Approaches to Managing MS in 2022: A Research Update

Presented by: Andrew Woo, MD, PhD

Alexis Crispino Kline:
Hello and good evening, everyone. My name is Alexis Kline, and I'm the Director of Mission Delivery and Grant Management with the Multiple Sclerosis Association of America. I'm delighted to welcome everyone here tonight for Approaches to Managing MS in 2022: A Research Update featuring Dr. Andy Woo. Before I hand the night over to him, though, I did want to take just a few moments to highlight some of MSAA's programs and services.

If you've connected with MSAA before, you've likely met them. MSAA's toll free National Helpline is staffed by individuals with a background in counseling or social work and are familiar with MS. Helpline specialists can share information about MSAA's programs and services, as well as the resources from the broader MS support community. For eligible individuals, MSAA also has equipment and cooling garment programs to provide tangible items that address some of the symptoms of MS, such as cooling vests for individuals experiencing heat sensitivity or four-prong walkers for mobility support. MSAA also hosts an MRI Access Fund for individuals who are facing barriers to obtaining a cranial or C-spine MRI to confirm a diagnosis of MS or to track disease progression. Finally, MSAA also has a robust online community, which includes programs such as the MyMSAA Forum and the MS Conversations Blog, as well as the MSI website, where programs like tonight's will be available on demand for viewing when you're available. If you have questions about these or would like more information about any of MSAA's programs, please don't hesitate to send us an email to give us a call or visit us and give us a chat.

And without further ado, I am delighted and honored to introduce our esteemed speaker for tonight, Dr. Andy Woo. Dr. Woo is in private practice at Santa Monica Neurological Consultants and serves as an Assistant Clinical Professor of Neurology at the David Geffen School of Medicine at UCLA and Cedars-Sinai Medical Center. Listed as one of America's top physicians by the Consumer Research Council of America, Dr. Woo also serves on the Navigating MS International Steering Committee and is a member of the Board of Directors for the Multiple Sclerosis Association of America. Dr. Woo, welcome and thank you so much for being here tonight.

Dr. Andrew Woo:
Thank you so much for having me. Let me share my screen here. Tonight, I am very honored to be with you all from hopefully all over the country and here in Los Angeles, although I know it looks like the Maldives in the back there, but it's actually Los Angeles. So tonight I'd like to go

over a number of things. I was asked to kind of give an overview of some research updates. But in order to do that, I think we have to kind of look at MS, do a little review about MS. I know many of you are very seasoned. But, I also like to nerd-out with you a little bit and cover a little bit of a brief immunology review, my PhD is in immunology, so I think just to get kind of a vocabulary to kind of understand what's on the horizon as far as research goes, I would like to go over a little bit of immunology.

I'll review a little bit about current treatments. A lot of the stuff here will be really more for your reference. So you guys can, I guess, you know, log on online and look at it later. So there will be some details here that are kind of beyond the scope of what we'll talk about. But I'll highlight a few things here and there about some of the current treatments, some tricks about symptom management, since I do have you for this evening. Having done patient programs over the years, I've learned from you guys some tricks from your caregivers, from yourselves that I always like to pass along to other patients.

And then one of my interests is... I'm Asian and Chinese New Year is coming up, you see some dumplings there on the left, so dietary stuff is a very interesting thing to me, and a lot of times people will come in and maybe you, yourself, will ask your nurse practitioner or your doctor, Hey, you know, what should I be eating? I'm taking my MS medication, but are there data for supplements or dietary stuff and what's really out there? So I like to kind of focus in on that as part of our research, anything on the horizon. Are there actually data supporting doing things as far as lifestyle changes for dietary stuff and the whole mystery about the gut microbiome, which transcends not just MS, but also other conditions with immune kind of things, like rheumatoid arthritis, also colitis, Crohn's disease, but also the gut microbiome now is a hot area of research, also for things like Alzheimer's/dementia, Parkinson's disease and even psychiatric conditions like depression and bipolar. So we'll dive into that and we'll also, of course, talk about some of the hot things on the horizon as far as some of the new medications that are kind of coming along the pipeline, like the BTK inhibitors, you may have heard of. Also some of the hot things about biomarkers. And also, last week there was a lot of press about Epstein-Barr virus, which we've been talking about for decades. And I think we probably need to address that as well.

All right, so MS background, I won't go into too much detail here, I think many of you have experienced many of these things here as far as having Lhermitte's Sign, that kind of electric feeling that can tip your head forward, down. Uhthoff's Phenomenon as far as the heat sensitivity. But when you look at this list here, I think many of you have experienced really the single most common symptom of MS is really the fatigue, the inexplicable fatigue. No matter how much rest you get. And I'm just going to kind of pass through some of these things here. As far as typical demographics here, as you know, more common in women than men. There are some genetics. People often ask us, especially during the first meeting, Hey, how likely is it that I might pass this on to my child? And certainly there are genetics involved in MS. There are over 150 genetic factors that have been identified over the years involved with MS. But if you have MS, the likelihood that your child would have MS is only about 4%. So even with identical twins, same DNA, same house, same marching band, the same everything, same DNA, identical twins, only about 35% of the twin sister gets MS. For identical twin brothers, it's only about 6% of the twin brother gets MS. So definitely genes are part of the factor, but not the only factor. In the HLA-DR, in HLA-DR2 and DQ are some of the genes that actually increase risk of getting MS. The DR2 increases about three-fold, increased risk of getting MS. Other things you see here in the red, other risk factors for increasing risk of getting MS, childhood obesity, cigarette smoking, exposure to pesticides. One thing I didn't list here is, not just head trauma, but multiple concussions between about the age of 11 and 19. There's is some of the more recent studies - low vitamin D levels and also Epstein-Barr virus, that we'll go into more detail in a moment.

What about stress? Now, this is a common question = people actually kind of wonder, Well, definitely I feel worse with my MS when I'm more stressed. Does stress actually cause MS? So stress doesn't cause MS, but an interesting study you may have heard of a number of years ago, almost ten years ago now, that stress actually can have an impact on the MRI scan. Not so much the real absence, because an interesting study where they just did talk therapy, less than an hour a week, about 50 minutes for six months versus a group of patients who didn't get that, and they followed their MRI scans. So, the 120 patients and those that got talk therapy, no medication intervention or anything else, and they actually changed their MRI spots, which is amazing to me, that just stress management, we can't emphasize that enough how important mindfulness is to decrease your stress because it literally changed their, not just the gadolinium enhancing lesions, but their T2 bright spots on their MRI scan just by stress management. So we always want to respect the whole Mind-Body continuum: exercise, diet, sleep, stress management, that type of thing. Very, very important for your lifestyle.

As you know, there are different types of MS, and oftentimes people kind of wonder, Well, what type I have, and in reality, you know, this is more important for the nerds like us who write the trials and things to try to pigeonhole people into different trials, groups and everything. But in reality patients sometimes kind of bounce back and forth and don't necessarily fit perfectly into an exact type. Most common type, Relapsing Remitting, a certain percentage over time, especially if untreated with medication, will transition over years, sometimes, to Secondary Progressive. Then a smaller percentage of people have what's called Primary Progressive over years, and they have a different type of progression. But that is a smaller percentage of patients over the years.

I won't spend too much time on diagnosis, but I will say that for those of you who've had spinal taps, I had a spinal tap... I needed spinal fluid for my research for my PhD, so one trick that I like to do to decrease the risk of getting a spinal headache, for those of you who had a spinal headache after a spinal tap, always ask for a pediatric 22 gauge needle, which is a smaller needle. It does take a little bit longer, but it really reduces the risk of getting a headache afterwards. Obviously, if you've already had it done, you probably don't need another spinal tap, but that's just a little trick we like to do to decrease the risk of getting a spinal tap headache. The evoked potential testing we don't do as much as we used to because the MRIs now are much more sensitive than they were years ago. And then, just one little note, I'll highlight some of the new testing methods you may hear about, T2* (T2 Star) and FLAIR* (FLAIR star). Those are some new techniques that are very, very sensitive for looking at some of the things we'll talk about later, such as the central vein sign and some other things that are kind of new in the MRI world, trying to diagnose earlier and there's some pathology things that are very interesting that might actually lead to some treatments that we'll talk about in a moment as well.

Prognosis - there are different types of MS, as you probably know, as far as when people first get their symptoms, some patients get a very first symptom, we call it clinically isolated syndrome, but there are patients that we actually find who don't have symptoms but have spots on their MRI scan. And oftentimes these are situations where we find it kind of by accident. So this is kind of around 2008 or so, Gary Nakhuda was one of the first really to describe this, where patients had MRI spots, or lesions, or plaques. And we kind of followed these pieces very carefully because they have a high likelihood of possibly of turning into MS. So that's called RIS (Radiologically Isolated Syndrome).

Move along here. So let me spend a little time talking about the immunology of MS. So when we're talking about, Yes, MS is one of these immune mediated conditions, you think about your

immune system as, Oh, it's your white blood cells, your B cells, which go on to produce antibodies when you get a vaccine, and your T-cells, which help regulate the immune system, and then your other white blood cells, like your macrophages, which are like your PAC men and PAC women, that kind of chomp on bacteria and viruses and funguses and all the evil forces out there, like the Boston Celtics, Dallas Cowboys and all the evil things here. I am, of course, a sad Steelers fan, kind of crying myself to sleep now. But so the immune system protects you from all those bad evil forces out there. But within MS, as you know, the immune system, it's actually too active. So what happens? It actually is so active, it actually starts attacking the covering of the nerve called myelin. So, if you look at your telephone cord, yes, the rubber coating is called myelin. And when it gets chewed up and inflamed by parts of the immune system, whether it's the cells or the antibodies or the complement proteins, that reaction shows up and irritation, the inflammation is called demyelination, and that actually shows up as the bright spots that you see on an MRI scan. So, yes, if you look under a microscope and you look at that bright spot on the MRI scan, what is that biologically? Yes, that's demyelination. Now, the good news is that over time, that may heal with or without treatment of steroids, pills steroids, I.V. steroids, or just with time, if you're lucky. However, underneath the wiring called the axons, sometimes that does not repair itself, and that's called axonal loss, and that shows up as kind of the dark spots.

So when you think about the immunology of MS, there are a lot of players there. There are a lot of people involved. So what are some of these factors that I'm talking about? So if you look, kind of at the bottom, let's see if I have a pointer here. Yeah, oh, all right, here you go. So, the cells of the immune system have to get into the brain and the spinal cord because to cause that information just very briefly, for example, the B cells here which go on to become plasma cells and spread antibodies, you have to cross what's called the blood brain barrier. It's like getting through security, TSA at the airport. You have to have the right ID markers, adhesion molecules and that type of thing in order to get across. And then, once inside the brain or spinal cord, then they set up shop, cause inflammation, they sometimes, what is called, present antigen. So they actually react sometimes with T-cells and other cells. And then they release all these chemicals and they cause more information. These chemicals are called cytokines. You may hear them called interleukins and these types of things. And then there are all these other cells I mentioned, like the macrophages. And those are the ones that are kind of chomp things. And the macrophages in the brain and spinal cord, they're called microglial cells. And the reason why I mention them is they are important for not only kind of scavenging cells and regulating some immune things, they are also very important for repairing things. And so when you guys say, Well, hey, you know what, is there anything that's going to repair my nerves? Can I fix stuff, can repair the myelin, remyelinate? Well, the microglial cells actually have a role in repair, not just clean up, and, you know, cleaning up the garage and sweeping up stuff, but also repairing things. And we'll talk about some things that may have a role. And medications may actually have a little bit of data towards repairing and remyelination.

And the other half of the story is, well what about these fried egg cells here, the oligodendrocytes. Those are the cells that actually make myelin and put the myelin rubber coating back on the cells. So there's this kind of a constant thing going on with inflammation, and inflammation kind of rubbing off the rubber there. But also the oligodendrocytes frantically trying to make myelin, but also this oligodendrocytes sometimes being told to stop working gets pink-slipped, gets government furloughed to stop working. That's called apoptosis, where it's told to kind of sit tight and not work anymore. And so there's this constant battle of signals of inflammation, cell death and that type of thing. So lots of things going on.

The other thing I want to mention is there's this kind of balance of immune cells in MS, kind of this inflammation and anti-inflammation, this kind of yin-yang, wax-on/wax-off kind of thing. So if

you look on the right side, we like this in MS because this kind of quiets the immune system. And the reason why I mention this is a lot of the research, you know, even the dietary stuff we talk about, we're going to be mentioning things like these things called T regulatory cells. The "T reg" cells, we actually like them because they kind of quiet the immune system and they secrete chemicals, cytokines, that kind of quiet the immune system. On the other half, on the left there, these are cells that increase inflammation, like interleukin 17, TH1, these effector cells, they actually increase inflammation, so we don't like them because they worsen MS. The T 17 cells, actually, not that old. It was only discovered in mice in 2005 and in humans in 2007 when your iPhone came out. So it's actually not that old a cell, it's a pretty new concept. So there's that delicate balance between inflammation and quieting inflammation. And when we talk about some of the dietary stuff, there is actually a balance that you can affect even through dietary means.

So just a quick review on some of the things that are out there currently that we're using and you guys are using for your MS. For acute attacks, as you know, steroids are what we use, either the I.V. steroids many of you have experienced, or pill steroids. And then for other kind of symptoms, again these are things that are used for the symptoms, for fatigue, the only things I'll kind of highlight without going through the entire list is, for those of you who do get benefit from things like Provigil® (modafinil), or Nuvigil® (armodafinil), you realize that now over the past several years, and chances are, we'll not cover it unless you have documented sleep apnea, where you work night shifts as a nurse, security guard, truck driver. Otherwise, it's crazy, crazy expensive. So yes, 30 pills might cost $400 or $600 at Rite Aid or CVS or Walgreens. However, go to GoodRX, because GoodRX, with a doctor's prescription, here in Los Angeles, the cost may be $22, $23 for 30 pills. Generic modafinil so ask your doctor for GoodRX if something like the Provigil or Nuvigil generic is effective for you. And that's true for any medication, whether it's heart medicine, cholesterol medication, if you have no insurance or insurance no longer covers things like, our Parkinson's patients, rasagiline, Lyrica® (pregabalin), if you're using that, for example, for spasms or numbness or tingling or back pain, those medications on GoodRX are much, much less expensive.

Another thing I'll just highlight here is for numbness, there are medications that are still being taught in medical school, in neurology programs the tricyclic antidepressants, the Elavil®, which is amitriptyline, Pamelor®, which is nortriptyline, these medications have a lot of pretty good data for what we call neuropathic pain. So they've been used historically in MS for numbness, for tingling, for nerve pain, for migraine headache prevention, and for neuropathy in diabetes. I was never a big fan of them because, number one, patients often get little bit tired on them. Number two, you often get a little bit of dry mouth. Number three, patients often gain a little bit of weight on them. So I think there are a number of other options. I was never a big fan, ever since my residency and in practice for this many years. And then in 2015, there have actually been a number of data sets in JAMA Internal Medicine, January 2015, JAMA Internal Medicine 2019, August and then British Journal and even Neurology in 2016, showing that these tricyclic antidepressants actually increased risk of dementia if you take them chronically for many years. And, because they dry out the acetylcholine chemical just like Benadryl®. So Benadryl, totally safe, we use it for rashes, etc. But if you start using Benadryl every night, either for sleep or you're taking things like Tylenol® PM or Motrin® PM or those types of medications, or Benadryl every night for insomnia over a three-year period, It actually does increase risk of Alzheimer's dementia by about 54%, and that was published back in 2015. So I've never been a big fan of these anticholinergic type medications like the tricyclic antidepressants or taking Benadryl too long over a three year period because that data has been out there and repeated in at least four different data sets. So, I'll just kind of comment on those two things.

What about the medication out there? Well, as far as treatment for MS, very different than when I was a resident years ago at UCLA in Othello. There are a lot of options out there, not just injections from 1993, but pills coming out in 2010, I.V. medications once a year, twice a year, etc. And now it's a big thing, with the Chinese New Year coming up, a lot of options. So a lot of different medications, not just for relapsing-remitting MS, but also for primary progressive MS, and secondary progressive MS. So really, for MS patients, what we're trying to find, really, the best medications for each individual MS patient. So it's a very exciting time. So to me, I'm Asian, everything's a buffet, everything is a food analogy. So a lot of options out there.

So what are they like? Well, the question - do they all taste like chicken? That's for you to decide with your physician. But there are options. There are self-injections. There are intravenous medications and there are pill options. So if you actually look at all the different formulations, and of course some of them have different brands. And depending on insurance with coverage, they're actually 22 different medications out there. And again, some of them are the same brand, but kind of different formulations. But there are a lot of options there. So my point is that really, if you're not on a disease modifying therapy, we call them DMTs, it's something you really should consider with your physician and your nurse practitioner.

What about the pills? You know, before 2010, everyone was saying, Oh, you know, it'd be great if there were pills out there. There are pills out there now and these have different mechanisms of action. Some of them are what we call these S1P receptors. Kind of homing receptors that kind of traffic, help the white blood cells, the lymphocytes, traffic through the bloodstream. But if you jam your GPS receptor, then they're not so interested in going up to the brain and spinal cord to cause inflammation. So they kind of hang out sequestered and hiding in your lymph nodes. And so that's how these Gilenya® and Mayzent® and Zeposia® and Ponvory™ kind of work. Aubagio® is a different mechanism. Tecfidera® is a different mechanism. Part of the reason why I want to mention that is that when we talk later about some of the trials looking at trying to decide between high efficacy and lower efficacy medications, that's kind of been the big debate over the years about when you have MS, should you start with some of the stronger or higher efficacy medications or should you save them for when patients are having more difficulty? The Gilenya and Mayzent are the only two pills... I'm sorry, the Zeposia and Ponvory, the S1P class, are the only pills considered the high efficacy class, along with some of the other intravenous medications like Lemtrada® and Ocrevus™ and the injection Kesimpta®, the B cell therapies, and also cladribine (Mavenclad®). So those are considered the high efficacy medications compared to the other 22 medications, and we make that distinction, so we'll talk about that a little bit later.

So why consider treatment if you're not on treatment? I won't go into great detail here, but there are many data sets over the years showing that MS does tend to progress over time. And there are many benefits to being on a disease modifying therapy. And so these are some of those reasons listed. So I won't go into great detail. But there are advantages to being on therapy, even if you feel fine, even if you haven't had a problem for a while. And there's something called the EPIC study that UCSF has been doing for over ten years, showing that even patients on treatment who feel fine, they actually are having some brain atrophy and shrinkage and things. So there are things that are actually happening kind of in a silent fashion. So there is progression even when patients are not on treatment, as well. So there are a lot of things being researched these days.

So, actually for symptoms, just want to touch upon a couple of things here. For symptom management, and these are not disease modifying therapies, Ampyra® was FDA approved in 2010 for walking speed. Nuedexta® is for some of the behavioral things for pseudobulbar palsy,

when patients are a little bit more reactive emotionally. I want to point out the LDN, Low Dose Naltrexone is not FDA approved. That's actually just something prescribed by a physician, it has to be made by a compounding pharmacy. But there is a little bit of data from Bruce Cree at UCSF, a small study showing that it did have some benefit for sense of well-being, for pain and self-reported cognition. There are some specific patient types for MS in children. Gilenya is FDA approved. There are some medications listed here for secondary progressive MS, and there's one medication for primary progressive MS, that's approved, and that's Ocrevus, which came out in March 2018. The I.V. medication twice a year.

Well, we also learned from looking behind us. So, you know, despite all these 22 medications we have in our buffet available, there are a lot of things that were looked at that, unfortunately, didn't work. And so here are some examples that were very exciting at the time. Different pills, looking at Myelin, you think, OK, well, if the covering of the nerve is a problem, what if you took the covering of the nerve, got your immune system to react to it and maybe try to develop some type of immunity to that? That was back in '93. That didn't work. Estrogen, as many of you know, during pregnancy, MS seems to get a little bit better, and after pregnancy, some patients may have a little bit of a flare up during that first couple weeks or months, but that seems to be tempered if the mother, if the woman is actually breastfeeding. And I'm Dr. Annette Langer-Gould has shown some of that data very nicely. But, so estrogens have been looked at. The estriol study, the oral estriol study, E3, actually was not able to show benefit, however. So a lot of these things listed here have been looked at and some of the T-cell receptor vaccines over the years have not been efficacious as well. So lots of things looked good in animal models, looked good preliminary in patients, but didn't seem to pan out.

So let's move on to some dietary things that I always find very interesting, and again, this is the thing that's good because this is something you could do to empower yourselves. This is a lifestyle thing. And there are actually some data sets that actually have positive data. So I've got the three M's of MS, the mangia, microbiome, and molecule. So what am I talking about? So what about vitamin D? A lot of people talk about vitamin D. Well, vitamin D actually does have some role in immunology. So there are a lot of genes with a vitamin D kind of extra adjacent to a number of the MS genes. There are actually vitamin D receptors on many of the cells of the immune system, on T cells, on the B cells, on the macrophages that we just saw on that little cartoon earlier. And vitamin D does seem to decrease some of those inflammatory chemicals released that are squirted out, the cytokines, and seem to decrease inflammation. Serum levels, just from an observational standpoint, way back, years ago, have been shown to have some, observationally, some correlation to, as far as developing MS, risk-wise, as well as relapses, atrophy, etc. So there are some data suggested from an observational standpoint.

Now the flip side is that it doesn't seem to be as true in African-Americans and Latinos. And then when the Cochrane Review looked at all the different trials, actually prospectively, saying, Alright, if you have MS, what if you were given vitamin D, does it really actually help your MS? And those studies have not really panned out. So again, observationally there seems to be a correlation as far as who gets MS, and that type of thing. But when you're actually studying it and giving people vitamin D, it doesn't seem to be panning out. However, we typically do check vitamin D levels at this point, just as long as it's safe for that particular patient.

What about salt? Well, not only in animal studies, but in patients as well. So the average American averages about three grams of salt, sodium per day. In Japan, it's about, I think, about five grams salt a day. I think Argentina is the highest about seven grams of sodium per day. But patients who have a low sodium with MS, tend to do better than patients who have a higher sodium content. So patients with MS who average about 4.6 grams of sodium per day

versus low sodium, 2.3 grams, they have almost about 3.95 times more relapses than the low sodium MS patients. So, you know, if you enjoy sushi, just reach for the green cap sodium soy sauce. If you're at the Texas State Fair, you know, maybe hold off on the fried butter. These are just ideas. No judging. But salt does seem to make a difference. And at least in the animal model, they actually know some of the mechanisms the sodium does seem to jack up - the serum glucocorticoid-induced kinase (sgk), which is an enzyme that kind of hyper educates and gets the Th17 cell kind of excited. So there are some kind of inflammatory pathway there that sodium does kind of incite a bit.

What about other things? Fish, caffeine, alcohol. There's an interesting study from Brussels, back in 2011, and followed about 1,372 patients and found that over almost 20, 22 years that patients who ate fish, or drank caffeine, and then, independent of that, drank alcohol, they actually had decreased progression of their MS, as determined by one of the disability scores that we use in trials. And so, Amanda Montague, and Alexis, and Kyle Pinion and I have developed a sardine brandy latte we'd like you to try. It's disgusting, but you're going to drink it because it's going to be good for you and we're going to market it and we're going to retire early. So there is something about the fish, whether it's the Omega-3 fatty acids, caffeine, as you probably know, has been studied for other things, and there's some data for it as far as cognition goes. And then alcohol, and again, this is, as far as there's just that one study, but there have been other data sets also suggestive about fish oils or actual fish. And Dr. Langer will show that as well. So there is something about that, the fish, the caffeine, and the alcohol. Now, there was a study. that people often ask, Okay, well if it's alcohol then what kind of alcohol? So there was a study at Brigham and the Harvard Group showing that it was 80 proof and higher had an effect, but below 80 proof did not seem to have an effect. And that's as far as developing MS. So again, I'm not telling you to drink alcohol, I'm not telling you what kind to drink, to alcohol, I'm just presenting the data, not telling you what to do.

All right. So what about specific diets? So you may have heard of one of the older diets. Dr. Swank had trained at Harvard, and when he was a fellow, he took on this project to look at different dietary things, so we're going to dove into that a little bit. And people have talked about, What about glutens? And what about the Mediterranean diet? There are a lot of data looking at the Mediterranean diet for heart disease and stroke prevention, Alzheimer's dementia that's already established that yes, it does actually decreased risk of strokes, heart attacks and Alzheimer's dementia. Mediterranean diet, you might be familiar with, is heavy on the fish, vegetables, olive oil and nuts and trying to avoid processed foods, trying to cut back on processed foods and concentrated sweets, and cutting back on red meat. Not necessarily excluding all red meat, but kind of, you know, favoring fish instead. So that type of thing. And the Wahls Diet you might be familiar with. Dr. Terry Wahls is a physician in Iowa who got diagnosed around the year 2000 with MS and was treated with medications for MS, and it was not doing as well as she wanted it to, and she kind of took it upon herself to change her diet, and she developed, kind of modified the Paleo Diet, and she modified it and she called it the Wahls Diet. So it's kind of a variation of the Paleo Diet with some calorie restriction and also a couple of added things as far as organ meats and bone broth. A lot of cruciferous vegetables, avoiding legumes, nuts, dairy, etc. I listed there the vegan diet, and then we'll talk a little bit about the intermittent fasting diets as well. So a number of different diets. Let's spend a moment just talking about the Swank Diet.

So Dr. Roy Swank again trained at Harvard and then found that, yes, patients in Norway who had MS, if they lived on the coast, where they ate a lot more fish than on the inland part of Norway? So from that and then when he kind of kept on thinking about that diet, when he eventually kind of started the whole neurology department in Oregon, in Portland, and he

developed this kind of Swank Diet, that's really kind of heavy on the polyunsaturated fatty acids, and the more fish, have not as much red meat. And that type of thing, which of course, is a very healthy diet. It's heart healthy. It's very good if you have diabetes or heart disease, high blood pressure, that type of thing. So he published a number of things over the years with his Swank Diet and kind of going with that theme, these polyunsaturated fatty acid diets, some of the data was negative, and then some of the data here at the bottom of the page was positive. But interestingly, it actually was more positive for the omega-6 fatty acids and not the omega-3 fatty acids.

And then so when you look at some of these other diets, you think, well, there's a lot of different diets to choose from, it's kind of confusing. There's a lot out there - the Swank Diet, gluten diets, the DASH Diet. Again, DASH is the Dietary Approaches to Stop Hypertension, which is again kind of similar to the Mediterranean diet as far as very heart healthy, and also the Wahls Diet we mentioned, the vegan diet and intermittent fasting diet, which I'll talk about in a minute. Sometimes it's hard to choose, sometimes it's hard to pick one. Hard to pick one, sorry, I apologize.

So, what are the actual data? Well, with the Swank Diet I mentioned, there is a little bit of positive data, but it's primarily with the omega-6 fatty acids, not omega-3, for some reason. The gluten diet, gluten elimination diets have really not panned out. There's a little bit of data for Mediterranean diet for fatigue and disability scores, and also the MIND diet, which is kind of in that same realm of the DASH diet, being kind of heart healthy, more fish, vegetables, olive oil, cutting out, or at least reducing red meat and that type of thing. And that's been published pretty recently. The Wahls Diet actually does not have any positive data. There's some open label studies, some small studies, but has not shown any kind of positive data for MS so far. A vegan diet has not shown any positive data to date.

However, the intermittent fasting diet does have four studies that are positive, two small animal studies and two patient studies. So if you're not familiar with intermittent fasting, you know Jimmy Kimmel lost about 25 pounds on it. A lot of actors do it. Terry Crews, Ben Affleck, a number of other people. So some people use it for weight loss. If you're kind of borderline diabetic, it will actually help reduce your sugars. But more importantly, for our purposes, it has a profound effect on inflammation. And so the two popular ways to do it are the 5:2 or the 16:8. 5:2 are first two days of the week. So if you do 5:2, basically two days a week you can restrict your calories, 500 calories two days a week, like a Tuesday, Friday or a Wednesday, Saturday for women, and for men 700 calories on just those two days. The other five days of the week, you would eat healthy. But what I think is actually more practical and easier is what's called 16:8, where during the day you kind of skip breakfast, maybe have your tea or coffee, then you don't eat until around noon, and from noon until 8:00 at night, you don't eat. So eight hours, you eat all your meals... Sorry, noon to 8:00, you eat your meals and then 8:00 at night until noon the next day, those 16 hours, you're not eating. So that's why you're fasting 16 hours, and eight hours you are eating. That's why they call it 16:8. So in either case, you're kind of fasting. Maybe you might be a little bit hungry, but your body gets used to it. What does that actually do? A lot of immunologic things, and we'll take a look at that.

So just to present some of the data, interestingly, in the animal model for MS, that is actually the standard model for which all of the 22 medications got FDA approved, it had a profound effect. And so what they found is that the animals actually did not get the MS, it's called EAE, Experimental Allergic Encephalitis. They can do it in mice and rabbits and guinea pigs and all sorts of different animals. The myelin sticks. So not only did they not get the MS, you can look here on the right side, the cells actually, at day three and day eleven, they didn't get the

inflammation. So the CD4 cells and all those kind of inflammation cells that we saw in that cartoon were not there, or much less so. And then when the myelin, here on that bottom kind of panel here, the myelin was actually preserved.

So again, this was not a medication. This is not anything fancy. The mice were not injected. They were simply, the mice were actually fed every other day. So not only were they intermittently fed, oh the mice, they were so skinny, they were so svelte, they were hanging out the pool, like sipping wine, having a little cheese, talking to their other mice friends, they looked great. So again, something simple is just intermittent fasting of the mice. No medication. Nothing. Nothing fancy. So, the same thing, there's a small patient study done, as well, that kind of correlates this. And this was done by Valter Longo's group, actually Longo's group over at USC. And this was published in 2016. So there's been, there's another small patient group that was done jointly between WashU and UConn, Connecticut, also. So there have actually been four studies now, two small patient groups and two small animal studies, as well, showing that there is some benefit to the intermittent fasting, which is quite simple, again nothing fancy, no injections, no medications. It's not even "what" you eat, it's the timing. So what is it about this that works? Let's dive in.

Well, what happens is you actually change your gut bacteria. It changes the diversity of your bacteria. Now, keep in mind, you have more bacteria in your gut than there are cells in your body. I mean, they tell you what to do. And what happens is you actually increase your bacteria, sorry, you increase your T regulatory cells and you decrease of your TH-17 cells. And remember, those are the ones we like. We like the T regs and you quiet down the inflammatory TH-17 cells. And other things that happen are you decrease leptin, which is inflammation, if you talk to any obesity expert, yes, obesity is a kind of low smoldering kind of inflammatory condition, and you increase adiponectin. And like I said before, obesity is actually a risk factor for those with MS. So there's a whole area of research looking at ceramides, and we'll talk about that as well. Ceramides seem to be higher in obese MS patients.

So what happens? Well, it turns out that MS patients have different bacteria than people who don't have MS. For example, on the left here, Methanobrevibacter smithii, which is one of the highest gas producing, methane producing bacteria in the gut, it's about seven times higher in somebody who has MS compared to somebody who doesn't. So the top two are kind of the most common ones that are jacked up in MS. Methanobrevibacter smithii and Akkermansil. So those two in particular. And then some of the other ones, Butryicimonas and Firmicutes and B-frag are much lower in MS patients compared to other patients. So you think, OK, well, that's great, but I still can't really connect the dots. What is it about these bacteria and how can I change that if I have MS? What can I do?

Well, it's really about having the right bacteria. The bacteria, when they break down your foods, they break down your foods into what are called short chain fatty acids, and there are three main ones. one is Propionic acid Propionate, one is Butyrate or Butyric acid, and one is called Acetate or Acetic acid, which you might know is the fancy term for vinegar. Right? So what is it about these short, these three short chain fatty acids and there are others as well? Well, these short chain fatty acids, they actually acetylate histones, for all you biochemical nerds, and histones are very important in the promoter region of the T reg cells and it gets the T reg cells to actually get advanced and mature. So it actually helps the T regulatory cells get excited and then they rise to prominence. And then, of course, they actually take over and it helps them quite down the TH-17 cells. So if you have the right bacteria or more of the right bacteria, you actually produce more short chain fatty acids, and the short chain fatty acids help the T reg

cells, and they kind of shut down the TH-17 cells, which ultimately decreases inflammation. So it's all about getting the right bacteria in your gut. Well, how do you do that?

Well, one thing you can do is eat more foods that break down and are sources of short chain fatty acids, like these listed here. Some of these starches, like oats and barley, pectins, like the green vegetables and fruits, apples, apricots and then supplements. And I'm going to, in the interest of time, just blow through a couple of things. There are two supplements for short chain fatty acids that have been studied for MS. One was with Dennis Bourdette'a group in Portland, where this over-the-counter supplement, ALA (Alpha Lipoic Acid) shut down brain atrophy about 67% over two years in secondary progressive patients, he had about 54 patients he followed. Likewise, a German group, Ralf Gold's group in Germany, looking at propionate, here about 300 patients, and actually looked at them six years prior to starting the propionate and then followed them for about three years after starting and they did, not everybody got MRI scans, but a subset of the 300 patients, some got MRI scans, they looked at disability, the looked at relapse rates, and they found a benefit for relapse rates, disability, thalamic and deep brain atrophy, a benefit to just over-the-counter propionate, which is proprionic acid. And also looking at the immune things like T regulatory cells and Interleukin 10 as well. So again, these are short chain fatty acids that actually had some benefit. They're just supplements.

Five things that I'll just kind of briefly mention, as far as supplements go. Lactobacillus you may have heard of, because that's one of the two kind of bacteria in probiotics. Probiotics always have Lactobacillus and phytobacterium. What we're talking about bile acids. We'll talk a little bit about parasites. Ceramides tend to be jacked up and higher in obese patients. And then fecal transplants.

So Lactobacillus, I won't go into great detail, but there are data both in the animal model and also for probiotics have been some small probiotic studies with MS as well that shows some interesting immunologic kind of data. Not so much clinical yet, but at least immunologic data.

With bile acids, so bile acids seem to be low both in adults and children with MS, and the bile acids actually are kind of relate to cholesterol metabolism, bile acids are very high in bear bile, so if your Chinese herbalist says, Hey, you've got to wrestle bears for their bear bile, you don't have to because you can actually buy something called TUDCA, which is tauroursodeoxycholic acid. TUDCA.

And there's actually a, Peter Calabresi, one of my med school classmates at Hopkins, his group is doing a study with TUDCA because the animal studies show that TUDCA shuts down MS in the animal model for MS, so they're actually doing a study in patients there.

So that's another way of looking at, again, the information from a different receptor, the TGR5 receptor on the microglial cell. Again, that's the scavenger, chomp-chomp cell in the brain and spinal cord, which may or may not have some effect on remyelination as well.

What about parasites? Well, Correale, back in 2007 showed that, Hey, this MS patient with parasites did better, sometimes even 19 times less relapses, than this MS patient who didn't have parasites. You know, hookworm, tapeworm, whipworm. So there have been some patient studies, small patient studies, about 16 patients were studied by another group looking at MS and parasites. And yes, they actually had about a 35% decrease in MRI spots, gadolinium enhancing MRI spots and also an increase in the T regulatory cells as well. So there are some immunologically interesting things going on there.

Ceramides I mentioned, these are things that are involved with insulin resistance, fatty liver. They are elevated in obese patients, but they also seem to correlate with inflammation. So that's a biomarker that's being looked at. And then, basically, fecal transfers are being studied now. There's a lot of interesting data for fecal transplants that works very well when people get C. Diff. Colitis. You may have heard of when patients are on antibiotics for too long, sometimes they get diarrhea because it wipes out your other bacteria and then the wimpy C. Diff. kind of rises to power and you get a terrible, very painful, hard to treat colitis. So, transferring bacteria from somebody else. So "mi casa es su casa" that can actually seem to help. Can you replenish the good bacteria? And it kind of takes place of that. So that is actually being studied with MS in a number of centers around the country, either by catheter, by colonoscopy placement or by capsules. So that's being studied now. We don't have any data yet.

And then I think I'll skip over this, but MAIT cells are a very kind of hot area of research, as well as some kind of interesting subsets of T cells that are very interesting in the gut.

So what treatments have a leg up? My sons are going to be horrified that I'm still using this years later, they're much older now, so I move on. So, when you think about, well, what drugs are best for MS, we get this question all the time. Well, what is... what should I get? What drugs should I take? What is the best drug for this? Well, neurologists are nerds. And so they do head to head studies. Here are some examples. There are many more I didn't list, but there are a lot of head to head studies over the years looking at, well, this versus that, that versus this. And then so those are some examples of studies looking at, you know, pitting one drug against the other. But again, everybody's MS is different for individuals.

People like pills, what are some of the pills kind of being looked at on the horizon? Mastinib is a French pill and is being looked at for progressive types of MS. So, mastinib, if you're French, works on mast cells, and mast cells may have a role in MS. We don't usually talk about mast cells because they are usually involved more with allergies and an antibody called IGE But they do have some role in Ms. TUDCA we talked about. The BTK inhibitors I'm going to talk about in a moment. Clemastine was a study done at UCSF a number of years ago, which is antihistamine over the counter. But it has some interesting, possibly even remyelinating type of properties, theoretically. So that's being looked at a little bit. Ibudilast is interesting also, because that's a Japanese medication that's anti-inflammatory that has some atrophy data that's kind of interesting. So that's being looked at. We talked about propionate. And then Boswellic acid. That's actually kind of a frankincense type thing. So that's lipoxygenase 5, that's been used in Europe for arthritis, aches and pains. But out of Heidelberg, in Germany, that actually has some interesting MS data as well, at least from a radiographic MRI standpoint.

So these are some of the things I mentioned, studies specifically for secondary progressive MS. The clemastine hematopoietic stem cell transplant, and that's previously what we called bone marrow transplant, which does involve usually immunoblation with a chemotherapy, usually a cyclophosphamide, a cytoxan. And then also mesenchymal cell transplant. So these are usually smaller studies at ECTRIMS. There's a presentation of about 18 patients from the Cleveland Clinic. And so that was about 28 weeks and it passed through that, and it seems to be safe, and about 67% or 68% of patients did have some improvement on one of the cognitive parameters they're looking at. A processing speed test called the Symbol Digit Modalities Test, the SDMT, and about 38% also had some improvement on a MS, kind of, walking scale as well. So again, it's preliminary. It's only been about 28 weeks for those roughly about 18 patients, but it seems to be safe and they seem to tolerate it, and again, that type of stem cell, which you can do really from just adipose, you know, fat tissue, from your love handles, it's not actually from the bone

marrow, and it does not involve ablation, where you use the chemotherapy to kind of knock out your immune system down to ground zero. So there's no chemotherapy involved.

Prior studies for secondary progressive, you may have heard about "statins", you know, the Crestor®, Lipitor®, Zocor® family, they have a lot of anti-inflammatory properties, so that's why they've been studied not just for cholesterol, and even when people have a stroke, and they don't have high cholesterol, but they still can help prevent future strokes because of their anti-inflammation property in the blood vessel, even studied for Alzheimer's dementia. They've also been studied both in animal models and some small patient studies as well.

So what about the new wave in MS, as we kind of finish up? We talked about these things. Let me spend a little time on the BTK inhibitors. This is really the next wave of medication for MS that you're going to hear about because there are a number of them that are right on the brink of coming out.

What are BTK inhibitors? These are pills, and they are novel because they affect something we haven't really seen before. They originally came out for oncology, kind of cancer type things, and also in the rheumatology world for different types of immune conditions, for rashes, for different kind of autoimmune skin and joint diseases. However, some of them have been modified a little bit, and now there are a number of them here in phase three, phase two and phase one thar are being studied, and the way they work is they actually affect B-cell maturation. Some of them have very, very good permeability in getting into the brain and across the blood brain barrier very well. But the nice little thing about them is this is a mechanism that has not really been seen in our other 22 medications. They have an effect on both the microglia and the macrophages. And you think, Oh, all right, well, that's interesting. We haven't really heard about that before. And at least in animal data in tadpoles, there's some data that there may be some remyelination, at least in the tadpole data looking at this particular type of molecule. So it's an enzyme that's involved with phosphorylation, for all of you biochem nerds out there. So this class of medications is very, very interesting, and we've learned a lot from our oncology colleagues about this class of medications since about 2013, I believe.

So in addition to BTK inhibitors, fecal transplants we talked about. Gold Nanocrystals. So, Gold Nanocrystals, and this is kind of complex, gold has an interesting effect on the metabolism of cells, as ATP, it gives your energy source and that type of thing, as far as stabilizing and decreasing what they call oxidative radicals, that shut cells down and kind of kill cells. So that study is being done really to look at the radiographic, what are called M.R. spectroscopy, of the brain. It's a kind of study of the brain from a metabolic standpoint. So it's more of a kind of radiographic picture study to see if it has an effect in that sense.

Epstein-Barr virus. Let's talk about that. So Epstein-Barr virus, as you probably know, is very common. From age five, about 50% of five-year-olds have been exposed. By your teens, about 80%, 85%. And then by adulthood, about 95% of people have had exposure to the Epstein-Barr virus. So yes, if you go get checked, check the antibodies, yeah 95% of adults. However, if you have MS, about 99% of people with MS have been exposed to Epstein-Barr virus. So a very interesting study just came out last week, Thursday, last week, really a week ago, right? And so that was published and they looked at the U.S. military and they followed patients for 20 years from 1993 to 2013, and they screened over 10 million people because they check everybody for HIV and other things. But they also looked at this data set, and this is from Ascherio's group at Harvard. And what they did was they found, they looked at Epstein-Barr virus and they wanted to see, well, was there a correlation to not having Epstein-Barr virus, getting Epstein-Barr virus, and did it increase the risk of getting MS? And it did. It actually increased the risk of getting MS

by about 32 fold. And interestingly, not only did they look at that, that was published last week here in Science, Thursday last week, just a week ago, they screened that many and then also NFL, neurofilament light chain was a serum marker that was also elevated in those patients compared to patients who didn't develop MS. In fact, it was actually increased, sometimes even almost six years before they actually even developed symptoms of MS. So when you're talking about, Hey, are there any kind of blood tests for MS? We don't have any, but this is one of those hot markers that people are talking about, the NFL.

So what actually happens with Epstein-Barr virus? Because you think, Alright, well if 95% of the population has it. Obviously, 95% of people are not getting MS. Well, if you have Epstein-Barr virus, there's this thing called molecular mimicry where there are parts of the Epstein-Barr virus, either in the nuclear antigen called EBNA, It has little parts on it called LMP1, which looks like the B cell receptor, LMP2A which looks like the CD4 molecule, where B cells kind of get tight with the T cells, it actually looks like your own parts. And so it can actually mimic certain things. And then the EBNA-1 itself sometimes actually looks like parts of your own myelin basic protein. Another part of the Epstein-Barr virus looks like an axolotl protein. Another part of the Epstein-Barr virus mimics and looks like a glial adhesion molecule. So basically, it's like, Oh, it's like the unwanted houseguest that shows up and yeah, they're kind of wearing your same sweatshirt that you wear and they're wearing a baseball cap that you wear and then they come to your home, they go through your closet and they start stealing your sweatshirt. They go in your freezer, they're eating your Haagen-Dazs and your Ben & Jerry's, they're stealing your Netflix password or their logging on your computer, they're getting on your Fortnite, they assume your gamertag, they're going to do a little Orange Justice, they're stealing everything.

And so the molecular mimicry, they're kind of mimicking all that stuff, and they're actually causing your immune system to react to them, and then they leave. But meanwhile, your immune system is all going out of sorts and starts attacking yourself. So that whole molecular mimicry, you start this immune reaction. And they may actually leave and be out of there, but they've actually triggered this whole immune response. So knowing the B cells get all kind of bent out of shape with all these kind of things that look like parts of the B cell, the T cells, there's data now also from a number of years, that these underactive T-cells actually traffic swarm to the brain, set up shop in the brain and are persistent, too. So to that end, there are now some trials going on looking at, well, what if you actually try to treat Epstein-Barr virus if people already have Epstein-Barr? Would that help people with MS If they already have Epstein-Barr? We don't know. All this data shows is that, yes, there really does seem to be a strong link between getting MS, but look, if you already have Epstein-Barr virus and you have MS, does it help to get rid of EBV? We don't know that answer. So there are two trials. one is with ATA188, It's a T cell treatment for, I think, it's a one or two year study, I think yeah. And then to actually try to eradicate Epstein-Barr virus in an MS patient who already has Epstein-Barr, and there's also a Moderna mRNA vaccine against Epstein-Barr to one of the envelope proteins. So they're looking at that. Again, we don't know if you already have EBV, is it too late? It may just be more of a triggering thing, but again, it seems critical, but that's not the only factor. Again, genetic factors, other factors as well.

Quick note. High dose versus low dose. There are many datasets already showing that, look, if you have MS, the data supports using a stronger medication rather than waiting later on to switch from a low dose, or low efficacy, to a higher dose, and that was shown in a UK study in 2017 by Harding. This recent August study, looking at Sweden, tends to be more aggressive using higher efficacy versus Denmark, which tends to use lower efficacy. That was published in August 2021 by Spelman in JAMA Neurology. And then there are also studies, the TREAT-MS trial and DELIVER-MS trial here and also here in the UK. Those studies are ongoing as well.

DISCO-MS, many of you kind of wonder, Well, if I've had MS for a long time, I'm older, do I still need to take medication if I haven't had an attack, and my MRI has been stable for at least five years and I'm over the age of 55? That's actually being studied right now. John Corboy is one of the lead people looking at that. A quick note about some of the MRI things, I'd be remiss if some of my former co-residents at UCLA, Nancy Sicotte, who I actually didn't mention in the MRI stuff.

Two hot things to know, one is called the Central Vein Sign. I'm not sure if you could see from where you're sitting, but Central Vein Sign is, sometimes these spots on an MRI scan are associated with a vein that looks kind of bright like this and also a, kind of almost looks like eye shadow, a dark kind of, if you almost look like, kind of a dark thing here, called a PRL a Paramagnetic Rim Lesion. What does that mean? So it's a batch of macrophages, again, those trapping cells that are full of iron on the outside, like an Oreo, and on the inside is kind of degeneration and axons and inflammation, and these are chronic plaques. Another way to look at it is on this one, you might see a little bit better. That's a PRL. So on the outside rim, it looks like an eye. So the outside Oreo cookie dark part, that's the ion filled macrophages, and on the inside is a chronic inflammation plaque.

So why is that important? So the inside chronic plaque, turns out that in nature in September, the first week in September, Nature Peter Calabresi and Danny Reich over at Hopkins and the NIH show that not only is that important from a pathologic standpoint in their animal model, it turns out that C1q part of the immune system with little proteins, that whole cascade, is actually dependent on C1q to cause that chronic plaque. And so they actually did an animal study showing, Well, if you block C1q, the animals didn't get sick, they didn't have the plaques, they couldn't cause that chronic demyelinating plaque. And so could that be possibly a treatment for MS or the chronic inflammation associated with those chronic plaques? So again, here it is. You have an MRI finding that's interesting. You have, Oh, you have the pathology, that's interesting, and, Oh, maybe that could lead to a treatment in animals and then maybe could lead to a treatment in patients.

And then, finish up there, BIOMARKERS, microRNA, there's been some interesting studies there. These are small RNAs that are little snippets, usually like like 22 pairs, and then they can actually have an effect on expression of genes. But there are some studies looking at that, and even encapsulating it. The Brigham Group is doing that in animal studies. Ceramides we talked about and NFL we talked about. A big NFL weekend, of course, for all you football fans out there.

So I'll finish up by saying don't believe everything you hear. We gave you lots of information, but stick with websites, like the MSAA website. We want to make sure you're being careful what you read, because there's a lot of misinformation out there. So read carefully. We sometimes say, Oh, things look good, but they're still dangerous. So, you know, here we are here. This guy's having a good hair day, but still could be dangerous, right? Sometimes things look good, but they're still dangerous AND they're stupid. So, think critically, right?

So what we do is we combine old ideas and new ideas. Look, we encourage you to take a medication, we encourage you to consider a DMT. We encourage you to still do your exercise, your sleep, your diet. See your physician, your nurse practitioner, but also consider some of these new ideas. So some of these new ideas we talked about, the dye stuff, the supplements, you can consider some of these other things. Yes, you can throw some berries in there, throw some caffeine in there.

If you want to take a supplement like TUDCA, great. If you really want to wrestle bears, wrestle bears. That's fine, too. If you want to consider fecal transplants, I think, well, you know, you take responsibility of your duties. So consider that. And by attending this program, you're taking care of your duties. So, you know, again, we always have this saying "MS is about ability, not disability". So whatever you can do to stay active and happy, you are trying to achieve nirvana, your own nirvana, your own happy space, whether it's nirvana, or Nirvana, or if you're a basketball fan like me, Nirvana and Krispy Kreme, Charles Barkley fan. I will stop there, and if we have any time, we will finish up with any questions.

Alexis Crispino Kline:
Well, Dr. Woo, thank you so much for this program. The chat and the Q&A was going crazy. Everybody was so excited and jazzed about the information that you shared. We did have questions come in, but I think that you touched on a lot of them. And we don't want to keep you for too much longer, either, so we just, I wanted to pop in here and say thank you to you for sharing your time tonight and thank you to everybody who joined us this evening for your very candid and kind feedback. And we hope that you all are staying well and staying safe. And, I guess, keep your fingers crossed for Dr. Woo's, his sports teams.

Dr. Andrew Woo:
Not this year. Not the Lakers, so... yeah. But, I'll give you some Chinese dumplings for the Chinese New Year, you know,

Alexis Crispino Kline:
Wonderful!

Dr. Andrew Woo:
And I think the one thing I didn't mention from a dietary standpoint is chocolate, M&Ms, very important. Very, very important. One of the four basic food groups. So that's published in Cell, Journal of Immunology, Nature. I mean, all of the big journals, they talk about chocolate, all the time.

Alexis Crispino Kline:
Delicious. That sounds wonderful. Well, thank you so much, Dr. Woo, and thank you to everyone who joined us tonight. Stay well.

Dr. Andrew Woo:
Great. All right. Thanks guys!

Alexis Crispino Kline:
Goodnight!