



Multiple Sclerosis
Association of America **Webinar Transcript**

Program Title: “What You Need to Know About COVID-19 and MS: Program 6”
Recorded On: August 17, 2020
Presenters: Barry Hendin, MD and Carrie Hersh, DO, MSc
MSAA Host: Peter Damiri

Peter Damiri: Hello and welcome to the Multiple Sclerosis Association of America's live Webinar, What You Need to Know About COVID-19 and MS Program 6. I am Peter Damiri, Vice President of Programs and Services for MSAA and your host for tonight's program.

On behalf of MSAA and our presenters we greatly appreciate the opportunity to keep you updated on this very important topic, and please know we hope you and your family are staying safe and keeping healthy in these uncertain times.

MSAA is extremely honored to welcome back our two MS expert advisors who will update us about the coronavirus pandemic and its impact on MS and answer your questions during our expanded Q&A session.

At this time I would like to introduce our special guest presenters, Dr. Barry Hendin and Dr. Carrie Hersh. Dr. Barry Hendin is MSAA's Chief Medical Officer and a practicing Neurologist at Phoenix Neurological Associates. He's also the Director of the Multiple Sclerosis Clinic at Banner University Medical Center and Clinical Professor of Neurology at the University of Arizona Medical School.

Dr. Carrie Hersh is the Chair of MSAA's Healthcare Advisory Council. She is a practicing Neurologist and Assistant Professor of Neurology for the Cleveland Clinic, Lou Ruvo Center for Brain Health in Las Vegas, Nevada. Thank you both again so much for being here tonight and keeping us updated on this very important topic.

Dr. Barry Hendin: Peter we are delighted to join you again. I speak for Dr. Hersh and myself in saying that we're pleased to be able to present again with the evolving information on COVID-19.

Peter Damiri: Great. Thank you Dr. Hendin. Well before we begin, I want to take this opportunity to thank our supporters, Bristol Myers Squibb, EMD Serono, Genentech, Novartis and Sanofi Genzyme for making this webinar series possible.

As you may know, MSAA is a national nonprofit organization dedicated to improving lives today for the MS community. In fact, this year marks MSAA's 50th anniversary as an MS advocacy organization. Listed here are just some of the many free programs available to people living with MS all across the country, along with our new COVID-19 and MS Pathfinder tool, which now provides ongoing updates and resources on the coronavirus.

Also please know MSAA has expanded our helpline hours to 8:00 pm Eastern between Mondays and Thursday. To learn more about our services please visit mymsaa.org or give us a call at 1-800-532-7667.

And lastly, tonight's program will be archived on our Web site very soon. During the program please type your questions into the chatbox on the screen and we'll present them at the end for our Q&A session.

Also if you are having any technical issues please type those concerns into the chatbox as well. So with all of that now covered I am very honored to once again introduce Dr. Barry Hendin who will kick off tonight's program.

Dr. Barry Hendin: Thank you again Peter. I - the first two slides appeal to me because of the humility attached to the slides. The first slide is what we know about coronavirus. The second slide that I'll be presenting is what we don't know with any level of certainty about the coronavirus and that - that's important for everybody to keep in mind.

There are as we know some basic things that we really do know by now, but we're only eight months into this pandemic, eight months' experience with this novel and mutating coronavirus that causes COVID-19.

And so although there may be people who tell you things definitively, I think Dr. Hersh and I believe that there's a lot that we would have to understand that is still formative. We're still learning and a lot of our answers are still in the stage of, what we know now, what we are learning more about in essence and what we still don't know sufficiently well.

So let me start with what we do know about the coronavirus. These - this is really basic. This is COVID-19 101. So we know that this is a novel coronavirus that causes the disease named COVID-19 and that the target for this disease is the respiratory system.

But we also know that this is not a social (inaudible) and other parts of the body are not affected. We know that heart can be affected, the renal function can be affected and there are other neurologic complications.

So people who have tracked the COVID-19 have also experienced other neurologic complications such as strokes or seizures, or an injury to the spinal cord or an injury to the peripheral nerve or alteration of sense of smell or taste.

So although we think of it as a respiratory target it is not exclusively respiratory and there are neurologic complications. What we do know is that...

Peter Damiri: Dr. Hendin...

(Crosstalk)

Dr. Barry Hendin: Yes.

Peter Damiri: Dr. Hendin I'm sorry. This is Peter. I was just interrupting but actually I think the audio sounds better. It was a little muffled earlier so I - it might've sounded better just as you were coming back on.

So I don't know if you were a little further away or not but I - and why don't you give it a try again?

Dr. Barry Hendin: I'll do it once again. So...

Peter Damiri: Oh that was...

(Crosstalk)

Dr. Barry Hendin: ...what I...

(Crosstalk)

Peter Damiri: That's perfect. Great. Thanks.

Dr. Barry Hendin: So what I started saying was that the two slides that I'll be doing really represent an exercise in humility and that is what we know and what we don't know because it's still early experience.

We're still eight months into this pandemic and we're still learning so what do we know about the coronavirus? We know that it is - primarily has a respiratory system target but that doesn't mean that

other parts of our body can't be affected, heart and kidney, for example, and that there can't be other neurologic complications besides those that people with MS worry about.

So in people with COVID-19 who don't have MS we've seen strokes and seizures and spinal cord injury and peripheral nerve injury and alteration in smell and taste. We also know that there are some basics that people should be relying on in order to reduce risk, things like wearing masks.

When you're in a situation where you are among others wear that mask. It's not clear how much we are protected by the mask we wear but it is clear that we reduce the risk to others, but also handwashing, social distancing, avoiding crowds and then what we would call pre-habilitation; not rehabilitation but pre-habilitation.

That is maintaining the best possible health by maintaining best diet, maintaining your weight at a proper level, exercising, if you smoke stopping smoking. In other words, it's a perfect time to pay attention to the other aspects of health that are so important in outcomes for COVID-19. Some people do well. Some people don't do quite so well.

It's clear that the healthiest people have a better outcome than those who have a lot of other medical problems especially if they're not controlled. We know that MS does not necessarily put you at greater risk for COVID-19.

That's an optimistic and favorable understanding but if you've got MS you are subject to all the other things that everybody else has. So if you have MS and have - are older than age 55, 65, age in and of itself creates this risk.

We talked before - comorbidities: heart disease, lung disease, uncontrolled diabetes, smoking, obesity. All of those create greater risk and so if you have MS it's not the MS that's going to put you at greater risk.

It really is more than anything else age and comorbidity. So the question would be do my disease-modifying therapies create increased risk and, therefore, should I stop them? It is generally the consensus in the treating community that you should not stop or change your disease-modifying therapy without a clear discussion with your clinician - with your treating clinician.

In fact, stopping some of the disease-modifying therapy increases the risk of a relapse and worsening disease activity, so by and large unless there's another reason to stop or change the disease-modifying therapy we recommend that you stay with the agent that's been prescribed in helping you, but certainly don't change or stop without discussing it with your clinician.

Then what don't we know? So that's what we know. What don't we know? We really are too early with insufficient numbers to be able to say that one particular disease-modifying therapy is the best or worst in the era of COVID-19.

This is something that we're currently exploring. In the early days of COVID-19 the - some of the European countries thought that there may be a differentiation between one group of agents and another.

I think in the US we're exploring that and saying that as of the moment we do not have sufficient evidence to say that one particular agent should be avoided or preferentially treated or used. We're also trying to - everybody's interested in what vaccines will be moving forward, and it's premature to say a lot of things about the vaccine.

How long will the immunity last? Will the immunity be complete? Will the degree of immunity be different in younger people versus older people? We do think on a hypothetical basis that there's some agents which will mute the immune response and others which will probably leave the immune response relatively unmuted or full - fully vigorous.

But these are things still to be worked out and it's still to be worked out whether this is a live virus or it's like the - a non - a live vaccine or a non-live vaccine and I suspect it'll be the latter. But all of this is still to be worked out and that is will there be immunity?

How profound will that immunity be and how long will it last we can't say without the vaccine. And then if you have antibodies can you be reinfected? It depends on how long the antibodies last and how high the antibody level is just like any other viral infection.

So it appears at least by common sense that people who have been infected will have some degree of immunity for some period of time, but again how much for how long we still are watching.

And then once you recover - have you fully recovered I think there is a - an exploration right now about the fact that some people seem to toss it off fairly easily. Some people are - don't have any symptoms despite the fact that they've gotten the virus.

Other people have profound illnesses and death but even those people who recover often recover with some degree of lasting symptomatology at least over a period of weeks and months and the - this is something again seven months in, eight months in, we're still exploring.

So with that discussion of the known and unknown, before we get to questions and answers I'd like to turn this over to Dr. Hersh for her thoughts about what we can do for our maintenance of the wellness and then health with COVID-19.

Dr. Carrie Hersh: Thank you much. Thank you so much Dr. Hendin. That was a very succinct and comprehensive overview of some of the attributes of COVID-19 we do understand as it pertains to the general population and, of course, more specifically to the MS population.

But I agree that this COVID-19 pandemic has humbled not only me but other members of the healthcare community in terms of how much we really don't know yet about this virus, and how it impacts people who carry other chronic autoimmune conditions and other chronic comorbidities that Dr. Hendin had discussed.

We are still learning a lot about this virus every day and fortunately there is a lot of work being done in the scientific community by the best and brightest and the MS scientific communities to try to collate better information on what is the COVID-19?

What is the risk to folks who live with MS and who are on certain disease-modifying therapies? And fortunately over the past six to eight months we have been able to learn quite a bit, but as Dr. Hendin had alluded to this really has humbled us in the MS scientific field in terms of how much we still have yet to learn.

So I would say that a lot of this information we will continue to learn along the way and, of course, we are happy to keep the MS community informed and involved as much as possible. So let me just go back and I want to review well what can we do in the current COVID-19 pandemic in order to try to prevent or thwart some of the risk factors that are involved in increasing one's susceptibility or one's risk of either developing the COVID-19 infection or having a worse time of it, and some of the things Dr. Hendin had already alluded to.

So some are what we call nonmodifiable risk factors and that does include one's age, so we've been able to see that those typically over the age of 60 years - they might have an overall inherently increased risk of developing COVID-19.

Folks who are physically disabled may also have an inherently increased risk of becoming susceptible to COVID-19, but there also are a number of what we call modifiable risk factors that one may be able to

work on either themselves or with the help of their MS healthcare provider or their primary care provider to decrease that overall risk.

And some of those things are reducing the severity or the risk of having certain vascular comorbidities, so those include uncontrolled high blood pressure. That includes uncontrolled diabetes.

That includes uncontrolled cardiovascular disease and tobacco smoking, vaping and chewing and we have been able to learn even in the short span of six months that these risk factors - if they go uncontrolled it does increase the risk of developing a viral infection.

So I would encourage those who are participating in today's event that if you do carry a diagnosis of MS and have some of these other modifiable risk factors that you may want to have a conversation with your primary care doctor and your MS healthcare team about ways that you might be able to reduce some of those risks.

This is a really good time to pay attention to your blood pressures, your sugar readings if you have a history of diabetes and to make sure that you are abiding by other recommendations such as tobacco cessation or trying to work on a program that will reduce the amount of tobacco that you are currently taking in.

So some other things that you can do that may not require the need of a doctor's visit - because I know that there are some concerns about the safety of going to the doctor's office and we'll actually be addressing that in a subsequent question.

But some things that you can just do day-to-day: getting plenty of sleep, being physically active. You know, right now it might be difficult to do some of the things that we previously enjoyed, maybe playing a sport that, you know, requires a lot of people or close-to-close interactions or going to a gym.

But there are other things that you can do either in your home or outside if you're actually living in a location where being outside is just not overly hot or overly cold. And then there are a lot of YouTube videos and virtual exercise classes that folks can go ahead and participate in that will help increase your level of physical activity on a day-to-day basis that not only we have been able to show has long-term benefits in folks who are living with MS purely based on MS disabilities, but also reducing the risks and consequences of some of these other vascular comorbidities.

Managing stress to the best of your ability is also another way that we can remain emotionally well. You know, right now this is a very stressful and emotionally charged environment that we are all living in, and we could all use help when it comes to managing stress.

So whether or not that's something that you have been able to self-identify as stress management exercises, some of those things might be taking up a hobby or doing things that give you a sense of inner peace like reading or listening to soft music, other things like yoga or tai chi.

There are some virtual yoga programs. We actually have one at the Cleveland Clinic that folks have found to be very helpful. And then when folks need a little bit of help maybe discussing options either with a local counselor or your MS healthcare provider team, there are certainly online resources that are provided by MS foundations.

So if you ever have any questions regarding what are ways that you can manage stress, getting your MS healthcare provider in the loop is a good idea so that way they can discuss options with you.

Drinking plenty of fluids especially now during the hot summer months - Dr. Hendin and I both practice in the desert, in the Sun Belt. Temperatures are very high right now. We're talking about 110 degrees plus.

So making sure that you are trying to keep cool, not being outside during peak heat temperatures, drinking lots of fluids throughout the day - all of this is very important and, of course, eating nutritious foods.

We usually recommend a nice anti-inflammatory nutritional regimen, the Mediterranean nutritional regimen that tends to encourage lean proteins, whole foods like colorful fruits and vegetables, multi-grains instead of light breads and white rice and, of course, high fiber and plenty of fluids is usually the best way to go as far as we understand when it comes to MS and COVID-19.

Taking a walk outside while abiding by social distancing recommendations is a great way to get fresh air and exercise. I will admit that when we put together these slides we were still during the springtime when most locations, you know, you would be able to go outside fairly comfortably.

Now where in certain locations it's very hot, it's very humid, you know, opportune times to go outside would probably either be early in the morning or later in the day after the sun goes down to try to avoid high temperatures and overheating, because we understand that increased heat and overexertion during high peak temperature hours can sometimes lead to transient worsening of MS symptoms which, of course, we would like to try to avoid.

Staying connected. So social distancing does not equal social disengagement and I actually don't like the concept social distancing. I think physical distancing is probably a better way to describe what the CDC is actually asking for all folks to be doing and keeping at least 6 feet away from another person to try to decrease the exposure to respiratory droplets in another human being.

But, you know, this does not mean that we can't still be connected and, you know, even though we would all like to be able to see our friends and our family face-to-face there are other means for remaining connected with our loved ones.

That could either be through telephone. That could be through Facetime. That can be through Zoom chat meetings, and again they're not ideal but we do have other methods that we can try to encourage at least until the time where we feel that the COVID-19 pandemic risks have decreased nationwide.

And mental health is extremely important, you know, and historically mental health, depression and anxiety have been stigmatized and this really should not be the case. It is so important especially during COVID-19 and I urge and encourage everyone on this line that if you are struggling please reach out to a trusted friend, a family member or your healthcare provider because there are certain programs, methods and folk out there who are more than happy to help during these challenging times.

Dr. Barry Hendin: Carrie shall we go through the questions that have already been submitted to us?

Dr. Carrie Hersh: I think that we can go back to the regular - yes the popular questions from registration.

Dr. Barry Hendin: Great.

Dr. Carrie Hersh: And then we can go to the questions that have been posed by this particular group.

Dr. Barry Hendin: Great. So Dr. Hersh and I will have a - at least answer some of the questions that have been pre-submitted and the first is, "Since seniors are more severely impacted if they contract COVID-19 virus, are people with primary progressive MS more vulnerable and is mortality higher for them than for seniors with other forms of MS?"

It's actually a very thoughtful question which is being asked. Let's begin with the - with what we told you to start with and then we'll try to answer that on a logical basis and what the evolving information says.

So we know that the - as Dr. Hersh also commented the older you are the more likely you are to have a poor outcome with COVID-19 and by poor outcome I mean hospitalization, intubation and death and the higher your level of disability the greater the risks are to you if you do get COVID-19.

So it stands to reason that if there was a group that was older or more severely impacted they would have greater risks. People with primary progressive MS are on average older than the people who start out with relapsing MS, and as such people with later MS, either primary progressive or secondary progressive, will just by the hint of their age be at greater risk for bad outcomes including mortality.

Add to that at least the emerging data. As some of you know there is a collection of the American data now with more than 800 cases through what's called COViMS, C-O-V-I-M-S, out of Washington University under the auspices of Dr. Anne Cross.

She's collected 800 - over 800 people with MS who've had COVID-19 and we were getting to at least see some of the patterns. The older you are, including later secondary progressive or primary progressive MS, the greater your risk.

The more disabled you are the greater your risk, which is to say people who are walking freely have less risk than people who are using walkers, and they have less risk than people who are in wheelchairs and they presumably have less risk than people who are bed down.

So the answer to your question is yes, statistically primary progressive MS carries a greater vulnerability and mortality but it's not because of the diagnosis. It's because of the age and greater disability often associated with both primary and secondary progressive MS. A very thoughtful question. Dr. Hersh?

Dr. Carrie Hersh: Okay. The second question actually Dr. Hendin had started to allude to. So the question is, "I was wondering if you collected any data on the number of people that have MS who have contracted COVID-19. How do they seem to do and is it any worse than a person without MS?"

So as Dr. Hendin has been alluding to, over the past six months or so, MS researchers have done a lot of work in trying to collate data in a standardized fashion across many different institutions in different countries, and there are a couple of pretty large MS and COVID-19 databases.

One is actually - was developed in Italy and is currently ongoing and collecting patient data and the other is the COViMS effort, which is a collaborative effort between the National MS Society, the MS Society of Canada that is being spearheaded by Dr. Anne Cross and Dr. Amber Salter.

And in the latter database, the COViMS database, which is actually made available publicly on their website, over 800 patients with confirmed MS have actually voluntarily been uploaded into this database by clinicians.

And overall over 85% to 90% of those patients have actually been described as either recovered from their COVID-19 infection or are actually in the process of recovering. And there is a large heterogeneity between different disease courses or MS phenotypes whether or not they're relapsing-remitting, primary progressive or secondary progressive. But it looks like overall the majority of patients who are having a more difficult time with COVID-19 are the ones who have those other comorbidities those of other risk factors that we have briefly talked about.

So patients who are over the age of 60 or 65 years, those who have cardiovascular disease, uncontrolled diabetes, high blood pressure, morbid obesity or who are chronic smokers. And we found that of the patients who did not do well, over 85% of them had at least one comorbidity listed.

In terms of disease-modifying therapies, and I know that that is a very hot and popular question among folks who are living with MS but also healthcare providers as well because the more information we have, the more we'll be able to help stratify risk and determine best treatment practices in the clinic.

And overall, all disease-modifying therapies that have been listed, for the most part, at least one patient has been determined to have been exposed to COVID-19. There doesn't seem to be a significant relationship to any disease-modifying therapy in particular except for maybe some of the immunosuppressant agents where we might have to be a little bit more careful, scrutinize the individuals who are undergoing treatment.

And I will say that these data are not completely sparsely out in terms of every individual on a certain disease-modifying therapy. What do they look like? What other comorbidities do they have? So there might actually be an unequal or disproportionate percentage of patients who are treated with certain immunosuppressive therapies or certain immunomodulator therapies that have other comorbidities that actually increase that risk of COVID-19 even further.

So this is - this data is really not to persuade people from being on disease-modifying therapies. In fact, it's felt to reassure the recommendations that we have been recommending even from the very beginning in terms of not stopping disease-modifying therapies unless otherwise specified by the healthcare provider.

Very similar data were actually reported by the Italian group who actually published their findings in Lancet Neurology of over 200 patients and 96% of their patient population were reported to only have a mild case of infection. So overall, the results appear to be slightly reassuring and they don't seem to contradict the guidelines that we have made even from the very beginning.

And they support that again, folks who have MS with comorbidity and disabilities combined with older age are exposed to the risk of maybe a worse evolution of the disease. And therefore we really need to focus on special care and preventing certain comorbidities and ensuring health and wellness in our patient population.

So, you know, overall I think that we're starting to garner some really helpful data and information. But how we extrapolate that to the general MS population in terms of treatment guidelines and consensus, we're still working on that.

Dr. Barry Hendin: So the next question is how safe is it to go on vacation or to stay at a bed and breakfast. And when I read this question, a smile came to my face because I thought to myself part of the answer is I don't think it's entirely safe ever to go on vacation because of the various things that may come up that are unaccepted. I say that a little bit tongue and cheek. But there's always been a risk before COVID-19 when we leave home and go on a vacation.

That means the risk of being on the road in our car, the risk of being on an airplane, the risk of the air traffic controllers going on strike and there being a hurricane where we land. Obviously those risks are now changed in the era of COVID-19 and to a large extent, vacations have been very significantly modified.

So for me, the answer is there is no one answer to how safe is it to go on vacation to stay at a bed and breakfast. But rather all the things that one would take into account; am I going into an area that is - that has a very high level of COVID-19 or an area that is relatively on the downswing and less?

How do I get there? If I've got to go on a crowded plane, aren't my risks greater than if I, at least for COVID-19 (era), than if I went by individual transportation such as a car? I think cruise ships, for the time being, are not an ideal way to - an ideal sort of vehicle of transportation or vehicle.

And at that point, how sure are you of the place you're going and what do you intend to do there? So I will tell you that my children by and large have gone on vacations; not all of them. But they tended to go on vacation in places where they were camping and out in the open and out in the air.

I think that there are safer ways where there is crowd avoidance. There are more difficult vacations with respect to mode of transportation, the place to which you go and the safety that place will create for you. That is, do you have confidence that that place will keep your room safe; that that place will keep you away from other people who may create risk, et cetera, et cetera?

It's a long answer. But my answer is there's always been risks about staying home or going on vacation. Those risks are heightened right now and they depend on vehicle, they depend on the place to which you'll be going and the circumstances there, not just the COVID intensity but how safe the environment is and how much you will trust the place in which you're staying. All of those are variables. I would not say as a blanket that you should not or that you should liberally go on vacation. Just stay smart. Dr. Hersh?

Dr. Carrie Hersh: Okay. And I'll cover the last question and I'll actually cover this pretty quickly so that way we can move on to the Q&A session. So the last question: "As a healthcare worker with MS, is there anything else you should do besides personal protective equipment and what the average person is doing?"

So I'm going to go ahead and say, and this is somewhat of an annoying answer, but please bear with me. Remember that just because one has a diagnosis of MS, it does not mean that one is at increased risk of developing a COVID-19 infection. So it really is on an individualized basis what their overall risk is in the workplace including as a healthcare worker.

So does this person have any other pre-existing comorbidities, are they older, do they have physical disabilities where it's difficult for them to mobilize and therefore might be at an increased risk of having respiratory infections and pneumonia just because they have trouble mobilizing?

So it really does depend on what other factors that particular individual has that may help stratify the risk of whether or not they might be at an increased risk of COVID-19 susceptibility working in a healthcare system.

So I would go ahead and say if someone with MS doesn't have any other risk factors, they're overall young and healthy and they are being treated with a disease-modifying therapy that doesn't have a significant impact on circulating white blood cells and lymphocytes and I would say they really don't have to do anything beyond what is already being recommended by the CDC and other folks who don't have MS.

But if that individual is a little bit older, they have maybe one or two uncontrolled risk factors, maybe they are on a disease-modifying therapy that reduces circulating white blood cells that may lead to increased susceptibility, that's really a conversation to have with your MS healthcare provider team and human resources to try to develop a plan that makes the individual feel safer in the workplace.

Dr. Barry Hendin: Great. And (Peter), would you like to address the questions which have come in to us?

Peter Damiri: Yes. Absolutely. Thank you for that. We had several questions today that came in and I'll start reading some off now. Are people with MS more likely to develop a cytokine storm if exposed to COVID-19?

Dr. Barry Hendin: I'll try to answer that. The first answer is that we don't know for sure. There has been some hopeful comment at least in the opinion that if you're on an anti-inflammatory agent, a disease-modifying therapy that reduces autoimmunity, reduces inflammation that there could be some at least hypothetical advantage in reducing the storm.

So it doesn't reduce the likelihood of your getting COVID-19 but it is at least possible that it reduces some of the cytokine storm and indeed some of the agents such as interferons have been looked at investigational to see whether those agents in some way be beneficial in outcomes of MS.

It's all still early and the answers are not yet clear except to say there is no evidence of having MS right now increases the likelihood of cytokine storm. Treatments could possibly reduce the cytokine storm but

it's not clear. And we are looking at some of the agents that are disease-modifying therapies to see if they may provide some mild benefit.

Peter Damiri: Okay. Thank you for that.

Dr. Barry Hendin: Peter.

Peter Damiri: Next question. Can you speak to what we know about memory loss as an aftereffect of COVID versus an MS symptom?

Dr. Barry Hendin: Dr. Hersh. Would you like to take that one?

Dr. Carrie Hersh: Yes. I'm not sure I completely understand the question. But I'll say this. There are certain disease-modifying therapies that are considered B cell depleters meaning that the overall mechanism of action of how they help safeguard from future inflammatory event that in effect does relapses in new MRI lesions in the brain and the spinal cord. They work at the level of decreasing the subpopulations of some peripherally circulating B cells that can impact some of the memory B cells.

But what I would go ahead and mention is that these medications, and I'm referring to rituximab, ocrelizumab and there is a new B cell depleter that is about to be launched. Their overall role is to decrease part of the peripheral B cell population but they do not decrease or eliminate the entire circulating B cell subpopulation. So one is still able to retain and maintain their earliest versions of those B cells that are closer to stem cells and the more mature cells that actually create antibodies.

Now with that being said, we previously discussed that there may be, and again, you know, these are hypotheticals based on what we understand about these B cells depleting medicines and how they have possibly blended the effect of other vaccines. There may be a blunted response to a future COVID-19 vaccine but we still don't quite understand to what extent and for how long.

So we really are going to require more information in terms of future trials specifically looking at patients who are on these disease-modifying therapies after these COVID-19 vaccines have already been approved and are available for use.

Dr. Barry Hendin: Dr. Hersh, let me see if I can jump in on this one too. First of all, I am very impressed with the sophistication of the immunologic answer you've given. I have a feeling, although I'm not sure, that the question was much more basic. And that is if I've got MS, I know that I may have some memory problems. Will COVID-19 increase my cognitive memory symptomatology? Let me give a thought about that and if you want to modify, please feel free to jump in.

Clearly, a large number of people with MS will complain of some kind of cognitive or memory symptomatology even before there was ever COVID-19. We know that in the recovery - that during the acute infection of COVID-19, people will have changes in their memory and thinking processes that we will call a delirium.

And we will know that in the recovery phase from a delirium, there may be some persistent memory changes. It isn't yet well worked out and I don't - I haven't seen a proper study to tell me about the long-term memory consequences of COVID-19, a problem that remember we've only had for seven months. And so there's no one who can tell us what the change is after a year or two or three.

But common sense says to me the following. If you're very sick and have MS, you may be more susceptible to a delirium. If you're already having memory problems, they may be worse during the acute infection. Infection makes everything - heightens everything with COVID-19 but also with other illnesses that cause fever. My guess is that the recovery phase for people with MS may include more fatigue and with more fatigue, some more memory symptomatology that's still to be worked out. Peter?

Peter Damiri: Thank you both for that. Yes. Sure. Next question. Can you talk a little bit about the connection between Vitamin D and COVID-19?

Dr. Barry Hendin: Dr. Hersh, I know that's one of your favorite topics and I'd love to hear what you have to say.

Dr. Carrie Hersh: Sure. I think that this question has actually come up with every webinar that we've had. And I'm actually quite impressed with the quality of the questions that have come in. This actually increases my humility as well.

But yes, there's actually been a lot of hot discussions in terms of Vitamin D and COVID-19. And, you know, from what we understand about Vitamin D, we do understand that there are certain immunological benefits and possible neuroprotection in MS if used as an adjunctive treatment to disease-modifying therapies.

The overall role of Vitamin D and MS still needs to be parsed out completely and there are clinical trials that are attempting to do that so we have more definitive information on exactly the role of Vitamin D and what benefits we actually do see in MS.

But we do understand that, you know, Vitamin D is not just a vitamin. It's also a hormone and it has other potential benefits that go outside of MS and that includes bone health, that includes cancer health and metabolism health as well. And there actually have been a variety of trials or studies albeit they have been relatively small looking at Vitamin D and whether or not someone has a decreased susceptibility risk of getting COVID -19 or if they have a (better off) time.

And those studies have actually shown that those patients actually had decreased inflammatory responses with COVID-19 and there may, may being the operative word, been some protective measures against COVID-19 susceptibility.

And so my overall opinion on this is that, you know, Vitamin D supplementation is something that we encourage for all of our patients who are living with MS. And certainly this is something that is considered to be safe during COVID-19 and I would certainly encourage the use of Vitamin D supplementation within the scope and practice of the primary care doctor of the MS clinician to make sure that Vitamin D levels are checked routinely and are being monitored.

Dr. Barry Hendin: Peter?

Peter Damiri: Great. Thank you for that. Sure. Next question. Does getting COVID-19 bring on any pseudo exacerbation or make the MS symptoms worse?

Dr. Barry Hendin: I'm happy to answer that. What - I kind of half answered that before but I'll try to answer it in a more directed way. Anything that causes a fever or an increase in body temperature may cause a worsening of MS symptoms. It's one of the things that we call a pseudo relapse.

So we know a history that a urinary tract infection or pneumonia will increase the risk of - I'm sorry, will increase MS symptoms. If you had numbness in your right leg three years ago due to an attack and it seemed to be fairly quiet, sometimes with (sort of) infection, things will act up and you'll get a reoccurrence of the old symptomatology, i.e., a pseudo relapse.

So to the extent that COVID-19 is associated often in its early phase with cough, respiratory symptom and fever, you'd expect there to be some increase in symptomatology at least due to the fever itself. My experience is that if you've got MS and have some kind of infection, not only will you have more risk of a pseudo relapse and that is a heightening of symptomatology but you're just going to feel much more done in than average. So the answer is yes.

Peter Damiri: Okay. Thank you. There were several questions about vaccines. And I know you discussed them in the presentation part of the program. But one in specific is the Oxford vaccine made with a live virus. And just in general, what other vaccines are in development?

Dr. Barry Hendin: Dr. Hersh?

Dr. Carrie Hersh: Yes. No. So that's a great question. So to date, there have been about 130 trials that have started looking at COVID-19 vaccines. And I believe that there are about somewhere between five and eight that have reached the Phase 3 clinical trial marker, so meaning that this is the last stage of clinical trial testing that is required before that particular drug or vaccine goes to the FDA for approval.

Phase 3 clinical trials typically require thousands of patients in vaccine trials in order to prove their safety and effectiveness. In the case of COVID-19, these Phase 3 clinical trials, one being done at Oxford, another one that is being spearheaded here locally with NIH funding through Moderna; they are requiring about 30,000 patients to be recruited into these clinical trials to showcase effectiveness and safety.

Both of these clinical trials are using a unique vaccine called an mRNA vaccine. This is a little bit different than your typical live attenuated vaccine or killed and activated vaccine where essentially they're taking a little piece of a genetic marker that codes for the viral captive protein that is located on the external surface of COVID-19 virus that allows it to attach to our own white blood cells and antibodies in order to create an autoimmune response.

So these mRNA vaccines that's exactly how they - the mechanism of action of how an autoimmune response, if it is created in an individual, happens where it is coding for essentially the viral captive protein markers where our own B cells and antibodies are being able to connect with it and then produce an immune response to it.

So it's a little exciting because the mechanism is a bit different than what we have previously seen and, you know, we still have yet to see the safety and effectiveness in those who are on certain disease-modifying therapies but I'm hopefully optimistic that we'll be able to see at least some immune response among allocations taking certain disease-modifying therapies but we'll have to wait and see with further clinical trials once these vaccines are approved.

Dr. Barry Hendin: Dr. Hersh, I'm going to put you on the spot just a little. We've said how humble we are about the fact that we don't know so much. And this is one of those absolute unknowns. Neither you nor I know when we're going to be seeing the first usable vaccine. Do you - when you speculate to patients or otherwise, when are you hoping to see the first vaccine available in the U.S. even if your speculation and optimism prove wrong?

Dr. Carrie Hersh: Yes. No. That's a great question. So my expectation is that we'll probably have a vaccine available by the end of the year, by the end of 2020. Of course, you know, with that being said, you know, a vaccine not only has to be approved but it also then has to become available to the mass public and it has to be affordable and readily available and then of course, readily used.

So the effectiveness of a global vaccination program is only going to be as successful as the number of folks who actually take that vaccine even if it's 100% effective and 100% safe; so that's under ideal conditions. But I'm hopeful that by the end of the year we will have a vaccine approved.

Dr. Barry Hendin: That's close to mine. I would have most optimistically ended this year for me. I won't be surprised if we're a little off and to see it in the first quarter or the first half of the coming year. But the later it is, the more disappointing because all of us are hoping for something that mitigates this pandemic.

And then I think as you pointed out, the questions will still remain. How much of an immune response will it provide in which people? The older you are, the less of an immune response you generally get. The

younger you are, the greater the immune response. And so we may have to see a variation in our populations. And then the question is how long will it last?

They're hoping I think that this will be a vaccine that gets to the core of the virus, which is mutating less and therefore will be a little bit more enduring. But this virus is a very clever one that is mutating and it doesn't mean we won't be needing periodic boosters. Those are my thoughts. But again, those are thoughts about the unknown.

So I think Peter, there are a number of questions which we haven't answered. Are there any that stood out; there's a last question that you wanted to ask?

Peter Damiri: Yes. And thank you both again for all those great explanations. There's one last question that kind of does tie into what you just mentioned. And the question is: Since there is no vaccine yet, how safe is it to go to regular doctors' appointments, get an MRI, get a mammogram and go to the dentist?

Dr. Barry Hendin: I'll try to answer that and again, if Dr. Hersh would like to add in, I'd be delighted. But there are things that change risk. And so some people get to their MRI for example in their private car. Some people get to their MRI on public transportation. Some people have infusion centers that are practicing high levels of safety. Some are probably a little more - or a little bit at least less clear in terms of their safety precaution.

So I think there isn't one answer. My general answer is - whereas I might have been on autopilot a year ago and said it's a year, it's time for your MRI or it's six months, it's time for your infusion. I at least ask myself the question each time about risk and benefit generally deciding that the old principles of making sure that we monitor MS - MRIs, making sure that we treat MS- infusions are still appropriate and my behaviors remain fairly close to what they were before. Dr. Hersh?

Dr. Carrie Hersh: No. I absolutely agree with your comments. You know and generally speaking, you know, we still have to take care of our patients. We still have to take care of our health. You know MS is a chronic long-standing condition.

And we still need to monitor. We need to monitor through surveillance MRIs. We need to monitor with labs. And we need to monitor by going to see the doctor.

So everything is about stratifying that risk-benefit ratio. And my overall concept is that if you feel that you can travel safely to see your doctor, to your Imaging Center and to your lab, that you are able to wear a mask and other healthcare providers are doing the same, maintaining social distancing, then I would say that overall the benefit of surveillance monitoring certainly outweighs the potential risk of COVID-19 contraction.

Dr. Barry Hendin: Thank you. Peter any final comments?

Peter Damiri: Well, just I want to thank you both so much for your time, your expertise, the presentation, and the excellent responses to the questions that were submitted ahead of time plus all the ones that came in during the program. So I really do appreciate it. A lot of great information and insights. And I'm sure very much appreciated by our audience as well.

So as I mentioned this does conclude our webinar tonight, "What you need to know about COVID-19 and MS Program Six." As you can imagine from the title we do have five additional COVID-19 and MS webinars. And they are all archived on our website at mysaa.org. And this webinar will join them as well probably in a few days to get that recorded and posted to our website so please check back.

I would also like to thank funders, Bristol Myers Squibb, EMD Serono, Genentech, Novartis, and Sanofi Genzyme for supporting this webinar series. As mentioned, the program will be archived so please check back. And I would invite you to take a brief survey that immediately follows this presentation to let us

know about thoughts on this program and other webinars you would like to see from MSAA in the future.
So, on the behalf of MSAA, Dr. Hendin, Dr. Hersh, thank you so much for watching and please stay safe.