Hello everyone and welcome to the TMA’s ask the expert podcast series. Today’s podcast is entitled Rheumatological conditions and ADEM, NMOSD, TM and ON. I’m Sam Hughes from the neuro immunology program at University of Texas Southwestern Medical Center in Dallas, Texas. I’ll be moderating this podcast today. The TMA is a nonprofit focused on support, education and research of rare neuro immune disorders. You can learn more about the TMA on the website at myelitis.org. The podcast today is being recorded and will be made available on the TMA website for download and for download via iTunes. During the call if you have any additional questions you can send a message through the chat option available with GoToWebinar for today’s podcast. We are pleased to be joined by Dr. Julius Birnbaum and Dr. Tracey Cho. Dr. Birnbaum graduated magna cum laude from Princeton University and received his M.D. from Columbia College of Physicians and Surgeons.

He earned his master's degree in Clinical Investigation at the Johns Hopkins Bloomberg School of Public Health. Dr. Birnbaum is the only physician in this country who is board certified in neurology, internal medicine and rheumatology. His clinical and research interests pertain to the neurological complications of rheumatic syndromes. With a focus on Sjogren's Syndrome, Dr. Tracy Cho is an associate professor of neurology at Harvard Medical School and director of the autoimmune and infectious Neurology Unit at Massachusetts General Hospital. He focuses clinically on meningitis, encephalitis and myelitis due to infections such as HIV and cysticercosis as well as neurological complications of systemic medical diseases like sarcoidosis and lupus. He also specializes in autoimmune neurological disorders that have NMDA receptor antibody encephalitis and other antibody mediated and encephalotomies. Welcome and thank you both for joining us today.

So before we dive into the questions that came from the community I wanted to set a kind of a foundation for us as we start this conversation. Speaking for myself as a non-physician and when I started into this world of immune mediated conditions it was certainly a little bit confusing to me to be talking about rheumatologic, the condition versus immune mediated conditions. And then the central nervous system disorders that are immune mediated and autoimmune disorders and there's a lot of vocabulary that kind of mesh together and is slightly confusing for me at least. And so I’m hoping that we can kind of like I said lay a foundation with kind of general definitions of what, when we talk about rheumatologic conditions, what do we really mean? Is that the same as autoimmune disorders or where are they different. And then why are disorders like neuromyelitis optica spectrum and transverse myelitis and other neuroimmune disorders maybe not considered rheumatologic conditions kind of where one ends and where the other began.
03:20 So if you put, Dr. Birnbaum throw it over to you, if you just kind of want to give us a little bit of an overview and foundation of what we talk about what we mean when we talk about these disorders.

03:33 Dr. Birnbaum: Sure. So, thank you for having me. I agree with you that a lot of the terminology that's used in clinical medicine to categorize these disorders can be confusing. The unifying feature of all these disorders is that the immune system which should be protecting us from infections and cancers starts acting aberrantly and this can result in different diseases. So when we think broadly of the field of rheumatology there's two facets to it. First these are disorders which we regard as being musculoskeletal so that can be pain in the shoulders or back of uncertain origin and those such as osteoarthritis who we consider to be not mediated by, or immune disorders. So for example osteoarthritis is more wear and tear. But the immune system is not acting aberrantly. The other half of rheumatology does deal with auto immune disorders. The unifying feature of these autoimmune disorders which make them rheumatological disorders is that they are associated with so-called systemic manifestation.

04:50 So for example when you think of a rheumatic disorder such as Sjogren's and lupus these are autoimmune disorders. But in different patients, different organs can be affected. This can include the heart, the lung, the kidney, and the skin. Now neurological disorders can occur in subsets of patients with rheumatic disorders. So again, I would define rheumatology as the practice of two facets. One is what we call musculoskeletal disorders and one is auto immune disorders and the rheumatological disorders broadly can affect many different parts of the body. And when we have autoimmune neurological disorders occurring in patients with the rheumatic diseases, the issue is what we call attribution. So specifically, it is a neurological disorder specifically due to rheumatic disorder or is the neurological disorder just presenting as a coincidental and secondary unrelated disease. So hopefully that provides some sort of vista of what constitutes rheumatological disorders and what constitutes neurological disorders and how they relate to each other.

06:16 Sam: And I think so our community is listening to this have by and large been diagnosed with one of these rare neuro immune disorders NMOSD, TM, ADEM that aren't really considered Rheumatologic conditions that are considered neurological conditions that are immune and origin.

06:38 And then there are some times those patients who have Sjogren's or Lupus that then like you're saying have a neurologic manifestation that we call transverse myelitis or some kind of brain or optic nerve lesion associated with it. So we considered these, and please correct me if I'm wrong, neurologic disorders even if they're auto immune in nature or immune mediated in nature if they are focused on the nervous system, either central or peripheral, as opposed to
maybe these rheumatologic conditions like a lupus or sarcoid that affect other organs and then in a rare subset of patients also affect the central nervous system. Am I understanding that properly, or would you describe that differently? Either Dr. Birnbaum or Dr. Cho? I'm happy to let you go ahead.

07:42 Dr. Cho: So I agree with Dr. Birnbaum's framework as laid out. I guess I would too address your question. I think we need to step back and define transverse myelitis which is a syndrome. It can be due to many different diseases whereas neuromyelitis optica is a specific disease due to a specific pathologic antibody, which has a target within the central nervous system. And likewise, ADEM is not. It's also a syndrome but it lies somewhere in between the Transverse Myelitis term which is quite broad and can be due to multiple different diseases, and NMO where it's such a specific diagnosis. ADEM is somewhere in between and that it is defined by typically an acute one-time episode of inflammation from a trigger firing on the immune system to target the myelin. So in regard to the frame which Dr. Birnbaum laid out if someone with lupus develops transverse myelitis there is the question of whether the myelitis is attributed to the lupus or whether the myelitis is due to a separate process.

09:12 And as the topic for this webinar and many of the questions submitted suggest there is a well-established link between NMO and other autoimmune diseases that affect other parts of the body and I think one of the key points that we’re going to get to today is whether NMO is indeed part of that broader systemic autoimmune disease or whether it is a separate disease and that with the latter being my take on the question of NMO. So the terminology really is confusing as you both have stated already and I think that we need to be precise when we’re talking about the attribution of transverse myelitis when we have a clear cause such as an NMO versus when we’re unsure of the exact cause. Before we can say whether or not it is related to a systemic disease process.

10:23 Dr. Birnbaum: Yeah that's like even talking about it can get pretty complicated and I think from the conversations I've been a part of and observed even with the clinicians and researchers talking a lot of these conversations occur just trying to define what everybody's saying what they mean when they say it. But I kind of moved into especially Dr. Cho, as you were saying are our patients who were diagnosed with NMOSD in particular what we see in many cases is also an increased risk of what we call, you know, comorbid rheumatologic conditions or these rheumatologic disorders that happen at the same time that are that we don't think are related to the NMO.

11:11 Sam: And without getting into you know all of the genetic underpinnings of why we think autoimmune disorders are connected as were you know researchers are
still working out. Dr. Cho, could you maybe speak a little bit to why we think that this comorbidity occurs with auto immune disorders and then what really are those are the conditions that we do see associated with these rare neuro immune disorders like NMO spectrum disorder?

11:44 Dr. Cho: Sure. So the underpinning I think is like you mentioned in generic terms a general tendency for the immune system to attack itself as opposed to cancer or infection as Dr. Birnbaum pointed out in his framework. It's well known that some patients with a certain auto immune disease have increased risk for other autoimmune diseases. And it just varies from individual to individual, how that manifests in terms of the specific diseases they get and what parts of their body are affected. So it's kind of a blanket statement. But certain autoimmune diseases tend to run in packs. And if you have one there's a slightly increased risk of having one or the others on the list. And for NMO spectrum disorders the most common associations are indeed with lupus and Sjogren's Syndrome. But there are many others that have been associated with increased risk and it goes in both directions meaning someone who develops NMO as their first disease could later develop and be diagnosed with a systemic autoimmune disease or someone who has a known autoimmune disease like lupus has a slight increased risk in developing future NMO and that the associations are not well laid out in terms of the exact mechanisms and we're not very good at predicting the exact risk associated but those are the two most common.

13:37 I also think that we will learn more about this as we better define the underpinnings of these different autoimmune diseases in terms of specific genes. Some of that is in the works but I think we've got a long way to go on that front.

14:01 Sam: So back to you Dr. Birnbaum. There are some questions that came in that are still kind of broadly about rheumatologic disorders like Dr. Cho was saying there are some conditions that are associated with NMO and these disorders that our community lives with.

14:19 But how are these different rheumatologic disorders like Sjogren's or lupus or rheumatoid arthritis even diagnosed and treated. And then how are those treatments how do they differ or similar to the immune treatments that we see for the recurrence neurologic disorders like NMO

Dr. Birnbaum: So another good question.

14:48 The rheumatic disorders basically are defined by a combination of patient's symptoms.

14:56 What we find on the physical examination and blood markers usually and these blood markers usually confirm in some way the presence of autoimmunity. So
there are disorders such as lupus which have protean symptoms and a diagnostic net is quite wide. But by and large there's certain cardinal features of for example skin manifestations such as the lupus I think everyone is familiar with a butterfly rash and then it's again trying to go through different organ systems, tease out different diseases. So again, Lupus many different organ systems are affected so we would ask for example is there hair loss, is there or are there ulcers in the nose or the mouth is there episodes of when you take a big breath it hurts too much or when you lie back and there's pain in the back and neck, and that could indicate inflammation in the lining around the lungs or the heart.

16:11

Any history of kidney stones any history of blood in the urine.

16:15

So these are symptoms that can affect different organs that we try and tease out and then there's a physical examination and generally we inspect hair texture, hair loss, if we look in the mouth if it's Sjogren's or we are looking at whether there is adequate saliva in the mouth will listen to the lungs will want to evaluate whether something called a rub which is grinding of lung or heart against different parts of the body, joint manifestations are a particular calling card of different rheumatic diseases so we'll look at the knees and the elbows the knuckles, we'll squeeze and evaluate for any tenderness, we'll see whether there's any swelling of the joints. So hopefully this is just to illustrate and compelling way of how many different things that we need to assess Rheumatic diseases. But based on that we have a formulation and we're able to siphon down to a few a set of symptoms and examination findings and then we look at the blood work and by and large there are certain abnormalities that are associated with diseases. Lupus might be associated with a very specific panel of antibodies and same as rheumatoid arthritis.

17:42

So at the end of the day it's the patient's symptoms which matter the most and the history is the most illustrative and forming feature. The rheumatic disorders interestingly are treated with some immunomodulatory agents that are similar to what are used for transverse myelitis and so transverse myelitis by and large you want to suppress the immune system. So that paradigm of suppressing the immune system is similar to some rheumatological disorders. There is also a subset of treatments which are called immunomodulatory disorders and these are medications which don't necessarily suppress the immune system but it modulates the immune system into behaving in a more tolerant way. Those classes of immunomodulatory medications tend to be more specific for rheumatological disorders as opposed to transverse myelitis. So for example immunosuppressive medications and that might include something called Rituxan or methotrexate or CellCept.
Those are medications that are shared between rheumatic and diseases, neuromyelitis optica sometimes ADEM but certain of the immunomodulatory medications are more specific and have a specialized niche in rheumatic disorders and are not widely used in transverse myelitis. So again, some areas of overlap in terms of disease treatment but also some areas in which medications are specific for rheumatological versus transverse myelitis.

So I’m kind of the follow up to that question when we are talking about NMO spectrum disorder patients you know the most common medication that they're on to prevent relapses are like you mentioned Rituxan, CellCept and even Imuran from time to time. So would you say that if I'm an NMO patient and I then go on to develop or lupus or some other rheumatic condition and I've been taking Rituxan and or one or the other medication, would you as a rheumatologist thing that they were going to keep what you're on what you're taking for the NMO covers this other disorder. And so we'll move forward with that or what circumstances would you look at a patient with a long standing diagnosis of one of these neurologic disorders who develops the rheumatic condition and say we need to work with neurologists or add another therapy - that kind of thing.

Yes it's an interesting question. I think that if you have a rheumatic disorder that's breaking through a medication that you use for Rituxan what you're doing is exactly correct. You have to think about whether that leads to abortment of treatment for the Transverse Myelitis or whether you want to keep that medication on board. And I think a lot of it depends upon the severity of the rheumatic disease flare.

So, if you're diagnosed with new rheumatic disease and it tends to be what we call musculoskeletal in nature, joint manifestations or sores in the mouth, I think then you try to keep the immunosuppressive agent or Rituxan onboard and it can be treated the rheumatic manifestations can be treated with short courses of steroids and managed in an expected way. In other cases if there's severe disease manifestations such as heart, lung, kidneys, then you would need to start medications that are specific and effective for those rheumatic diseases and in those disorders you would try to see whether you could come up with a regimen that would also be useful for minimizing risk of relapsing transverse myelitis and sometimes we add to immunosuppressive agents when necessary. It wouldn’t be the first step because of the risk of infection. But in situations in which you're kind of trapped in a corner we have used two combinations of immunosuppressive therapies both successfully and also with a tolerable risk of minimizing infection. So depending upon the severity of the flare and what that rheumatic disease is.
And it kind of moves into some other questions that came up about the potential drug interactions for lack of a better term with these immune agents.

So I guess first question is like you said, Dr. Birnbaum, many of the Rheumatic conditions that can become comorbid with NMO can be managed by the same the same immune medication. Is there any rheumatic disorder that you might expect to see or would not be surprised to see manifest in an NMO patient that would require one of the more specific immunomodulatory agents that is in the room pathologic world that we don't necessarily see in the NMO world. And if so do you kind of go into more detail about concerns you might have about the interactions of medication.

Using either specific immunomodulatory medications normally used for NMO that use for rheumatic diseases that might be useful for NMO?

Or useful or really even if you have a condition that's diagnosed alongside the NMO rheumatic condition diagnosed alongside the NMO that normally would have a difference and not Rituxan, CellCept or Imuran a medication used for it. There are concerns about the safety like you were getting at before multiple immune agencies that want.

So it's interesting.

There is a widening net of therapies that might be useful for NMO and is used for rheumatic diseases. So for example the medication Actemra, or Tocilizumab, which is approved by the FDA for the treatment of rheumatoid arthritis. It's being investigated for efficacy in NMO and has been shown to greatly reduce neuropathic pain in NMO. So there is a reason to think that certain immunomodulatory medications that are just currently approved for specific rheumatic diseases might be more ubiquitously effective for NMO and this is certainly a fertile area for research when you combine two immunosuppressive medications you do incur the added risk of an infection.

the point that I'd like to illustrate is that there's other autoimmune disorders such as inflammatory myositis when there's inflammation in the muscles, a subset of these patients could develop really debilitating and severe lung disease. And in these patients two or three immunosuppressive agents are used and there's the risk of infection. But I think at the end of the day it needs to be geared towards how severe the disease is. I think one thing to emphasize is a lot of times when patients are in immunosuppressive therapy there's a concern you know can I go near my daughter and I think that when we use immunosuppressive therapy we are not completely knocking out the immune system and we're not treating it as chemotherapy. You still have an immune
system that hopefully is effective in fighting off infections. So I would say that you want to try immunosuppressive mono therapy if you can.

26:31 But when you need to use multiple immunosuppressive agents you still have an immune system, you still have the ability to some extent to fight off infections. And when it's necessary it needs to be tailored toward the aggressiveness of the rheumatic disease.

26:50 Sam: That's a good point. I am going to turn it over to you Dr. Cho. Dr. Birnbaum and I have been talking for a little bit now.

26:57 Dr. Cho: I have one thing to add to that topic before you leave it. I don't know how many of your members have a possible diagnosis of MS that's often on the differential for transverse myelitis and as some providers offer MS medications for patients whose only manifestation is transverse myelitis. I would just add that the interferons that are used, the injections that are the sort of traditional first line medications in MS have been known to exacerbate or worsen, or cause a flare up of some underlying autoimmune diseases or rheumatic diseases.

27:58 So those medicines I've had a few patients that I've seen after they were seen by my MS colleagues and we ultimately used medicines like Dr. Birnbaum mentioned like mycophenolate mofetil (CellCept) that might be beneficial for both MS or Lupus to avoid the risk with the interferons. So, I think it does bear mentioning that some of these medicines both for neurologic and non-neurologic diseases that can activate the immune system sometimes rarely can trigger a flare up of an underlying autoimmune disease and we try to avoid those in those situations.

28:47 Sam: I appreciate that point. I think especially in the NMO world I think it's been made pretty clear in the literature that the interferons like you said that are used in first line MS meds that exacerbate the NMO disease process. And there are certainly those patients who are diagnosed, you know, before the advent of the NMO antibody that were treated like MS and had worse disease after that. So, I think in our world we think about MS interferons worsening in NMO. But we don't necessarily think a lot about it if the transverse myelitis is from an underlying rheumatic condition that the interferons normally used in multiple sclerosis might even exacerbate those conditions. Am I understanding that properly?

29:42 Dr. Cho: Yes. Even when it's due to MS I would not use MS interferon specifically if they have an underlying rheumatic disease like Lupus.

29:50 Sam: And so sticking with you Dr. Cho, there's some of the questions came come and relate to each other in a way I think globally. When we talk about rheumatic
conditions and these rare neuro immune conditions, patients kind of fall into two categories. There’s those who have some kind of rheumatologic condition and then they develop neurologic manifestations of that disease like a transverse myelitis or they’re then diagnosed with NMO that is occurring alongside their Lupus or whatever. And then there are those patients who have transverse myelitis and they’re treated like say basically an idiopathic transverse myelitis and then a couple of years later they develop a rheumatic disease process and then there’s the question that the patients have come up where is my TM, was that really a onetime event, or was that the first manifestation of my Lupus or my inflammatory arthritis and should I be worried about reoccurrence of my neurologic condition.

31:16 I think that this is a big unknown with that kind of subpopulation of our patients specifically the TM patients who for a few years have been told that this is an idiopathic onetime event. Now they have some kind of rheumatologic condition, inflammatory arthritis or what have you. And the fear of the unknown that they might have another attack of TM. Could you speak a little bit to kind of how you as a medical provider look at that kind of case and how you monitor it?

31:52 Dr. Cho: Sure. So that is a great question. And I guess the starting point for me would be what was the nature of the transverse myelitis. And I think of certain big buckets or categories in patients who have a partial transverse myelitis that is only affecting one or two segments of their spinal cord.

32:17 If the first question is do they have any other indications that they might have multiple sclerosis or be at high risk for developing multiple sclerosis. And I think that pathway is well recognized by neurologists and it’s kind of a routine work up when patients present with. So the categories there would be a idiopathic transverse myelitis with no other indications of MS and those patients are at relatively low risk for having a recurrence, whereas the patients who have any indication that they’ve had prior MRI findings that are suggestive of MS even if they hadn’t had symptoms those patients are at high risk for developing MS. When the lesion is larger, the Transverse Myelitis lesion is a longitudinally extensive lesion, that is classically more compatible with NMO then the sort of predictive algorithms are different. And we know that patients who have the NMO antibody are at high risk for recurrence. Now, when I see patients who have any kind of myelitis, whether it is short or long, I check for the NMO antibody as well as the myelin oligodendrocyte glycoprotein or MOG antibody which can sometimes mimic NMO, and if those are positive, then those patients, their treatment is different, because their risk of recurrence is high. If those antibodies are not present, then it is a judgment call on the part of the patient and the physician about what the risk of recurrence is and whether they need to be on an immunomodulatory agent or an immunosuppressive agent to prevent a recurrence. So in the patient you’re describing that has a prior
occurrence of transverse myelitis with a presumably negative workup of signs of MS or antibodies for NMO who later develops symptoms and signs of an autoimmune rheumatologic condition,

34:45 My immediate concern would be that the patient has NMO because of what we discussed earlier with a high rate of co-occurrence of NMO with other autoimmune diseases and I would look hard again as we know the NMO test is not perfect. Sometimes on repeat testing it becomes positive. And so it's not that having another autoimmune rheumatologic condition guarantees that you're going to have a recurrence if you've had transverse myelitis but I think it would make me suspicious enough that I would look again for NMO and if it's still negative then I think it's again a grey zone that requires judgment from the patient and physician on a case by case basis and also depends on how severe the nature of the rheumatologic symptoms are in terms of whether to treat. So that's kind of a vague answer. I think it really depends that the risk for recurrence really depends on the nature of the original myelitis and whether it was a long segment or a short segment, whether there was any signs of MS, obviously whether the antibodies for NMO or MOG were present.

36:08 and my personal general take would be to follow those patients carefully for any development of other neurologic symptoms and have a very low threshold for treating them for recurrence.

36:27 Sam: Dr. Birnbaum would you have anything to add Dr. Cho's statement.

36:34 Dr. Birnbaum: Well yeah the one thing I would think about is it is always these questions about when someone has myelitis.

36:42 And for the most part be it like transverse myelitis or ADEM or neuromyelitis optica as Dr. Cho was saying is questions like What's their relationship to the underlying rheumatic disease. And I think the understanding of this relationship has greatly changed over time. So for example in the 70s and 1970 1980s MS, multiple sclerosis and Lupus were thought to have a similar mechanism. And so that led to the term of a combined together called lupoid sclerosis. And I think that the treatment back then of MS and Lupus went hand in hand. What we're recognizing now is that the disorders that we see NMOSD, neuromyelitis optic or ADEM when they occur in a lupus patient these are generally two disorders that are coincidental meaning that the ADEM and the neuromyelitis optica is not a direct extension of Lupus or Sjogren's but rather these are two distinct autoimmune disorders.

37:51 Now they share certain pathways and that's why the treatments that are useful for neuromyelitis optica can be used for Lupus and vice versa but really they do not share an overlapping cause. So and to be brief Lupus is not a causative
disease that directly leads to neuromyelitis optica. So these neurological disorders are not a direct manifestation of Lupus or Sjogren's, they present in a coincidental fashion. And the reason why it's not unusual for a patient with one autoimmune disease to develop another autoimmune disease so the same way that a patient with neuromyelitis optica has a higher risk for example of autoimmune thyroid disease or Hashimoto's thyroiditis. That's why patients with Lupus or Sjogren's are at a higher risk of developing these neurological disorders. But that doesn't mean that they're directly causative. So again they are coincidental. There is a higher rate of these disorders occurring but there really needs to be a reformulation that these neurological disorders such as ADEM and neuromyelitis optica are not direct manifestations of entomological disease.

39:14 Sam: Yes that's a good point. Dr. Birnbaum I'll stay with you for this next question. It's a little bit more granular.

39:23 A lot of the rheumatic conditions we've been referencing are Lupus and others but there's a question that came then about a TM attack that was thought to be a part of Sjogren's and that the question is really how do you look for the onset of Sjogren's besides high AMA blood level so other than blood work how do you really look for Sjogren's in particular inpatients.

39:54 And if somebody comes to you with transverse myelitis at what point do you start going deeper than blood work kind of diagnostic to rule out things like Sjogren's Disease?

Dr. Birnbaum: So Sjogren's could be challenging to diagnose and sometimes the mean onset between the symptoms of dry eyes and dry mouth and the diagnosis can be 10 years.

40:27 It used to be about 10 years and now with greater recognition of Sjogren's that's back down to five years. The symptoms of dry eyes, dry mouth can be elusive in the beginning. So if you ask specifically for dry eyes, dry mouth you may have an answer suggesting that there's no underlying what we call sicca symptoms. But you have to probe a little bit deeper so not just asking for dry eyes but you know can you wear contacts and do you use artificial tears and when you ask for dry mouth you want specifically on examination look under the tongue and see whether there's what we call saliva pooling which it should be whether the mouth is dry. So the symptoms dry eyes, dry mouth that might become obvious after years they could be somewhat subtle in the beginning. We want to have tests which prove the eyes are dry and these are generally not done widely in ophthalmology offices and they probably should be.
And there's tests such as taking out a tear strip and seeing how wet the tear strip becomes and you actually measure this when you put it in the corner of the eyes and you could see how much moisture wicks out. And again we want to have cardinal serological features - blood type markers and these tend to be certain antibodies such as called anti-Ro antibodies. If these antibodies are negative and there's a high suspicion for Sjogren's then we do a lip biopsy and this is looking for characteristic findings in ducts in certain patterns of inflammation. So if you take that work up together it can be laborious sometimes and how detailed the workup needs to be depends upon how much the symptoms crop up at the beginning. So again, Sjogren’s could be under recognized and a lot of times the symptoms of dry eyes, dry mouth are somewhat marginalized and they're not thought to be for example as worthy of attention as the severe heart lung disease that occurs in Lupus.

But the symptoms can be quite distressing and I think Sjogren's is being raised to be more on the radar screen and everybody and I think it's pretty much what doctor Cho says. I totally agree. When you have someone with myelitis and to dating or coming before Sjogren's syndrome you want to be more specific about what the nature of that myelitis attack is. So again, like he said it's you know are we dealing with a partial myelitis are we dealing with something that might be on the spectrum of multiple sclerosis or you know and especially when we agreed when we do see a Sjogren's patient we're very suspicious for neuromyelitis optica popping up.

But again you know these are disorders that tend to co-occur both autoimmune diseases that share certain features what we call the antibodies are being churned out but at the end of the day you want to precisely categorize what the nature and type of the myelitis attack presented as. But again, if it is for example neuromyelitis optica it should be regarded as a coincidental disease co-occurring but it's not a direct manifestation of a Sjogren's again. Just to summarize the diagnosis of Sjogren’s needs to be worked up in detail and what Dr. Cho says the myelitis needs to be categorized and ultimately even if it is neuromyelitis optica it's going to prove not to be directly caused by Sjogren's and others don't have.

Yeah I would love to. I'm glad Dr. Birnbaum re-emphasized that I was going to echo what he said about neuromyelitis optica being an additional disease that is causing the myelitis in these cases that happens to occur in someone who also has Sjogren's

So getting back to the question as it was framed I guess. I don't routinely look for Sjogren's Syndrome in someone who has a longitudinal myelitis as the cause for that myelitis but there are certain forms of symptoms like in particular if it's sensory only symptoms that sometimes can imitate myelitis. The dorsal root
ganglia the nerve cells just outside the spinal cord that control sensation can sometimes be affected by Sjogren's syndrome and that's a very specific syndrome for Sjogren's that would make me look hard for it even in someone who had never had dry eyes or dry mouth or the other symptoms. So I think Dr. Birnbaum point is I agree with completely that you know 15 years ago when someone had myelitis looking for Sjogren's was part of the work up when we saw Sjogren's was causing the myelitis. While we now know is that almost all of those cases where someone ended up with myelitis and Sjogren's was because they had NMO in addition to their Sjogren's.

46:08 And so it's rare that someone has what would be termed a Sjogren's myelitis without NMO and I know there are no very few things in medicine that are 100 percent. So it's not that it's impossible. But I think that most neurologists who deal with myelitis now would assume that that the two are occurring rather than being caused by the Sjogren's.

46:39 Sam: Interesting point Dr. Cho.

46:40 So as we get into the last 10 to 15 minutes there's one had a group of questions that came in that are more about symptomatic management really specifically about pain and sensation changes. Often we see that with transverse myelitis whether it be in the context of an idiopathic event or NMO. But we also see pain and sensation changes with different rheumatologic conditions as you all have been discussing. So the questions that have come in are really asking Are there any practical suggestions regarding pain management? Since this is a big challenge just singularly with these disorders on their own but then if you combine them together that potentially have different reasons why the pain exists. Do you as clinicians have practical advice on how to manage the pain whether it be through pharmaceutical interventions, physical therapy, other kinds of pain management that you work with? Dr. Cho would you like to start off answering that question?

47:53 Dr. Cho: Sure. It's a good and tough question.

47:57 I think my short answer is that we have a sort of limited arsenal for neuropathic pain that all physicians turn to the same list.

48:15 And those are not generally as effective for inflammatory pain in other structures outside the nervous system that our seen in that with rheumatologic disorders, there are some patients who have vague rheumatologic symptoms that are not necessarily directly due to inflammation. Some of those patients may have some relief in their sort of general body aches and pains with medications that we often use for nerve pain in particular the tricyclic antidepressants like nortriptyline or amitriptyline or the other category that we
often use or the gabapentin and pregabalin, but in general I would say that you probably have to treat the nature of the pain depending on whether it is specifically affecting the nerves or the spinal cord somewhat independently from the rheumatologic symptoms but I would defer to Dr. Birnbaum on the symptomatic treatment for the type of pain that is seen more often in lupus and rheumatoid arthritis and other rheumatologic autoimmune conditions.

49:41 Dr. Birnbaum: Yeah no I agree it could be very tough issue to manage.

49:51 The interesting thing is when we see rheumatic diseases like Lupus or Sjogren's, they can develop very debilitating sensory neuropathy. And these neuropathies can have a predilection for attacking very very tiny nerves and it causes a small fiber neuropathy and certain features of small fiber neuropathies are similar to myelopathy. So it's pain that can be diffuse in nature and can be refractory or not responding to one medication.

50:27 So a lot of the medications that we use for neuropathic pain are also used in seizure disorders. So the treatment paradigm and seizure disorders that may have relevance for neuropathic pain is the mantra of treat towards efficacy or toxicity. And when you treat neuropathic pain under that paradigm there's an explicit awareness at the outset that hopefully when you ramp up the dosage there will be relief of pain but there very well may be the experience of unpleasant side effects. But that's the therapeutic window between success and treatment side effects some is very very narrow in their empathic pain. And I think that needs to be stated at the outset so. Well we tend to see is patients treated with neuropathic pain who do not have their dosages which are high enough to treat and provide some efficacy. Now oftentimes there's these treatments are not tolerated because of side effects.

51:41 But again you want to commit to a treatment and you want to ride that treatment wave until there's some demonstration of success and then the other thing is that often I do is the combination of treatments for neuropathic pain and that's polypharmacy so sometimes polypharmacy or the one medication gets a bad rap. And that's true if there is no rational design for why you're using polypharmacy but when it comes to neuropathic pain if you combine symptomatic treatments and each of those medications have different mechanisms of action then does a rational use of these medications and polypharmacy is actually the way to go. So you know by and large you can mix and match treatment for neuropathic pain depending upon mechanism depending upon what patients are saying. But I think that often when it comes to neuropathic pain the dosages have been too low and there's not a commitment towards using two agents often you try one agent that doesn't work, you drop it.
And again that's not to say this is going to be a panacea for all medicate for all patients but hopefully that will provide a window so that there is some alleviation of pain.

Very interesting thank you both for that. And last five minutes or so of the podcast I wanted to turn it over to Dr. Birnbaum and Dr. Cho kind of give us their kind of rounding out final thoughts takeaways for the conversation today for those members of our community who have these dual diagnoses of transverse myelitis or NMO and rheumatologic condition and things to think about things to keep in your arsenal as you you're working with your healthcare team. Questions that to have in mind. And so if I can start with you Dr. Cho any final thoughts or takeaways you have from the conversation today.

Yes I think that Dr. Birnbaum is a good example of why you need good communication between your neurologist and rheumatologist so he can just talk to himself. But for everyone else in the country if you have a rheumatologist for your rheumatologic autoimmune disorder you still need a neurologist if you have neurological symptoms and in particular if you have transverse myelitis and it is not straightforward how those interact. And so you can see even on the same questions. Dr. Birnbaum and I have slightly different perspectives even though we have a lot of overlap just by the nature of our training and the types of patients that we see most often and the types of medicines that we use routinely. So I think it's essential to have concerted care with experts who talk to each other and it is always good to ask those experts about any new symptoms that you have whether it could be any recurrence of your myelitis and then asking the rheumatologist whether the neurologic symptoms could be related to their rheumatologic disease and then again on the on the treatment side ask each physician whether the treatment that you're getting for the one condition may have any impact on the other condition.

Dr Birnbaum your thoughts.

I totally agree I think that communication between neurologists and rheumatologists is absolutely essential. When I think that honestly drives me crazy is if a patient has seen a neurologist a rheumatologist that has a very complicated disease course and a lot of different therapeutic options and she comes to me or even on fall she says Well my doctor says to tell me why I should try treatment A or B or C and that's not fair to you because you know you're already dealing with a complex illness. And then to encumber you to be the primary person who acts as a physician is really not there. So the physician/neurologist conversation should happen with other physicians and that you should be involved but you shouldn't be a sounding board. And in the place of
direct contact with neurologists and rheumatologist. So I agree and I've seen just too often patients being put in the way and having to deal with that.

56:58 And I don't think that's fair. The other thing I will say is that I would be very, it's not often but be careful about if you have a diagnosis of an inflammatory neurological disorder when you have a new diagnosis of rheumatological disorder pops up. Be very very careful because a lot of the so-called antibodies these blood markers that are thought to be somewhat specific for rheumatic disorders they can occur in neurological disorders so having an antibody blood marker that could be seen in Lupus or Sjogren's is not sufficient. You need to have the signs and the symptoms. So I would tread very very carefully and really make sure that you have a rheumatologist that you trust if you're presenting with a new diagnosis from that disease make sure that it's an actual disease defined by symptoms and examination findings and not just a blood marker because sometimes the rheumatologic disease diagnosis can be quite questionable. So really have that diagnosis fully and have that discussion fully with your rheumatologist.

58:13 Sam: Thank you. That is an important point. And like you both said and as we know so much in all of our lives, communication is key. And I hear so much from patients a lot of times what they have to be when they have multiple physicians is basically the communication liaison between them. And so it's important to be sensitive to that. I agree with that as well.

58:40 So to finish off our podcast today I want to thank you both Dr. Birnbaum and Dr. Cho for your time and your expertise sharing that with the community today. Thank you to everybody who sent in questions and is listening out there and all the members of the community who participate in this. We appreciate your time as well. Be looking forward to the next podcast at the beginning of 2018. And until then I hope everybody has a happy holiday season and Happy New Year. And that everybody has a great week end as well. Thank you all very much.