Open Q&A with SRNA James T. Lubin Fellows

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[00:00:00] **Dr. GG deFiebre:** To wrap up, we're gonna host an open Q&A session featuring four of SRNA's James T. Lubin Fellows: Dr. Haiwen Chen, Dr. Cynthia Wang, Dr. Jonathan Galli, and Dr. Sydney Lee. So, thank you so much for joining us. We have many questions for you. So, to start, do you mind just introducing yourself? We can go, I can call out folks and just say where you are now, and then we can get into questions. Dr. Galli.

[00:00:36] **Dr. Jonathan Galli:** Thanks GG. I apologize everybody, I am just kicking the cold, so my voice is shot today. I am Jonathan Galli. I did my fellowship training at the University of Utah where I have stayed on as faculty. And I'm between our university and our Salt Lake VA, where I take care of a myriad of basically patients with any kind of demyelinating disease that include from MS as well as MOG, NMO and everything else under the sun.

[00:01:13] **Dr. GG deFiebre:** Got it. Thank you. And Dr. Chen?

[00:01:16] **Dr. Haiwen Chen:** Hi. I am Haiwen Chen. I did my fellowship at Hopkins, and, like Jonathan, I also stayed on as faculty. So, I'm a pediatric neuroimmunologist at Hopkins. I was actually the first one at Hopkins. Now we're up to two. And so, I see patients currently at Hopkins. We're actually starting to expand and work on building a multidisciplinary clinic for neuroimmune patients at Kennedy Krieger as well.

[00:01:40] **Dr. GG deFiebre:** Thanks. And Dr. Lee?

[00:01:43] **Dr. Sydney Lee:** Hi, I am Sydney Lee. So, I'm currently doing my autoimmune neurology fellowship at the University of Utah here in Salt Lake City.

[00:01:52] **Dr. GG deFiebre:** Thank you. And Dr. Wang?

[00:01:54] **Dr. Cynthia Wang:** Hi, I am Cynthia Wang. I'm a pediatric neuroimmunologist. So, I did my fellowship at UT Southwestern. And I've been on faculty in Dallas since 2018. Yeah. Thanks for the invitation to join you.

[00:02:11] **Dr. GG deFiebre:** So, to start, for those who were diagnosed a long time ago do they need to know if their TM diagnosis, they're given a TM diagnosis at first, was actually something like ADEM or MOG or NMO Dr. Galli, do you want to start?

[00:02:26] **Dr. Jonathan Galli:** Yeah, that's a great question. So, I run into this not infrequently where I'll have patients who come to me with a diagnosis of transverse myelitis with, I would say partial evaluation, or it was just like they hung that up as the diagnosis. I think it's always really important to make sure that if that's your initial diagnosis, to make sure that you're ruling out other things.

[00:03:02] My biggest rule of thumb, and the biggest thing I talk to my patients about is this could be idiopathic transverse myelitis. But we sure do want to rule out anything else. And really the big important feature of doing so is making sure that you're not missing something that potentially down the road could relapse.

[00:03:22] And so if the biggest thing I'll talk to patients about, and questions I've had through the years, is if I've been given the just run-of-the-mill TM diagnosis, should I seek a second opinion or see somebody else? I think the biggest thing is to make sure that you're not missing something else that potentially could rear his head in the future.

[00:03:46] **Dr. GG deFiebre:** Got it. Thank you. And then related to that Dr. Chen, someone said, I haven't had a relapse so far since my initial diagnosis. How do I know whether I'm in the clear or should I still stay alert for a potential relapse?

[00:04:00] **Dr. Haiwen Chen:** Yeah, those are really hard questions to answer. So, I will piggyback off of what Jonathan said that ten, maybe 15 years ago, a lot of things were labeled transverse myelitis. And when we look back now, we've gotten much more specific testing. So, I think it's always worthwhile to reevaluate and if possible, have a more specific diagnosis that could give more ideas about the risk of relapse.

[00:04:28] So in a study of over a thousand cases at our myelopathy center, a couple years ago, we looked at myelopathy that presented for evaluation of all ages including kids and adults. And we found that actually two thirds of them were inflammatory, about one third were actually non-inflammatory. And then within that inflammatory diagnosis we've gotten much better assays.

[00:04:51] Like it's hard to diagnose MOG after the fact oftentimes. But for at least things like NMOSD, for MS, for things like potentially other more rare neuroimmune diseases if we can come to a better, more specific diagnosis, we can better advise as to the risk of relapse and in different sort of cases that advice is gonna be a little different. So, I think what Jonathan is saying, if we can get to a more specific diagnosis and understand what the underlying cause is, we can advise much more appropriately.

[00:05:27] **Dr. GG deFiebre:** And then Dr. Wang, are there any tips from the clinician perspective for how someone might deal with the kind of uncertainty around prognosis and treatment? Someone gets diagnosed with one of these things and we don't obviously have a crystal ball to see what will happen in the future. But anything you've found in your practice with patients?

[00:05:47] **Dr. Cynthia Wang:** Yeah, that's a great question. I think a lot of times, again, arriving at the correct, most specific diagnosis will give you a sense like, is this, for instance MOGAD, maybe 50/50% chance of relapse?

[00:06:02] Is it idiopathic TM where maybe the risk is much, much lower? And so, I think like the other Fellows have said, that prior Fellows have said it's very important to get to that diagnosis. And then if it is your neuromyelitis optica, then hopefully you're on a medication.

[00:06:23] The question is that an efficacious medicine and how is monitoring being done? Is it always going to be a clinically significant attack where you would know based on how your body feels versus do you need periodic testing? Most of the time we don't, unlike conditions like multiple sclerosis, usually there are not silent lesions.

[00:06:45] Those are the questions that would be pertinent if you have a specific diagnosis. Then if you, I guess more like just practically speaking, maybe I'm speaking mostly for MOGAD patients where it is that 50/50. So, like you're not in the camp where you know you're on treatment and hopefully it's efficacious and you're not in the camp where it's like AFM or idiopathic TM where it should be quite low, but it could happen this year.

[00:07:14] So what do we do? Sometimes I'll just give families like a steroid dose pack or something when they travel. If they happen to be away in Europe or Asia or somewhere, they can before they even arrive to medical care, if they have been well educated on what relapse might look like, they can start that. So that's the most I can give for the ones where it's like really 50/50, I don't know. And I think that can cause a lot more anxiety than maybe some of the other categories.

[00:07:46] **Dr. GG deFiebre:** What do we know about the exact cause or trigger of attacks and how to prevent them from happening other than maybe just with medications?

[00:07:57] **Dr. Sydney Lee:** Yeah, thank you. That's a really good question. There can be a variety of reasons why relapses happen. Sometimes we don't know, so they can come on out of the blue for no rhyme or reason. And so sometimes there's really nothing to prevent that from happening, aside from everything that we do in terms of our treatments and our monitoring.

[00:08:24] In some cases, infection can be a trigger. Often that can be a trigger for the initial attack. And I think it can also be a trigger for having a relapse. But it's usually more that kind of initial presentation. So, I think just doing your best to stay healthy in all aspects. Getting your annual flu vaccine, that's a good idea.

[00:08:50] Taking care of yourself, avoiding stress. I think all of these things, it's not clear if that really causes a relapse. Certainly, it could result in a pseudo relapse. So oftentimes it's one of those things that we don't know why it happened. But yeah, I think taking care of your general health and then if a relapse were to happen, then you're in a better spot to actually manage that and recover from that.

[00:09:26] **Dr. GG deFiebre:** Thank you. We did get a question too about, besides general things like a healthy lifestyle and diet, are there any specific supplements that can potentially help for autoimmune diseases? This person in particular was diagnosed with MOGAD and healing from attacks. They mentioned things like alpha lipoic acid, lion's mane extract, et cetera. I know we often get questions about things like supplements. Dr. Galli?

[00:09:51] **Dr. Jonathan Galli:** Yeah, this is always a very popular question. So, the kind of long and short of it with a lot of the supplements is the clinical trials that we will do with many of our medications are much more robust than what happens with the supplements.

[00:10:17] And so usually even if something's going to demonstrate a benefit, it's been based on a much smaller study. And so that's, I always tell my patients that take that all with a grain of salt in the sense that if I had a supplement that I could give my patients, it was this miracle thing, I'd be doing it.

[00:10:41] I can just, I can tell everybody on here right now. Unfortunately, there's not that. Now there are certain supplements, alpha lipoic acid probably has the most data. There's a little bit of MS study; there's a little bit of neuropathy studies that show some benefit.

[00:11:02] And so where I usually go with this is it's again, everything we do is risk versus benefit, cost versus benefit. So, I have some patients that will take alpha lipoic acid, and it will help, usually it's more of a neuropathic pain type thing that we're treating with it. And they will tell me, “You know what, I feel better.”

[00:11:23] In that case if I feel like the supplement is safe, if cost-wise it's not too much out of pocket for you every month, I am always fine with you taking it. Now that being said, again, none of these on their own are probably enough to manage your condition. I don't think about it from the sense that you're, gonna prevent relapse with alpha lipoic acid. That I don't expect.

[00:11:53] And my caveat with patients is I'm cool with whatever supplements you want to take. We'll bring them up at your appointments mostly from just making sure they get along with all the other medications you're on. But never substitute your immune therapy with a supplement because there really is no benefit data to suggest that it's going to be more effective than the medication that your doctor's prescribing.

[00:12:22] **Dr. GG deFiebre:** Got it. And yeah, we have some resources on supplements and alternative therapies in a resource library, but it is a bit of a challenging topic without all of the data to support it. The next question is, can be, I know, controversial. We're talking about vaccines. But are there any sort of particular recommendations for vaccinations for those with rare neuroimmune disorders? Dr. Chen?

[00:12:46] **Dr. Haiwen Chen:** So, I generally recommend all of your scheduled routine vaccines. Oftentimes immediately after attack, we may recommend like your annual flu shot or COVID boosters. Let's maybe wait a couple of months before doing that just to let things calm down. And more so than anything else I think, we always have this fear that if people have a relapse and they were going to relapse anyway and the timing of the vaccine didn't work out right, that may actually end up being a contraindication that's listed, or they may take it as a contraindication, or their PCP may take it as an a contraindication forever there forward.

[00:13:26] So I think just to make things a little cleaner and easier for everyone's like future vaccination causes we often will say, let's just wait a few months before the next set. But I certainly recommend, especially for my pediatric patients, that they get all of their regularly scheduled vaccines.

[00:13:48] The risk of some of the infections that the vaccines prevent from are often very severe. And in this case, in these cases now we have measles outbreaks, polio outbreaks all of those things have really dire consequences as well. So that's why we have those vaccines and why they're important.

[00:14:06] **Dr. GG deFiebre:** Thank you. And then someone mentioned that they were diagnosed with TM and NMOSD in 2022 and have been on azathioprine since then but are so far relapse free. But they were also already on IVIG since 2016 due to a preexisting primary immune deficiency.

[00:14:26] And so they have a suspicion that this may be giving them additional protection against relapse and many members of our community are on IVIG or subcutaneous IG in addition to preventative treatments. Dr. Lee, just wondering if there's any sort of research on or information on whether IVIG or subcutaneous IG provides any additional sort of protection against relapse?

[00:14:51] **Dr. Sydney Lee:** Yeah, we do have some patients who are on a more standard immunotherapy and then they may have the addition of maintenance IVIG. And we do have some people who tell us that they feel better when they're on IVIG. I would say right now there's varying evidence and it depends on what the underlying diagnosis is. So, for instance, for something like NMOSD, we wouldn't routinely add on IVIG. We know that kind of the other immunotherapies are the recommended standard of care.

[00:15:32] Whereas something like MOGAD, if there is an indication to start preventive immunotherapy, then we might consider something like maintenance IVIG. Where we have seen a benefit for IVIG is in patients who have a rare neuroimmune disorder plus an underlying immune deficiency. So, for example, something like common variable immune deficiency or CVID.

[00:16:00] So that is generally where people run into recurrent infections. We see that their immunoglobulin levels are trending low over time. So that's a case where if we're suspicious for something like CVID, then the addition of IVIG actually makes a lot of sense. And in those cases, people do tend to feel a lot better.

[00:16:23] They stop having recurrent infections. So that's a more clear indication. But I think it's always an ongoing discussion with your physician to see if something like that is right for you. Because IVIG does carry some risks, so it's always weighing that risk-benefit and seeing if that is something that is really helping to go forward.

[00:16:50] **Dr. GG deFiebre:** And then Dr. Wang, so this person was originally diagnosed with. transverse myelitis, but, and Devic's Disease or Devic's Disease NMO. But then were tested for MOGAD and are positive for MOGAD. So, their diagnosis has changed. But they said that their symptoms actually seem to be closer to NMOSD though. So, what did they do from here to move forward with their illness? Does the diagnosis matter as much as the symptoms or what's the overlap there as well?

[00:17:21] **Dr. Cynthia Wang:** Yeah, I'll speak to how I would approach that. I think where that test, where the assay, was sent is important and then the titer is important. So, if it's a very clear cut, high aquaporin-4 NMO IgG, that would be, I don't know, I think that trumps the MOG. Unless the MOG, and some people can have multiple antibodies, but MOG is one that tends to have I think less specificity or it's more likely to be like false positives.

[00:17:54] And I should say the assay can be reported on certain levels. Under one to a hundred for the labs I think we usually use in the United States is considered a low titer MOG. So, if it's a low titer MOG and it's a clear-cut aquaporin-4 NMO, IgG very high, then the NMO or aquaporin-4 is, I would consider the primary disorder.

[00:18:23] Are there some cases where it has features of both and they overlap a lot clinically and we don't know. Thankfully there are some medicines that are being studied or used in both conditions, like satralizumab, for instance, or we tend to use B-cell suppression therapies for both and it's probably more effective in neuromyelitis optica.

[00:18:46] But that could be something your physician discusses with you. How do we try to even if there is a bit of ambiguity, what is the most effective drug for you? And yeah, you can as long as it's affected, you're not having clinical relapses, you're not having any radiological activity, I think just that treatment seems to be working. So, it may matter a little bit less what we call it. But I, think again, if you got that Devic's Disease, aquaporin-4 antibodies, I would very much say 99% go with that diagnosis.

[00:19:26] **Dr. GG deFiebre:** And then is there any impact of GLP-1 medications like Ozempic on something like NMO or any of the rare neuroimmune disorders? Dr. Galli?

[00:19:37] **Dr. Jonathan Galli:** It's a good question. I, to be honest, I'm not sure if there's any very recent trials that have looked at specific use. As far as benefit, I know there's been some suggestion, more in the MS literature, as far as there may be some benefit. Now, again, getting back to what does benefit entail?

[00:20:01] So the way I think about it is, is the GLP-1 going to prevent a relapse or have a disease modifying outcome? Probably not, right? Because it's not an anti-inflammatory. But where I find it useful is I have had and I actually encourage my patients who are trying to lose weight, especially if they're trying to be more active.

[00:20:28] And where I run into these medications being very helpful is I'm sure many of you with transverse myelitis, NMO, MOG, what have you, where you have some physical limitation. If you are, I use this guy as an example, but I had a patient who's about 20 pounds overweight and he could not walk more than a mile.

[00:20:53] And it was not without him trying, he literally just couldn't do it from a cord lesion plus extra weight. And so, he used a GLP-1, and I forget which one, but he used that for three to six months, lost the weight that allowed him to start walking more. That allowed him to lose more weight.

[00:21:18] So he was then able to walk two, three more miles per day. And really from that standpoint he's so much healthier and now he's more ambulatory because he's not, he’s lost the weight. So, in those cases they can be very helpful. So, I think the big important thing to take home there can be benefit. Especially if you're trying from a weight loss standpoint, blood sugar management standpoint, they can be very helpful.

[00:21:49] And I always tell my patients, I have no contraindication or no reason you can't use them. So, I always encourage my patients if there's a reasonable cause for the medication, absolutely go forward with it.

[00:22:05] **Dr. GG deFiebre:** Got it. Thanks. And then if someone experiences variability of pain or other symptoms throughout the day, what can they do? Is there a way to stabilize symptoms or is there a reason this might be happening? Dr. Chen?

[00:22:18] **Dr. Haiwen Chen:** Yeah, pain is a really difficult symptom to treat. Oftentimes it's multifaceted and oftentimes the approach that we have to take to it has to be very multidisciplinary or multidimensional. Certainly, if there's pain related to like spasticity or prior injury, things like baclofen or things that kind of help decrease the spasticity may help with the pain. If there are nerve pain associated, then we may use medications that target more nerve pain related symptoms, things like gabapentin or Lyrica.

[00:22:55] And then what I've also found is that besides just the physical experience of pain, it can be also become over time a cognitive and psychological experience wrapped in with that physical experience. So, in addition to medications I also like to have, take a more broader approach, have them see potentially like a psychologist to help them work through how they live and deal with that pain.

[00:23:26] And then the last part is going back to the physical activities, the exercise and therapies, physical therapists, occupational therapists, and all of those activity and exercise and therapies also usually help, especially when the pain is potentially related to things, again, like the spasticity or, neuropathic pain. So ideally you target it from a lot of different approaches because it tends to work better when you try a lot of different means.

[00:24:00] **Dr. GG deFiebre:** Thank you. And then Dr. Lee, what does someone need to know about autoimmune or immunity dysfunction? Do any of the treatments cause immune deficiency?

[00:24:11] **Dr. Sydney Lee:** Yeah, it's often a balance. We can think of autoimmune diseases as involving an overactive immune system, and then you could think of like an immune deficiency on the other end of the spectrum. However, we tend to feel like it's actually a little bit more of a complicated picture.

[00:24:35] So rather than having either an overactive immune system or an underactive immune system, often people with autoimmune diseases, we say there's like a dysregulation of the immune system. So, it can be reacting abnormally in some ways and then not in other ways. And that can obviously present in different ways.

[00:25:01] So when we have somebody with a rare neuroimmune disease and we start them on immunotherapy, that immunotherapy is really to try to target that part of the immune system that is acting abnormally. So, we're really trying to target that underlying disease process at hand if we can, if we have more targeted therapies.

[00:25:24] And then certainly a lot of our medications that we use for that do cause immunosuppression. I would say that's a really common side effect that we have to be careful of. But it's important. Each medication is different. It's going to have a different mechanism of action. So, you know, one might make you more susceptible to all infection, and you might have to take some precautions versus some of our therapies are much more targeted and you might be at risk for very specific infections.

[00:25:58] So I think it's important to really talk with your care team and who's prescribing the medication and get to understand what those side effects might be. So certainly, we dampen part of the immune system and then there still may be this underlying immune dysregulation going on. So, it's trying to like, bring everything back into balance. But I think we feel like it's a pretty, it can be a pretty complicated picture sometimes.

[00:26:34] **Dr. GG deFiebre:** And then on the topic of treatments Dr. Wang, someone said their rituximab treatment was stopped because of suspected GI inflammation caused by the drug. Is this something that you've heard about before? Or if this inflammation is a chronic symptom despite being taken off of the drug?

[00:26:54] **Dr. Cynthia Wang:** I don't think I've come across that complaint specifically. I guess it really depends on if they have a more specific diagnosis for what type of GI inflammation. It's hard for me to say if it is rituximab being used for NMOSD, then certainly they have higher chance of having other autoimmune disorders. So, I don't know if it could be like celiac or inflammatory bowel disorders. So yeah, I think that becomes a very nuanced question, but personally I haven't had any complaints about necessarily GI side effects from the CD20 drugs like rituximab.

[00:27:36] **Dr. GG deFiebre:** Then I just have one more question for each of you. Dr. Galli, how do MOGAD patients who live by themselves prepare for the unexpected, like relapse or seizure? If there's no one nearby, especially if they're not able to call emergency services. What would you usually recommend to patients if that is a potential issue?

[00:27:56] **Dr. Jonathan Galli:** Oh, my goodness, that's a loaded question. I would say I would, try to, before things got, hopefully you're on treatment and, preventing those things from happening. So that's the first thing is I think first and foremost is making sure you're in with a good neurologist who's got all that stuff covered.

[00:28:23] But I think I have the same mentality when I'm in the hospital caring for patients is I like a good contingency plan before everything hits the shingles. And so, I would say and this is easier said than done, if you live very rural but have a contingency plan, have an emergency contact, where if something goes wrong, you can reach out to them.

[00:28:53] They at least somewhat know your condition at least to some extent and can explain it to basically EMS. Because if you get yourself into a situation where there's something emergent where you have a bad fall, you have a seizure, seizure gets a little dicey.

[00:29:10] Obviously if you're having a seizure, you're not necessarily going to be aware. But I think having a close somebody who can help be your basically emergency contact. And if you're in a situation where, if you were to have a fall or a seizure, something along those lines where let's say you're unconscious, I do think the no brand, this is not brand specific, just the commercial always makes me give the name, but the a Life Alert type system I think can be very helpful.

[00:29:44] Where if you do have a fall, it alerts EMS right away. So that way I think it gives and a lot, I have patients that try to find it, but it really gives I think, a lot of peace of mind where if something were to happen, you at least have some way to alert EMS and who can help you out.

[00:30:05] **Dr. GG deFiebre:** Got it. Thank you. And then, Dr. Chen, has there been any research on relieving pain due to myelin sheath and nerve breakdown? And are there any new treatments for neuropathic pain in the works?

[00:30:19] **Dr. Haiwen Chen:** Ok. So, I would say that there's certainly a myriad of different pharmacologic tools that we have to try. And unfortunately, it's a little bit of trial and error because what one works for one person may not work for another. I'm not aware of any new or clearly efficacious treatments to assist in the remyelination process. I know that people are working on that and there have been some things in the past that maybe looked promising but have not necessarily borne out to be clearly effective.

[00:31:04] So it is still a bit of a work in progress. But yeah, there's not like a one-size-fits-all kind of approach to it. So unfortunately, it is, you do have to try a few things, and like I said a more multidimensional approach often works well together where you try different approaches at the same time to try to help each other out or complement each other.

[00:31:30] **Dr. GG deFiebre:** And then Dr. Lee, someone's neurologist said that with a lesion from idiopathic TM, there's the possibility of progression to MS. So recommends continued monitoring with MRIs for additional lesions. Have you seen this progression in your experience?

[00:31:47] **Dr. Sydney Lee:** Yeah, that's a really good question. I can't say in my experience so far, I've run into that. But I think it goes back to what Dr. Galli was saying at the very beginning with one of our questions. How it's always important to reconsider and revisit the diagnosis. So, if somebody's given an initial diagnosis of TM you always want to be thinking about what that could evolve into or whether or not that was truly like a single initial attack.

[00:32:21] So certainly we know that some instances of multiple sclerosis do start with a first episode of TM and that will have certain features, right? It's going to be more likely a short segment lesion. You might have other clues in terms of lesions on the MRI brain. You might have a lumbar puncture showing oligoclonal bands.

[00:32:46] So you know, there may be some features with that initial attack that could help point you in one direction or another. So, I think it really depends on the case. It's very hard to predict whether something can progress or not. But I think it is reasonable to keep revisiting that over time and not a bad idea if that question is still on the table to have some follow-up MRIs just to see if anything is changing.

[00:33:21] **Dr. GG deFiebre:** And then Dr. Wang, will there ever be a way to reverse myelin damage?

[00:33:29] **Dr. Cynthia Wang:** I will say I tuned in before this, and I know Dr. Greenberg talked a little bit about the Q cell study but wasn't able to share efficacy data. So, I'm certainly, I haven't been able to get information from him.

[00:33:43] I wish I did and knew. But I think that's a very promising study. I work mostly with children, so you know, they're not gonna test or do many of those studies yet in children until they've at least done it in adults. So hopefully some of my colleagues may know more about the remyelination drugs, but as far as I know that there's not been any, I think, slam dunk. This is

[00:34:08] how you have to do it. And again, I think we've touched upon a lot of themes and hopefully the rest of the speakers earlier today have discussed. I really do think there's a lot in thinking more about lifestyle. Really drilling down on is your diet as healthy as you can?

[00:34:28] Even before thinking about supplements, like what can you do to improve your diet? What can you do to improve your sleep? Exercise. Stress reduction. I heard about the ACT therapy, and that's like amazing. People are finding out those things. So yeah, I think really exploring those things that we know help for not just these rare neuroimmune conditions, but for so many other parts of the human experience and human disease.

[00:34:54] I think I would really not chase some of these things until like we as the specialists tell you like, yes this is it, this is what you've been waiting for in terms of a silver bullet. But I doubt that it's going to happen anytime soon. I think it is going to be multifactorial. And again, this multidisciplinary approach that we try to take and discuss with our patients and families.

[00:35:22] **Dr. GG deFiebre:** Thank you all so much for answering rapid fire questions of varying topics. Appreciate you all being willing to join us and answer these questions and for everything you do for our patient community. So, thank you so much.