

Community Q&A

You can watch the video of this event at: youtu.be/ZgkQIMctalQ

[00:00:04] **Krissy Dilger:** We're here for an ADEM Together event with Dr. Cindy Wang, who is a former James T. Lubin fellow and a neurologist at the University of Texas Southwestern and Children's, Dallas.

[00:00:23] **Dr. Cindy Wang:** Yes.

[00:00:25] **Krissy Dilger:** Awesome. So, thank you so much, Dr. Wang, for joining us. We're excited to have you here and to hopefully answer a few questions about acute disseminated encephalomyelitis. I guess we can just get started, and if people join as we go along, that's totally fine. But I guess if we could just start the session with a brief overview of what constitutes acute disseminated encephalomyelitis?

[00:00:58] **Dr. Cindy Wang:** Thanks Krissy, and thanks to SRNA for inviting me. It's always such a joy just to be able to communicate and interact with members of the community. So, yeah, acute disseminated encephalitis is a condition where it can really affect many different age groups, many ethnicities, races. And I think the unifying features are, it is a condition that comes on quite abruptly, can lead to many neurological symptoms depending on where we see an abnormal immune response.

[00:01:33] There is often a history of an infection either in the days to weeks prior to the onset of neurological symptoms. And it is mostly a diagnosis of both the kind of the history of the presentation as well as some imaging MRI features that would be consistent with the diagnosis of ADEM. Yeah, I've certainly seen it in multiple types of presentations, and I'm even surprised now, sometimes I see a different part of the brain being involved, and I have to think, like, "Is this ADEM or is this something else?" But always looking at sort of where the inflammation happens seems to help us with figuring that part out.

[00:02:18] **Krissy Dilger:** Great. Well, that's a great introduction to the topic. So, thank you for that overview. And I'd like to just jump into questions. So, if any participants want to either join and give your question live or put it in the chat, that's also an option throughout the session, please feel free. We welcome any questions, but we can get started with a community members-submitted question who asks, "What are the long-term effects of ADEM?"

[00:03:03] **Dr. Cindy Wang:** Yeah, that's a really great question. And I think there is kind of an overall statement we can make that a lot of people who have these very devastating and abrupt and distressing neurological symptoms do end up a lot better. That recovery usually takes, you know, the time scale of a few weeks to months. I think one thing that is more notable to me is that time period in the hospital and what potential treatment decisions or complications can occur.

[00:03:40] Do you have a way of influencing the prognosis? So, things that tend to be associated with worse prognosis, if a person has a very significant decrease in what we call mental status, if they're very sleepy,

lethargic, they might have other potential medical complications, such as having a need for ventilation, mechanical ventilation, being in the intensive care unit can lead to a host of other potential hospital-related consequences if they're immobile for a long time for instance.

[00:04:22] So, yeah, I think in terms of treating the underlying cause, we usually start one or several immunotherapies that help stop the inflammation, and that is often enough to reverse a lot of the damage that this disease causes. But it might be more related to the potential hospital-related complications that happen how somebody does.

[00:04:49] And then another thing I'm acutely aware of is that there are some physiologic elements to ADEM where if you have two great of brain inflammation that outpaces our ability to tackle that with our immunotherapies, then that can lead to other secondary complications, such as cerebral edema or brain swelling that becomes hard to manage.

[00:05:13] So, yeah, it's a very important question, but I would say the first thing to look at is how is the short-term response to treatment, how do we look, like, a few weeks after onset of symptoms, a few months. Then when things have stabilized, usually after three months or so, how can we appraise the current situation and plan a strategy to return to school, to work and also be mindful of the resources that's going to help that person to be positioned for success.

[00:05:52] **Krissy Dilger:** Great. Thank you. And so, you mentioned return to school and work, I guess what are the specific factors that children diagnosed with ADEM have to deal with or should be cognizant of versus adults?

[00:06:12] **Dr. Cindy Wang:** So, ADEM describes primarily brain inflammation, that's like the requisite feature of it, but it can sometimes be accompanied by optic neuritis, which could lead to visual impairment. Sometimes it's associated with myelitis or spinal cord inflammation, which mobility issues could be part of it. So, I think being mindful of those are part of the ADEM that can help with devising, do we need any visual aids? Do we need help with mobility?

[00:06:45] So, those are not limitations to the person returning to school. And then it does really just depend where in the brain and to what extent the brain is involved, because a lot of ADEM involves swelling in the white matter, which are the cables and the connections of the brain, we often see some decrease in processing speed. It can also decrease the way different parts of the brain are connected together.

[00:07:09] So, how do we integrate our motor skills with our vision and our sensations with our decision-making? So, a lot of those things may not quite be back to normal. Again, leading to potentially increased processing time or potentially difficulty in paying attention, making memories or retrieving those memories. So, that's a really great question, because I think sometimes, we can only kind of guess what that might be.

[00:07:38] But the real, I think, help is to get a formal neuropsychological evaluation where standardized tools can help appraise those areas of cognition and mood. And then with the experience of a neuropsychologist, come up with a plan for that person's educational level or vocational level.

[00:08:03] **Krissy Dilger:** And we had another question about treating pain. How would someone go about having a conversation with their physician about treatment of pain?

[00:08:19] **Dr. Cindy Wang:** Hopefully the physician is open-minded and asking a lot of questions. I think sometimes we face the issue if you go to someone who's really not familiar with these conditions, they just

feel overwhelmed and that they're not able to help you. But I think you can start by giving them some features of how the—and this might require some introspection and some journaling just to know, like, what is the pattern of the pain? Is it a certain time of day?

[00:08:48] What areas of the body is it? What kind of features can describe the pain? I know pain is like the hardest thing, especially trying to get a child to describe it is very tough. But anything that you can help, at least the doctor in figuring out could this be pain, because we're fatigued, and we need better sleep, and we need better nutrition to just generally improve fatigue or diffuse tiredness that might be leading to pain.

[00:09:19] Is this related to say, like, mobility, or if one leg is working harder than the other one, is there some compensation that we need to treat more of arthritis or joint pain? Is it what we call neuropathic pain? Is it kind of sharp, burning, tingling where the nerves are getting mixed signals from the body and the brain can't integrate that? And then some medications that calm down those faulty signals can be helpful.

[00:09:52] Is it muscle spasms in which some anti spasm medications can help with loosening those muscles? So, yeah, that's why it really isn't like one size fits all. And I think if a doctor really doesn't ask you those questions and stops at like, "I'm going to give you a prescription for an opioid medication, or this helps pain in general," then I would be suspicious of that and that, that might not be the tailored and personalized approach that you would need.

[00:10:24] **Krissy Dilger:** Great point. I agree completely. So, someone asks, "Is there a way to manage symptoms or effects of ADEM without medication?" Any [crosstalk] natural.

[00:10:47] **Dr. Cindy Wang:** In terms of thinking about medications—and I think medications may be like pills, but they could also be like interventions like therapies. They can be like those school or workplace accommodations. So, it really depends on the type of symptom. When we think about treatment, I think there's maybe like two classes of treatment that—well, there's multiple ways.

[00:11:12] But let's think maybe first by timing, if you're presenting with the illness then we try to decrease the inflammation as soon as possible. So, that would be things that somebody receives in the hospital such as intravenous hydrosteroids, plasmapheresis, IVIG that kind of decreases the inflammation. So, we hopefully don't get any secondary damage by injury to the brain and the wires to the optic nerves in the spinal cord.

[00:11:38] And then there's the question is ADEM, in which we think that this is a one-time hit and never going to come back, or do we think it's part of a condition where we can find blood work or spinal fluid testing—an antibody that tells us this may be an actor that comes back in the future. Sometimes we can't resolve that question at the very beginning, especially in cases of ADEM, in which we find these antibodies to something called MOG or myelin oligodendrocyte glycoprotein.

[00:12:10] In those cases, most literature suggests that there's a 50/50 chance or so of it returning in a different form or same form in the future. So, I guess those are sort of, in terms of immune treatments, the short term and the long-term treatments. And the long-term treatments really are a discussion with somebody who has experience in this field and also can appraise your specific preferences, your kind of aversion or openness to risk or things like that and how you recovered from that first attack. Those are some considerations.

[00:12:47] I think a lot of other questions may be aimed at what is the supportive care or what are the medicines that improve symptoms or improve quality of life? So, going back to the person who asked about pain—that can certainly be a really powerful and all-encompassing thing that can impact quality of life. And again, that could be a combination of medications, therapy.

[00:13:16] Sometimes people have found biofeedback or retraining, kind of how your brain appraises pain through the assistance of pain management providers, can be helpful. And then, yeah, it really just depends. Some people will have seizures during their ADEM. And although a lot of that inflammation improves and seizures come under better control, somebody might be left with some long-term injury to the brain or scarring. In which case, seizures are more likely to occur.

[00:00:58] And that might be a conversation with a neurologist, like, "What's the likelihood of seizures? And does it make sense to be on a daily medicine to prevent seizures or just managing seizures if they do happen?" Yeah, I think there is such a need for multidisciplinary care. So, I think getting perspectives of not just a neurologist who can make your initial diagnosis, but also the people that help with people recover after any sort of brain injury, such as traumatic brain injury or stroke.

[00:14:24] And I'm really talking about the wonderful people in rehabilitation medicine. They will really just appraise what symptoms you're having. And then there are evidence-based approaches that we don't need to just draw from the ADEM literature or the demyelinating disease literature. We can draw from other fields where we get left with similar results where our central nervous system is injured.

[00:14:57] **Krissy Dilger:** We also received a question: "What's on the horizon for research in ADEM? And when we think about a quote-unquote 'cure,' what would that look like for ADEM?"

[00:15:21] **Dr. Cindy Wang:** Yeah, and again, I think in the forms of relapsing ADEM that we mostly draw our understanding from individuals who test positive for MOG antibodies. There is some suggestion if a person continues to make these antibodies at high levels that that might pretend a higher risk of relapse. Many of the therapies that we use are sort of like temporizing measures, they alter the immune system in a way that we hope will decrease its ability to overreact and engage in that abnormal response again.

[00:15:58] There's none that is like a single dose or several doses of medicine and then you're done. Most of those things are therapies such as intravenous immunoglobulin where you might get infusions of these healthy human antibodies on a monthly basis. There's another medication called Tocilizumab, which works on a chemical called IL-6, which seems to be really important in getting immune cells to mount a response and react.

[00:16:25] And then there are other things that we draw from the literature from neuromyelitis optica where we're suppressing some of the antibody producing cells such as B cells and kind of taking them out of the picture, so they can't coordinate this sophisticated response with T cells and other elements of the immune system. I'm not sure what cure would look like.

[00:16:46] I think there is certainly a lot of interest in how can we retrain the immune system in making it tolerant—kind of forgetting this memory of MOG and that it's a bad actor to the immune system. And I think that's where I think there should be a lot of optimism right now in terms of what technology and what advances might be able to do that help with our human, I guess, limitations and assembling solutions from a lot of complicated data, because I think these conditions are not, you know, there's not a one-to-one genetic risk.

[00:17:27] It is a collection of different life experiences, environmental exposures, things your immune system may have seen when you're quite young that trained it in a certain way. So, I think a lot of people just look to AI to help solve the things. But I think we need human input, you know, what are the problems that are important to solve? And is a cure what's best or is it finding one of these treatments that is not taking a lot of time, does not carry many side effects?

[00:18:02] Is it a model where we can look to things like managing things like high blood pressure or diabetes? Or is it very important to hit the condition from the beginning in which ways they treat maybe cancer to try to induce some remission? Yeah, and I think I'm hopeful, excited, but I don't say that we're quite there in answering these questions quite yet. But the more we engage with the community in forms like this I think the more we can at least try to arrive to answers that would be satisfying to the people most affected by the conditions.

[00:18:39] **Krissy Dilger:** Thank you. This question was submitted by a community member who has a child who had ADEM, and they tested negative for MOG during the initial attack. But this parent is wondering if there should be any tests done post-ADEM after a year, after that initial attack, should their child be retested for MOG? And is it normal for hands to be trembly after a year, but aren't consistently trembly?

[00:19:17] **Dr. Cindy Wang:** Yeah, I'll take, I think there's kind of two pieces of that question. If you're MOG negative at onset, does it make sense? Are we more likely to find, maybe, a false positive or answer? Because that's one thing we found out with some of these tests for MOG, certain labs—there can be low MOG-positive results that are more like red herrings and actually aren't consistent with MOG.

[00:19:45] So, if a person was tested at the onset in the peak of their symptoms and they were MOG negative and this was sent to a lab such as the Mayo clinic or ARUP or a lab that is well versed in testing for MOG then I think it should be a conversation, you know, would this do any good or would this lead to potentially more questions?

[00:20:06] Personally, I haven't really seen a case where somebody was a negative and then became or retested at a level that was a clear MOG positive. So, the more common situation is that they were negative, or it was low in the beginning, and then we retested, and it was either at that low level or even lower. So, probably does not make sense. And then also is the diagnosis ADEM or should other things be considered that might look like ADEM?

[00:20:36] And that can be a wide variety of different things in the pediatric age group. So, yeah, I think reappraising all the information and thinking is this the most likely diagnosis. Things that would not fit with ADEM are symptoms that progressively get worse. So, if the trembling was something that was consistent and worsened continuously over months to years, then that would not be really in my mind fitting with a diagnosis of ADEM.

[00:21:05] This is a one-time inflammation attack. What you're describing—what the questioner was describing about the fluctuating symptoms is really common in ADEM, because like everything we have good days and bad days, we might have poor sleep, or we might have an illness and then those neurons or those axons that are trying their best to compensate and in times may not be able to compensate. And then we kind of have almost like an unmasking or what we call pseudo exacerbation of old symptoms returning in some form due to some sort of bodily stress.

[00:21:44] And our team and nurses are very well attuned to that. And the first thing that may not be exactly what you want to hear is just we need a rest; we need to try to decrease stimulation and see if those symptoms start to resolve this. So, that probably does support this theory that these are just kind of a temporary unmasking of old symptoms rather than new inflammation that we need to work up.

[00:22:10] **Krissy Dilger:** Thank you for that explanation. And then someone just asked, "Who would be the person who treats long term adult ADEM? Would that be a neurologist, a general practitioner? Who can someone go to?"

[00:22:27] **Dr. Cindy Wang:** Yeah, and it might depend on the region and who's most equipped to do that. I think for the forms in which we want to consider relapse as a possibility, a neurologist or neuroimmunologist would be good, because this is a rapidly developing field with new research and treatments. If it's a person who does not have any of the other autoantibodies and they've had a sufficient amount of time where it doesn't look like they have a relapsing disease or a progressive disease that requires somebody to put on their thinking hat and make sure that that's the correct diagnosis.

[00:23:11] Then it may just be shifting to the mindset of like how can I manage my symptoms at this point in my life? And that could be different depending on, is this a child or adult? Is this someone who has a job that they can return to, or is it something that the disabilities related to ADEM would make it very hard? So, and I think that does require sort of a kind of a discussion, not a one size fits all approach.

[00:23:44] **Krissy Dilger:** Makes sense. And then we did get a question about IVIG therapy. So, this person has ADEM with MOG antibodies, and they just want to know what, they asked what the ideal duration for IVIG therapy was. And I guess without more context, I'll just say, what are the decisions that go into deciding how to treat someone with IVIG?

[00:24:16] **Dr. Cindy Wang:** Yeah, I would say most of the time it's initiated after somebody has had at least two attacks. So, I think at the very minimum, you should have two episodes that there is some documentation that the immune system is abnormal, it's activated again, and that might be episodes that are at least three months apart and potentially different symptoms in those episodes.

[00:24:42] And then it becomes a question of, how did we recover? Did we recover quite completely? Is this something where, like, a person had very severe vision loss from that first attack, and we really can't risk another attack taking away further vision from either eye? Or you have one eye that is doing all the work—that kind of thing.

[00:25:09] Again, we borrow so much from other fields, and I think with multiple sclerosis and neuromyelitis optica, we know that those are more chronic and relapsing conditions. So, there's not really a set point to when we stop therapy. But I think with MOG ADEM, we look a little bit more to autoimmune encephalitis literature where it is also sort of an infection trigger event and the relapse risk is often lower than with MOG ADEM, maybe in the 20% range.

[00:25:42] In that field oftentimes, a practitioner will treat someone with maybe a year or two of immune therapy just to make sure that we induce kind of a long standing or at least some remission. And then during that period it may be an ongoing discussion of how we're tolerating these medications. If we're a person in school and we have to do IVIG, but that takes maybe three or four days out of a month where they're missing classes and really valuable things then that may not be the right treatment.

[00:26:17] And either a different treatment that might be less time consuming or have better potential side effect profiles could be considered. So, it just really depends, a lot of the medications are infusions, others are oral treatments. But a lot of times if there is uncertainty, merely kind of monitoring approach can also be the right fit for someone. Most of the time, after you've been through an incident like this, you and your family are very attuned to anything, any new neurological symptoms.

[00:26:53] So, if you're counseled well, that if you do have, say, eye pain or changes in thinking that persists over several days, then we can go back to getting treatment for the acute episode or testing for the acute episode. Because thankfully a lot of times if it's recognized quickly relapses respond really well to steroids and other immune therapies.

[00:27:19] **Krissy Dilger:** Great, thank you. I know we kind of already touched on this, but someone did have a question about recovery. What does that look like? What would you tell someone who's concerned about their future in terms of the prognosis and what that looks like?

[00:27:41] **Dr. Cindy Wang:** Yeah, I think those questions weigh on so many people and I think we often think the physician can give us some more level of certainty and some direction. And I think certainly that's really important, but I think also feeling that you know yourself, you know your body, you can reflect and know what are your priorities is really important.

[00:28:05] I find that a lot of people in talking to other people in the SRNA community, they often can arrive at a solution that a doctor hasn't thought of by finding similarities with your story or your illness and someone else's and not reinventing the wheel, seeing what they've tried and trying to make a plan. I think part of that is also feeling empowered that you have some way of impacting how well you do, because if there is this need for certainty where we can offer certainty as physicians, that often increases mood or anxiety disorders.

[00:28:41] And that certainly can lead to mental health issues related to these conditions. And since they are so sudden and striking and oftentimes somebody previously healthy gets struck with these conditions and gets very acutely sick—that can have a toll, I think, mentally on the person and their family.

[00:29:05] So, I think really connecting through some of the support groups, improving your own knowledge, having a dialogue with your physician and knowing they may not have the answers is sometimes important in kind of thinking about what can you do in this present moment to improve your condition, whether that's through engaging with people or getting social support is really invaluable.

[00:29:32] **Krissy Dilger:** Those are great plans, yeah. Something that comes up a lot in discussions with our community members is the conversation around child versus adult ADEM. And it's, I guess, historically thought that ADEM mostly only occurred in children, but may, but to some of our community members, they may have this event happen in adulthood or just in general, I think, it might occur more often in adulthood than is represented in the literature. Is that true? Can you speak to any of that? The question of, "Is ADEM predominantly found in children?" Is that changing?

[00:30:22] **Dr. Cindy Wang:** I would say most of the literature suggests ADEM in the form of encephalopathy and multifocal brain lesions happens more in childhood. And that may be something about a child's immune development and brain development. We know with the MOG protein that there is differing, I guess, times and levels of expression in different parts of the nervous system.

[00:30:48] So, a child might be more at risk of having an immune response directed toward the brain. But as you get older, maybe in school age or older and in adults, it seems like the MOG that is in optic nerves or more of a target for the immune system. So, I guess, ADEM can be a first presentation, and then sometimes people can have other parts of the nervous system affected later in age.

[00:31:18] And I would say, yeah, optic neuritis and myelitis tend to be more, I think, I guess with a more developmentally sophisticated immune system—seems to go after those areas of the nervous system. And then I think again, trying to understand, like, is this a consequence of the attack that happened when someone is younger and then are kind of fluctuating symptoms are just fluctuating of that underlying condition, versus is this something new, is also important to think about.

[00:00:58] And then, yeah, and if you're an adult it's possible that we didn't have the tools to test you for some of the causes of ADEM. So, testing for MOG even testing or considering some metabolic or genetic

conditions that can mimic ADEM is important. So, I think if you don't feel like you've conclusively answered that question, getting a specialist to weigh in is important.

[00:32:18] **Krissy Dilger:** And we've talked a little bit about how the MOG antibody is now being tested for in people with ADEM, and there is some overlap and people, not always, but in some patients who are diagnosed with ADEM. Is there any thought that maybe there might be another antibody that we haven't figured out yet is associated with ADEM? Is there any thought in the research community right now going towards that?

[00:32:54] **Dr. Cindy Wang:** Yeah, you know MOG came from some multiple sclerosis research, and there were other myelin antigens, something called myelin basic protein and others. And the MOG history was that the assay or the test of MOG was not very good up until maybe a decade ago. So, I think those other things that are expressed in myelin may certainly cause an immune response.

[00:33:21] I think the unique thing about MOG is that it develops a bit later than a lot of the other proteins in immune systems. And it may be that the immune system was never trained on MOG from the beginning. So, this is where I feel like understanding more biology and all of these interesting things that maybe technology can help us figure out is—are there proteins that also sort of evolved later in maturation that could be good ways of like devising new tests to see if a subset of patients have that.

[00:33:56] Because I would say about 50% of patients that I think could certainly have or have features that look like MOG don't have MOG. So, I think, yeah, those are really important things to discuss, because that population for most of what we've known are not relapsing. So, what is it about what their immune system is doing is different is really important to answer.

[00:34:24] **Krissy Dilger:** Sure. So, I think we're out of questions. I know we're a little early for the hour, but that was all the questions that were submitted. But I did want to thank you so much for joining us today and answering all these important questions, and we're always so lucky to have such a knowledgeable person to come in and answer questions for us. Thank you.

[00:34:50] **Dr. Cindy Wang:** Yeah, hopefully at some point I'll have more direct answers and not these vague answers. But I feel like I'm always happy to be at symposiums and other things to learn more from the community and the scientists who are at the cutting edge of these conditions.

[00:35:10] **Krissy Dilger:** Awesome. Well, thank you so much, Dr. Wang, and we'll see you again, I'm sure.

[00:35:14] **Dr. Cindy Wang:** Okay, appreciate it. Bye.