Is it a relapse or recurrence?

Deliberations on acute and long-term treatment guidance

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[00:00:00] **Dr. Spencer Hutto:** I'm Spencer Hutto again. I have the pleasure of running the panel about relapses versus recrudescence and how does that factor into acute treatment deliberations. What do we think about how that adjusts our long-term treatment approach. And so, we have a couple of new faces with us on the panel. And so, begin with Dr. Conor Kelly, if you all don't mind, introduce yourselves as we go down line?

[00:00:27] **Dr. Gabriela Bou:** Hi, my name's Gabriela Bou. I'm also one of the neuroimmunologists at Emory Executive Park.

[00:00:32] **Dr. Varun Kannan:** I'm still Varun; I'm still a pediatric neurologist.

[00:00:36] **Dr. Spencer Hutto:** Alright, so I thought we'd just begin by a couple of questions that I have. And so, we'll begin with some questions that some people in the audience at least are going to be a little bit more familiar with.

[00:00:45] What actually is a relapse? What does recrudescence look like? And then we'll kind of move on to some additional questions, and then we'll make some space at the end for questions from the audience. And so why don't we just begin by examining the concept of a relapse. So, Dr. Kelly, if you don't mind, just review for us what does it mean to actually have a relapse? What's that like?

[00:01:07] **Dr. Conor Kelly:** Yeah, so when I think about a relapse of disease activity, I think about occurrence of new or worsening of prior symptoms caused by the inflammatory disease activity. If it's due to a like a spinal cord relapse, you can have new numbness, tingling, weakness, urinary retention and optic neuritis, decreased vision and all depends on where it's occurring within the nervous system.

[00:01:39] Most oftentimes it's associated with a new lesion, but they can be visible on MRI but not always, not all MRIs are created equal. And then it varies between disease processes.

[00:01:57] **Dr. Spencer Hutto:** And then for Dr. Bou, I just wanted to think a little bit about and sort of along those lines, sometimes symptoms can occur that might be very similar to a relapse, and it really feels exactly the same.

[00:02:09] And sometimes actually it just also looks the same without an actual new inflammatory event taking place. Maybe it's due to like a UTI or some other sort of an electrolyte disturbance or something like that, a so-called recrudescence. Can you kind of walk us through a little bit about what that may mean?

[00:02:25] **Dr. Gabriela Bou:** So, you can have a general recurrence or recrudescence of symptoms that look very similar to a symptom, to symptoms that a person had during a prior attack. And oftentimes they will mimic the exact symptoms or very similar to the exact symptoms that were had during a prior attack. And this can happen many times when the body is in a state of physiologic stress.

[00:02:47] So, for example, when there's an infection, for example, like Dr. Hutto mentioned, a UTI, very often patients can experience the same symptoms in the setting of them having these infectious symptoms as well can happen with other sort of infections as well, like an upper respiratory infection.

[00:03:05] And there are other situations in which the symptoms can come back as well, such as when a patient is overheated transiently just for a short amount of time. You may notice that some symptoms come back for a short period of time. And typically, in that case they may not be as long, they may not last as long as when a relapse occurs.

[00:03:26] Sometimes when an infection happens, the symptoms may be lasting for even more than 24 hours. Sometimes it takes actually having to evaluate and get some studies done to try to figure out which one it is.

[00:03:40] **Dr. Conor Kelly:** Piggybacking off of Dr. Bou, how many people here have been stuck in Atlanta traffic before? Just show of hands. So, as an Atlantan, I am probably more of a traffic expert first and then neurologist second. So, I think it can be helpful to kind of conceptualize this viewing the central nervous system like a roadmap where in the suburbs it's a lot of subdivisions, a lot of back road options, and your brain develops pretty good constant good workarounds.

[00:04:20] But if you think, if you shut down a lane on I-20 at 2:00 AM you're not really going to have many issues. Probably won't notice it, but come rush hour, and you can think about systemic stress, lack of sleep, those symptoms will come back out like in infections.

[00:04:43] **Dr. Varun Kannan:** It's almost like after an initial inflammatory attack, there's always a little bit of scar tissue left over. And most of the time when you're feeling otherwise healthy, even if there's not new disease activity, you might feel some of that, but you're able to compensate for it until something stresses out your system, jams up traffic, like heat, like an infection, or even emotional stress that all of a sudden you feel those old symptoms come back.

[00:05:10] And I think an example that illustrates this is from decades ago before we had MRIs. One of the ways that neurologists would diagnose multiple sclerosis is called a hot bath test. They would measure your vision and your strength when you're at a normal temperature, and they would put you in a hot bath for about 10 minutes, and then they would measure your vision and strength afterwards, and you would see it almost immediately decline, and then you cool down and it pops right back up to baseline.

[00:05:35] So obviously that's very crude and we wouldn't put you through that anymore, but I think it's a good example that kind of illustrates this point, that you can have very real symptoms even though there's not new disease happening. But as the person experiencing that, it's really hard to tell the difference, which is why if you're feeling that, you should call us so we can work you through it.

[00:05:55] **Dr. Spencer Hutto:** I'm trying to think about bathtubs in the neuroimmunology clinic. That would be a first. So that's sort of a good segue, I think, to talking about what do we do when we experience new symptoms of concern? As a neurohospitalist, I try to counsel patients on the possibility that if symptoms re-occur, it could be potentially one or the other.

[00:06:16] And it's not the patient's job to know which one it is when they present at the hospital. It's just their job to kind of get there and give us a chance to work them up further. And so, I think Dr. Kannan would be a perfect person to kind of ask this question too, because he works in the clinic and he also works in the hospital.

[00:06:29] And so what sort of recommendations do you have for patients when they're concerned about the possibility of a relapse? Is it something where they should message you first or call the clinic? Should they go directly to the hospital? What sorts of advice do you give them?

[00:06:45] **Dr. Varun Kannan:** Yeah, ideally after we've established a diagnosis and kind of talked about what your new baseline is, living with this new diagnosis, we also counsel there may be fluctuations triggered by these typical stressors.

[00:06:58] What would that feel like and what would we expect if it was just a, a fluctuation versus new disease activity? So certainly, if you have a new symptom that you never had before, that's not a recurrence, that's something new. And we want you to just come in, either call us or just come straight to the emergency room of wherever hospital that we typically have your care at.

[00:07:18] But if it's an old symptom and you felt like you've had this before then you think about that list of triggers. Like, are you sick? Do you have a fever? Have you been outside in the heat? Do you feel emotionally, physically exhausted for whatever reason? Try to address that thing. If you have a fever, try to cool down, take some Tylenol.

[00:07:38] If you're hot and dehydrated, drink some water, take a rest. And if it's a fluctuating symptom, usually on the order of minutes to hours, it should get better. But a general rule of thumb we have is if it's really sticking around for 24 hours or more, we should probably do another scan and at least examine you.

[00:07:55] And it still might be something like a UTI, and it might need antibiotics for a few days before those symptoms get better. We don't know that without seeing you. So certainly at 24 hours of old symptoms or any new symptoms, let us know.

[00:08:09] **Dr. Spencer Hutto:** And I hadn't thought of this question before, but I feel like sometimes I get this when I'm in the hospital. So, Georgia is a very big state and some of you are probably traveling from all corners of the state or maybe even from outside of the state. And so, when you experience symptoms wherever you are, sometimes that's a challenging situation, I think to know where's the best place to go, what do you do from there?

[00:08:28] And so do you all give advice to people on when there is a decision made about let's go seek additional care, be evaluated in person, what sort of advice do you give someone where maybe they're going to have to make a tough call about exactly where they end up going and seeking care.

[00:08:44] Do you all have advice for patients who, maybe they're not living next door to the Arthur M. Blank, to a hospital or maybe Emory University Hospital, how should they prioritize where they end up going.

[00:08:59] **Dr. Conor Kelly:** I think it depends on the individual and the disease and the severity of symptoms. So, I kind of counsel on an individualized basis. It's a hard question to answer. If it's new, sudden onset, stroke-like symptoms, I wouldn't want someone driving five hours to come to Atlanta. In most instances in adults, I'm all right with local hospitals. But I usually counsel patients to one, be on MyChart so they have access to my notes that they can provide to their providers.

[00:09:51] And I usually try to give some anticipatory guidance in there for what to expect. But it's somewhat of a case-by-case basis.

[00:10:01] **Dr. Gabriela Bou:** I would say that I think of it pretty similarly. I think with some of the more common demyelinating disorders, such as multiple sclerosis, there are many hospitals that have neurology services that are probably well equipped to be able to determine whether there's a relapse or a recurrence of symptoms for other reasons.

[00:10:21] And especially if patients are really, really far away, it may be in
[their] best interest to actually go to one of those local hospitals. If it's a kind of disorder that may be very, very rare, patients may be best served by going to the more academic institution in the state, then in certain scenarios the advice may be to try to make it to that hospital. So, it is a case-by-case basis.

[00:10:48] **Dr. Varun Kannan:** An additional challenge with pediatrics, like I mentioned before, is for young kids we have to sedate for MRIs, and most community hospitals that aren't in the major cities don't have a pediatric anesthesiologist at all. So that's a challenge where if our younger kids were concerned about a relapse, then we're going to have to bring them to our center anyway.

[00:11:08] And then it really depends on the severity. So, if it's something where we feel like it's a true symptom, but it's not particularly severe, we are okay with the parents driving to Atlanta, which may in Georgia may be anywhere from an hour to a four-hour drive and still be within the state.

[00:11:23] But if it's something severe, sudden onset, we really just want you to go to the closest hospital, get stabilized, and then they can transfer you to us if they think that's appropriate and they have access to call us at the major center at all hours of the day. I think the same is true at the adult Emory facility as well.

[00:11:39] There's always an on-call neurology team, and we are available for your local community medical team to access.

[00:11:46] **Dr. Spencer Hutto:** I was just going to add that all hospitals have access to steroids and so at the very least, they can bring you in. They can do some initial round of workup to figure out exactly what's going on and give you steroids kind of in the meantime.

[00:11:58] And if the decision is made that you need to seek a higher level of care or go to a different institution, then transfer is always kind of a possibility. And importantly, in the adult population, the possibility that something else could have occurred at some point maybe that's not your primary disorder becomes increasingly likely.

[00:12:19] You could also have a stroke that may cause weakness on one side of the body, which sometimes inflammation can do as well. And so those are always important things, I think, to kind of keep in mind. Alright. And then I was just curious if somebody could set the expectation for us in terms of, so you come to the hospital, what's that going to look like with concern for relapse? What sort of tests are going to be done? How long might a patient stay? That sort of thing?

[00:12:45] **Dr. Conor Kelly:** Certainly. So, we've kind of touched upon two important things. One would be assessing for other causes of recrudescence which becomes less relevant if there are new symptoms or symptoms that are worse than you've ever had before.

[00:13:06] Repeat imaging, and if the situation's concerning and consistent with new disease activity, usually almost always IV steroids, oftentimes plasma exchange, and in some diseases intravenous immunoglobulins. Sometimes after discussion between the inpatient team and your outpatient provider, the decision might be made to switch your chronic disease modifying therapy while inpatient, but that's a little less common.

[00:13:50] **Dr. Spencer Hutto:** Okay. All right. And then Dr. Bou, I was curious if you could touch on, what are some of the factors that we consider if somebody does come into relapse, they're on some medication beforehand, and it looks like indeed a new inflammatory event has occurred. What are some of the things that you factor in when you think about whether or not the patient's treatment had failed them?

[00:14:12] **Dr. Gabriela Bou:** So, we take many different things into consideration when patients come in and there has been evidence that there are new brain or spinal cord lesions while they're on disease modifying therapy. So, one of the things that we take into consideration are what are the other options for disease modifying therapy and what are the benefits versus risks of each different option.

[00:14:36] And we also take into consideration whether there's been any problem with getting access to maybe the current disease modifying therapy, any delay. Or anything that could have caused it to not be as effective as it may have. In some cases, maybe there was a problem with accessing it and delay, and maybe the disease modifying therapy itself would have been effective.

[00:14:55] And what we actually need to work on is just making sure that there's access at all times. If it's a situation in which the medication has been administered perfectly, and there's been a new relapse despite that, then at that point we really want to consider what are the other options for each given disorder and what are the other treatment options and level of tolerability.

[00:15:20] If there are other options that maybe they work a certain different way and they, they have a side effect profile that is generally tolerable and it'll be a discussion, a shared decision made between us and patients about whether we want to try to see if a different sort of therapy that works a little bit differently may be actually more effective at preventing these relapses.

[00:15:44] **Dr. Varun Kannan:** In those situations where a true new disease relapse occurs, steroids are used again to buy us time to help calm down whatever disease activity has happened and then make a decision together about what the next best step of treatment was.

[00:15:58] If we try option one and you still had a relapse on option one, then we go talk about options 2, 3, 4, and 5. And you always should get to weigh in on what would be the best, looking at the risks and benefits of that. That's an important point too, unfortunately we still see relapses happen when we know a treatment works, but you're not getting the treatment because of an insurance barrier, which doesn't mean the treatment doesn't work, it means our system doesn't work, which is harder for us to address, but we try our best.

[00:16:26] **Dr. Spencer Hutto:** Alright, so I have another question for Dr. Kannan, but after that I thought we would open up the floor to questions. So be thinking about those, and we're going to get to those next. So, Dr. Kannan, I was wondering if you could also weigh in on how do we navigate vaccinations in the setting of treatment. And then just sort of an additional piggyback I think off the prior session - how does diagnosis and treatment affect school and education? If there are some additional things you'd like to add on that point.

[00:16:52] **Dr. Varun Kannan:** Yes, vaccines come up a lot, as you can imagine in my patient population and kind of in three regards. The first is usually, my child got a vaccine a couple of weeks before this attack happened. Did the vaccine cause it? A really hard thing to prove. Kids get a lot of vaccines, especially early on.

[00:17:10] What they get more often than vaccines are viruses. So, it can be really, really hard to tell if a demyelinating event happened because of a vaccine or because of a viral infection. And like I mentioned, sometimes you don't always have a symptom of a viral infection. Our data certainly suggests that viruses are more likely to cause these things to happen than the vaccine itself.

[00:17:32] This came up a lot with COVID and side effects of the COVID vaccine. For example, there's a side effect of certain vaccines called myocarditis or heart inflammation. We actually saw that you're 20 times more likely to get myocarditis from the infection itself than from the vaccine. Similar consideration with the flu vaccine.

[00:17:51] There used to be concerns that the flu vaccine would give you a different disease that's demyelinating called Guillain-Barré Syndrome, where you have demyelination of the nerves that go into your arms and legs. But again, we've looked at the data, and it seems like you're 17 times more likely to get Guillain-Barré Syndrome from the flu than from the flu shot.

[00:18:07] So just looking at a numbers game, it still seems like the safest thing you can do is still protect yourself from viruses that are preventable with vaccines. Another question that comes up is, now that I'm on treatment or my child is on treatment, how do I continue getting vaccines that are recommended?

[00:18:23] It depends on the kind of treatment you're on. Dr. Hutto showed us detailed immune pathways that these medicines work on. Those immune pathways are also how vaccines work. Some of these treatments interfere with effectiveness of vaccines. We can still use vaccines in patients that are getting these treatments.

[00:18:39] We just have to time it perfectly. So, we kind of have to work with you, the family and your primary care doc who's prescribing the vaccines to find the schedule that works to protect the child or the adult. And then regarding school - so again, as a pediatrician, school is kind of our best barometer of how a child is doing in overall health.

[00:19:01] Not only neurologically, but emotionally. So, we really rely on mental health specialists like psychiatrists and neuropsychologists to do formal assessments. But we ask you every visit in the pediatric office, how is school going? How are grades? How are extracurriculars? What are you doing for fun?

[00:19:19] Are you able to enjoy your childhood and do the things you want to do despite having challenges with your disease? We're not in the school system, but we know how to navigate the school system, what supports are available. Most of our clinics have support staff who help kids integrate back into school.

[00:19:37] So at CHOA we have a couple of schoolteachers on staff that help. For example, if you're in the hospital during a relapse, they'll actually work with your school to have you do remote work and catch up and then help transition back into a regular school environment if that's what your plan is.

[00:19:55] **Dr. Spencer Hutto:** With that I'd like to turn it over to the audience, if anybody has any questions.

[00:20:00] **Audience Member**: I know y'all discussed like heat and stressors can affect those occurrences. Does puberty play a role in that? I know my daughter's going to be coming up on that, and I just have concerns

that I won't be able to differentiate between a recurrence and her mood because she did relapse the one time, very angry and very upset, and I don't know if puberty plays a role.

[00:20:23] **Dr. Varun Kannan:** The short answer is yes. Puberty does a lot of things to the body, including the nervous system. Even outside of demyelinating and immune diseases, for example, oftentimes migraines, which are pretty common in adolescents, start around the time of puberty. And sometimes we see that migraine spike happen even before the pubertal body changes happen.

[00:20:42] So the hormone surge is there before you know it. And that certainly plays a role in immune system activity as well. So, does that mean a relapse is going to happen with puberty? No, but it does mean that we're going to be on lookout for any changes, and certainly those same rules apply
[for] any new neurological symptoms that's concerning for a new attack.

[00:21:02] And then if it is a mood swing or heat-related or anything like that, try to address what seems to be triggering it, and if you address it and it's still happening and certainly getting worse, hits that 24-hour threshold, call us.

[00:21:19] **Audience Member**: Can you also speak to the other end in terms of menopause?

[00:21:26] **Dr. Conor Kelly:** I cannot, but they can. That is an area of active and ongoing investigation, which is an odd answer. Certainly, many different things happen in the immune system as we age on both ends. Generally, the immune system calms down a little bit which in some instances can calm down the autoimmune diseases affecting the central nervous system. Not all the time. But there's not a lot of great data on it.

[00:22:16] **Dr. Gabriela Bou:** To add a little bit more to that, and it's not related to specifically research that's happening in that area, but just to kind of speak to some of the symptoms that patients have brought up to me in regard to menopause. Oftentimes I have had patients tell me that they've had fatigue that's worsening, sometimes mood swings.

[00:22:35] And sometimes it can be a little bit difficult to parse out does this have to do with the underlying condition, or does this have to do with menopause? And so oftentimes we'll try to sort those out. We'll often recommend seeing the OB/GYN, also to have discussions and do a workup regarding where someone is in regard to menopause or around perimenopause, which is the time period around menopause.

[00:23:03] And we often do monitor as well with MRIs from the neurology standpoint to look for any signs of new disease activity and to make sure that our disease modifying therapies are working. So, it's not always the easiest thing to know for sure whether one is related, whether it's more menopause or the underlying inflammatory disorder that may be causing these symptoms.

[00:23:31] But oftentimes we do an evaluation to make sure that we are seeing objective stability of the disease by way of not seeing any new lesions, not seeing any new areas of inflammation, and working with OB/GYNs to see whether this in fact could be part of menopause and could be treated with some of the standard treatments for menopause symptoms.

[00:23:54] **Dr. Conor Kelly:** Another thing that we kind of touched on earlier, but I kind of want to expand upon a little bit that becomes especially important as we age is just to remind your other medical providers that just because you have this very rare disease that affects you in a lot of ways, doesn't mean that you don't have other things going on as well.

[00:24:20] So I mostly see multiple sclerosis, which can cause a wide range of symptoms, and patients will come to me reporting a certain symptom that I don't think is related to multiple sclerosis at all but someone else thought was. I've actually seen two patients who went to the ER and were told that they were having MS hug, but they were actually having appendicitis. So just please be strong advocates for yourselves within the medical system.

[00:25:01] **Dr. Spencer Hutto:** So, one of the things that I think is so good about today is hearing what things are important to you all and what areas that are perhaps under researched. So, this is a good collaboration.

[00:25:11] It has me thinking about neurosarcoid because a lot of the patients that I see in their forties and more commonly ladies actually. And so that's sort of something to think about. And there has been research in this, in multiple sclerosis, so obviously a different disorder, the longer people have it, the more likely they are to enter a progressive phase that's less characterized by acute inflammatory attacks.

[00:25:33] And so I'm sure that there have been a lot of investigations actually about how pregnancy effects disease activity, at least in NMO, and I'm sure that now that they are trying to settle those questions. One next question to think about, sort of along that spectrum may be the impact of menopause.

[00:25:49] And so hopefully we'll have more data. Certainly, with some of these disorders we're reaching the point I think where people are getting to that stage of life. And so hopefully we'll have more information soon.

[00:26:01] **Audience Member**: So, addressing the older people again, it seems that immune responses to vaccines have a time limit in some cases. And recrudescence after primary disease or vaccination as age goes on is a not very widely covered topic, is my opinion. My sister-in-law got pertussis at age 50. I'm personally interested in whether or not polio reactivates.

[00:26:51] **Dr. Varun Kannan:** Yeah, I mostly interface with vaccinations in the early parts of life, but certainly there are high risk medical situations whereas an adult you can get revaccinated for certain disorders if you're felt to be high risk. I don't know if these neurological syndromes technically count, but certainly things like heart disease and lung disease do. You could probably argue that secondarily to neurological disease, you may not have perfect lung function, in which case revaccination to protect you later in life would make sense to me. But that's from a kid doctor.

[00:27:23] **Audience Member**: I also have a question about, well, you spoke about it earlier, but about vaccines in particular, because I continue to struggle weighing the risks of taking them or not. And I've always taken vaccines my whole life. And then I got diagnosed. Specifically with the COVID vaccine. I was hesitant to take the follow-up one that you take because I had relapsed shortly after.

[00:27:51] Not saying that it caused that, but my doctor had said, when I had asked, should I take these vaccines every year, she had said, "Well, how did you take it the first time?" And I was like, "It was fine until I relapsed." So same thing with like the flu. Flu vaccines every year, every time I take it, I get the flu. Every time I don't take it; I don't get the flu.

[00:28:11] Again, not saying correlation equals causation, but because of my personal experience, I have this hesitancy despite understanding that vaccines are very important and that the risks of just getting the disease unvaccinated could be very great.

[00:28:29] But because I have this history, I hesitate. And so, I'm kind of seeking maybe more insight on how to judge when it's appropriate to take it because I don't want it to create potential for relapse.

[00:28:42] **Dr. Varun Kannan:** I mean, I think you're kind of thinking along the correct lines already, which is it's okay to be hesitant and it's okay to ask questions. We make recommendations based on population level data. There are exceptions and you are not a population. You're one person and this affects you. So, we give you the data and kind of help you interpret it and make a recommendation. But as an individual you don't have to follow that. That doesn't mean you're not following a recommendation overall.

[00:29:09] We're just saying that we don't know, this is what numbers say, but you're gambling it feels like with your own health. and it's okay to make your own personal informed decision as long as you know the risks and benefits each way, right? Which is, there might be a risk with flu vaccination or COVID vaccination.

[00:29:27] There's definitely a risk with flu infection or COVID infection. There are other ways to protect yourself from these infections and vaccination, which is of course things we learned about in 2020. So, if you're on immune therapy, if you feel that you qualify as immune suppressed, you can take steps to protect yourself from getting sick.

[00:29:45] That don't necessarily have to involve vaccines, but overall, the data still says vaccines help people with or without autoimmune disease. So that is also a non-answer, but I get the sense that you're very well informed on this and making the right decision for yourself.

[00:30:05] **Audience Member**: I definitely have a question about myocarditis and the COVID vaccine, but I'm not going to go with that one. My other question - I have multiple sclerosis and earlier this year I had the flu, which caused a pseudo-exacerbation that my neurologist determined that that's what it was.

[00:30:28] So my question is, how do you know if you have a pseudo-exacerbation? Because it didn't feel any better in the middle of it. And then do you think that pseudo-exacerbations have lasting impact?

[00:30:43] **Dr. Gabriela Bou:** So sometimes in the initial stage, it may not be always possible to tell without actually getting imaging sometimes whether pseudo-exacerbation or pseudo-relapse is that, or if it's an actual new lesion. So, in some cases as you had mentioned, with an infection, you can have some symptoms that are extremely similar and mimic what a relapse would look like. And in some cases, they last more than 24 hours which is typically what we consider our threshold to start being worried about whether some symptoms are potentially due to a new relapse.

[00:31:20] In certain scenarios, if you do notice that you are having symptoms of infection at the same time that you do have new neurologic symptoms, then that would really drive us to try to figure out if there's an infection that's causing it. But sometimes in the hospital we have to do evaluation for everything, and in certain scenarios if the symptoms are disabling and they're lasting a very long time, we may actually have to get some neuroimaging to confirm that there in fact has not been a relapse in the setting of new lesions and that we've basically excluded that and then proven that this has been most likely due to the infection. But sometimes it can be difficult to tell in the beginning. It may require more evaluation.

[00:32:06] **Dr. Varun Kannan:** I certainly think imaging in that situation makes sense. especially with a disease like MS, where if there are new attacks, new lesions, new enhancement, that tells us immediately this is new stuff, we have to treat it with steroids.

[00:32:18] In the absence of that, you asked about can that cause new damage? I don't think that causes new inflammation damage, but a different way to ask that is, you had influenza - could influenza have changed your brain somehow chronically? We don't know. We learned a lot about long COVID in 2020 and since then, but COVID isn't the only virus that has long lasting symptoms that may be neurological or psychiatric in

nature that we don't understand. EBV has certainly been shown to have an association with that too. So, it might be the infection itself rather than the underlying disease process.

[00:32:56] **Audience Member**: Hi, my name is Lakeisha. I am from South Carolina. I live in a very rural area, so we don't have top-notch doctors like you guys have here. My question goes back a little bit but still ties to the last question.

[00:33:11] I went into the hospital thinking, assuming I was having a pseudo-flare, some type of relapse, and I was treated for a mini stroke. How do you suggest I advocate for more testing? Because they did everything for a mini stroke and really nothing for what I assume was a pseudo-flare.

[00:33:38] **Dr. Conor Kelly:** That's difficult because I don't really know what a mini stroke is. That's a term that gets thrown around a lot sometimes in the medical community imprecisely. What they may have meant is a TIA, a transient ischemic attack, where the symptoms usually last less than 24 hours and go away, and there shouldn't usually be a new spot on the MRI.

[00:34:11] And usually in a vascular event, like a stroke, it's a sudden onset of new symptoms, rarely worsening of old symptoms. And the MRI should give you the answer typically, especially if in differentiating between a demyelinating event versus an ischemic event. So, it really all kind of depends on the clinical picture.

[00:34:52] But I would generally recommend imaging, testing for stomach infections, and anything else that could cause recrudescence of prior symptoms. And I'm assuming that this was recurrence of prior symptoms but definitely imaging and then consideration that this may be a new relapse, depending on what all is found during those investigations.

[00:35:25] **Dr. Gabriela Bou:** I think in the scenario in which the imaging doesn't show anything new, so there's no signs of an acute, a new stroke on imaging, and there's no signs of a demyelinating lesion, so basically, the imaging shows nothing new, but you are having some symptoms. I think one of the ways to advocate for yourself would be, in that scenario, to make sure to emphasize to the healthcare providers that are evaluating you about what your history is and ask them to take into consideration that you have this history and

[00:35:56] evaluate for whether these symptoms are new or if they're very, very similar to past attacks that you may have had. And I think that can sort of help some of the physicians, the providers that you're seeing, try to figure out whether this is more of a pseudo-relapse rather than a transient ischemic attack.

[00:36:14] **Dr. Spencer Hutto:** Can I just say, I work primarily as a neurohospitalist. And so just have a little bit of a humble moment, that sometimes you all, almost everybody in this room has an extremely rare disorder, which means that if you are not one of the people seated at the front here or over at that table, they may actually not know everything there is to know about these rare conditions.

[00:36:36] And therefore, some of the providers may be less familiar with the concept of a relapse or a pseudo relapse. And so, they may not be familiar with that. And so even providers are people who need to be educated periodically, and you know the most about your disorder. So, I really second what was said, that it's important to kind of let them know what you have, let them know how it works.

[00:36:56] You know that sometimes you'll have a relapse. Sometimes you may have a pseudo relapse and maybe it's even you who says like, hey, have you checked for UTI, are my electrolytes okay, do I have pneumonia, do I have the flu? Something like that. And so, some education there can sometimes be very

important. And so, we have time for one question, and then I think everybody will be eager to eat. But it's a, it's a lunch and a eat and greet, so you can, you can always find us.

[00:37:19] **Audience Member**: If we notice a pretty significant change in eating habits, should that be a concern? Does that mean anything?

[00:37:29] **Dr. Varun Kannan:** Yes. It also depends on what underlying condition we're dealing with and knowing, was there eating/GI/appetite-related symptoms initially or with previous attacks, or is this something new?

[00:37:44] And like I said, it can be hard to tell. And oftentimes as neurologists we probably undervalue the gut kind of symptoms and GI symptoms. So certainly, if this was something that was active, an active issue early in the disease and diagnosis and it's coming back, we worry about a pseudo relapse or a new relapse.

[00:38:03] But if it's something completely new, then that probably warrants a full medical workup. So, whether you're a kid or an adult living with these diseases, you should have a primary care doctor that's a generalist that can help triage these initially non-neurological seeming issues like feeding issues, urinary issues. And then if they think, hmm, this is having a neurological flare to it, then we can escalate, talk to us and then decide if imaging or other treatment is warranted.

[00:38:32] **Dr. Spencer Hutto:** And so, with that, I'd say thank you to the audience for your attention and to the panel for answering all of these questions.