

Long-Term Neurologic After Effects of Ebola

[Announcer] This program is presented by the Centers for Disease Control and Prevention.

[Sarah Gregory] Hi, this is Sarah Gregory. Today I'm talking with Dr. James Sejvar, a CDC neuroepidemiologist, about a recent article regarding the neurological consequences of Ebola. Welcome, Dr. Sejvar.

[James Sejvar] Thank you. It's great to be here.

[Sarah Gregory] You work at CDC in zoonotic and infectious diseases. You're a neuroepidemiologist. How is that different from any other epi and what's your area of specialty?

[James Sejvar] Well, I'm trained as a neurologist, but then I also have additional training in applied field epidemiology and infectious diseases, which kinda makes me a neuroepidemiologist, if you will. There's certain aspects of neurology that make epidemiologic investigations somewhat more difficult than in other situations. For instance, neurologic illnesses oftentimes have very vague periods of onset or whatnot. So, it makes it difficult to determine a, you know, an onset period for an epidemiologic study. So, there's really a need for people that speak, you know, kinda both languages, if you will—neurology and epidemiology. And so, my main area of focus is neuroinfectious diseases, which is basically the investigation of infectious diseases of the nervous system, such as encephalitis, meningitis, acute flaccid paralysis.

[Sarah Gregory] I know you do a great deal of traveling to far-flung places. What do you do, say, in Kazakhstan or Vietnam?

[James Sejvar] Well, my job, because of my area of expertise, I kind of work throughout CDC. I'm centered in the National Center for Zoonotic and Infectious Diseases, but I also work with the environmental health group, the vaccine group, to provide subject matter expertise to them. My job is kinda two-fold. One aspect is outbreak response and then the other is more evaluation of, you know, long-term, ongoing projects. Now, the outbreak response is a really enjoyable part of my job. You know, it can just be, you know, a call in the middle of the day about an outbreak of an unusual, unexplained neurologic illness, and within 24 hours, I'm on a plane with a number of other experts, going on to try and find out, you know, what the cause of the neurologic outbreak is and how to implement prevention measures and hopefully solve the case, if you will. Now, the other aspect is ongoing projects, and this, within this capacity, I basically try to look at the clinical, epidemiologic, and long-term outcomes of neurologic infectious diseases, such as different forms of encephalitis or meningitis. In this capacity, I do more of training of local collaborators and basically overseeing the projects, if you will. So, I kind of have a split, split job here at CDC.

[Sarah Gregory] While you, you're not an author on this study, you have obviously expertise in this field. So this study is about the long-term neurologic sequelae of the Ebola virus. Let's start off by you explaining what "sequelae" means.

[James Sejvar] Well, sequelae is basically the aftereffects of an acute illness, if you will. After somebody, you know, survives and gets through an acute illness, sometimes they can be left with remaining signs and symptoms that can persist long after the acute illness. For instance, somebody may develop encephalitis and they'll survive and recover from that episode of

encephalitis, but they'll be left with memory difficulties or persistent weakness in their limbs that can last for months or even years. And so, that's what we mean by a sequelae.

[Sarah Gregory] When did doctors first suspect that Ebola might have these long-term neurological consequences?

[James Sejvar] Well, doctors have kind of long suspected that there might be long-term neurologic aftereffects from Ebola, but in previous Ebola outbreaks, the outbreaks had been relatively small and, unfortunately, have been very few people that have survived past the acute illness. Now, the more recent, large outbreak in West Africa had many thousands of patients and a significant proportion of those patients did survive past the acute stage of illness. And so this gave scientists a unique ability to systematically assess for the, you know, potential, you know, long-term aftereffects of Ebola virus, including effects on the nervous system. So, this is, has been something that has been, you know, long suspected but only more recently been able to be able to be systematically assessed.

[Sarah Gregory] Who were the patients studied and where did they come from?

[James Sejvar] Well, the patients in this study were patients who had experienced Ebola virus disease and had survived the acute illness. They're residents of an area in Sierra Leone. And they had been being followed up long term to track the progression of their illness and see how they, see their recovery process. And so, out of over approximately 300-odd patients, they identified 35 patients who had severe neurologic or psychiatric sequelae that they then were able to follow over a period of over a year.

[Sarah Gregory] The study looked at patients with both neurologic and psychiatric symptoms. Could you explain the differences between these two kinds of symptoms?

[James Sejvar] Yeah, so both of these symptoms are effects on the nervous system. Probably the simplest way of kind of conceptualizing the difference between the two is that neurologic symptoms tend to affect the body, if you will, whereas psychiatric symptoms affect the mind. Now, neurologic symptoms oftentimes present with something that you can basically see with your own eyes—weakness in the limbs or slurred speech or, you know, a facial droop or seizures, you know, things that are observable and can be, you know, observed with the eye and examined. With psychiatric sequelae, they're more subtle and they involve things like depression, anxiety, behavioral disorders. They, they're basically symptoms that relate to thought and behavior. And that's really the big difference between the two.

[Sarah Gregory] What kinds of conditions did the researchers find in the study's cohorts group?

[James Sejvar] Well, they actually found a variety of different findings, quite frankly. The most common finding that they found was headaches. People, a lot of people complained bitterly of severe headaches, different types of headaches, and in some cases, the headaches were severe enough to, you know, render them incapacitated. In addition, though, they found some other findings, including eye findings, that caused difficulty with vision and even blindness. Some patients suffered from strokes. There were some patients that had what are called peripheral neuropathies. Now, these are illnesses of the nerves that cause things like numbness and tingling. So, really, there was a very vast variety of findings that the, that the authors found among these survivors.

[Sarah Gregory] Do we know why Ebola has apparently caused these kinds of lasting health conditions?

[James Sejvar] We really don't, at this point and, quite frankly, we can't be absolutely certain that Ebola is even the, sort of, the cause of these conditions. It might seem a little semantical, but there's a difference between a causal association and a association that is temporal, in other words, associated in time. What we do know is that, at the time that these people were recovering from their Ebola illness, they developed these varying, you know, neurologic signs and symptoms. But what we don't know is, if we had done a case-control study, in other words, looking at some of the patients who had Ebola, and compared them to patients who didn't have Ebola, whether the various neurologic findings found in the Ebola group were just representative of findings that we would find in the general population. So, but based on the sheer number of patients in the Ebola group that did have these findings, and the unusual nature of the findings, it's fairly quite likely that Ebola did have a role to play in these neurologic findings. Now, how and why they would have developed these various neurologic sequelae is unclear, as well. It's possible that the Ebola virus itself invaded the nervous system and caused damage to the brain cells or the other, you know, cells in the nervous system causing direct damage. It's also possible that the damage was due to the body's immune response to the virus, so kind of an indirect effect, because of the immune system in the patient's body reacting to the presence of the virus. But, the fundamental answer is we really don't know at this point why Ebola seemed to lead to these neurologic sequelae.

[Sarah Gregory] What kinds of testing were done to determine the neurologic sequelae?

[James Sejvar] Well, the fundamental testing was just basically physical examination—testing the nervous system by a trained neurologist or looking at psychiatric symptoms by psychiatrists. And you can actually tell a great deal about the sequelae from examining the patient and finding, you know, lesions or, in other words, findings that point to certain areas of the nervous system that are affected or certain psychiatric manifestations that point towards a certain psychiatric diagnosis. So, that was really the fundamental way of evaluating these patients. Now, in some cases, when it was clinically indicated, there were some other, sort of more special tests that were done, including scans of the brain, detailed examinations of the eyes to look for the reasons for the visual problems and the blindness. In some cases, cerebrospinal fluid, or CSF, was collected, and this is the fluid that basically bathes the brain and the spinal cord. And this was collected in order to see whether there was, we could find presence of the virus in the CSF, which would indicate presence of the virus in the nervous system. And so, in some cases that was performed. And then, in some cases, other testing, such as formal detailed neuropsychiatric testing using computers was performed to more effectively gauge the psychiatric sequelae. So, those were the main sort of ways of assessing these patients.

[Sarah Gregory] So, with the brain scan and the spinal fluid, looking at the spinal fluid, they saw things?

[James Sejvar] Well, yeah, in some cases they did. In certain cases, they found what we call cerebral atrophy, which means a kind of a shrinking of the brain. And that can be due to a number of different reasons, but their suspicion was it was due to the Ebola infection of the brain. In some other scans they found evidence of strokes, and so there was a concern that, in certain situations, certain individuals can develop strokes in the setting of the Ebola. In the cerebrospinal fluid, in fact, they did find some evidence of the presence of the virus in the CSF,

indicating that it seems like the virus is able to get in, get access to the central nervous system and could be a reason for the neurologic effects of the virus.

[Sarah Gregory] So, the virus is still in the spinal fluid, even though they're theoretically well, or cured, or whatever the word is?

[James Sejvar] Right, right. So, there's, there is concern about viral persistence. There doesn't seem to be persistence of the virus in the nervous system, but at least during the acute illness, there can be the detection of the presence of the virus, indicating that the virus is in there, in the nervous system. And so, it's not clear whether perhaps there is some viral persistence in the nervous system, or it's just the, you know, the acute injury that leads to the long-term sequelae, because of the initial injury to the brain and the spinal cord.

[Sarah Gregory] What's the long-term prognosis for these people?

[James Sejvar] Well, that's really kind of hard to, hard to gauge at this point. I think time is going to be the ultimate teller of the long-term prognosis. The authors did give some positive results that, in some cases, people had, that had, you know, suffered from the severe headaches, the memory loss, the psychiatric symptoms, showed improvement after one year. So, there does appear to be the possibility that, in some cases, there can be improvement over time. In some cases, however, particularly in people with very severe sequelae, there was little or no improvement over the period of a year. So, there seems to be kind of varying outcomes and, really, I think it's gonna be, you know, time will tell and, you know, further investigations into the long-term outcomes as to what the ultimate prognosis in these patients is going to be.

[Sarah Gregory] Can people get it again?

[James Sejvar] As far as we know, once you've gotten Ebola, your body creates antibodies that lead you to be protected from reinfection. It's kind of like you're immunizing yourself, if you will.

[Sarah Gregory] That's why I guess a vaccine would be effective, if they come up with one.

[James Sejvar] Right, right. And they do have, they've come up with a vaccine and they're actually trying to use it in the current outbreak in the Democratic Republic of Congo.

[Sarah Gregory] So, where do we go from here? Vaccine? Will these findings lead to better treatment of survivors?

[James Sejvar] I think that this is going to lead to better treatment. Just the knowledge that people recovering from Ebola virus disease develop these headaches, these eye findings, these peripheral neuropathies. The clinicians are gonna know to look for these things, they're gonna be more astutely looking for these various sequelae, and in doing so, they'll be able to diagnose and treat and act more fast. And this could lead to better outcomes for the patients in the, in the short term. In addition, knowing what happens in the months and years after the acute illness, clinicians will be able to more effectively describe to patients, survivors, and their families what to expect in the months and the years to come, after the infection. Because, you know, obviously, once people develop an illness, they want to know, you know, "Doc, how am I gonna do?" And so, this will allow clinicians to have that information to better inform the patients and families of what to expect. So, I think that, in itself, is a positive thing that's gonna result from this research.

[Sarah Gregory] Well, thank you so much, Dr. Sejvar, for taking the time to do this podcast today.

[James Sejvar] It was my pleasure. Thank you.

[Sarah Gregory] Listeners can read the entire article, Case Series of Severe Neurologic Sequelae of Ebola Virus Disease during Epidemic, Sierra Leone, online at cdc.gov/eid.

I'm Sarah Gregory for *Emerging Infectious Diseases*.

[Announcer] For the most accurate health information, visit cdc.gov or call 1-800-CDC-INFO.