

# Neurologic Complications Associated with Coronavirus

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

[Sarah Gregory] Hello, I'm Sarah Gregory, and today I'm talking with Dr. Karima Benameur. She's a neurologist and associate professor in the Department of Neurology at Emory School of Medicine. We'll be discussing neurologic complications from coronavirus disease.

Welcome, Dr. Benameur.

[Karima Benameur] Thank you, Sarah. Thank you for having me.

[Sarah Gregory] Your study is about encephalopathy and encephalitis associated with coronavirus. What's the difference between the two?

[Karima Benameur] So, encephalopathy is a general term that means that your consciousness or your level of consciousness has been altered. So, somebody who is confused we would say is encephalopathic. And it's a spectrum, you can be encephalopathic from being confused to encephalopathic being almost comatose. Encephalitis is a little bit more specific. “-itis” is what defines inflammation related to something. So, encephalitis means inflammation of the brain.

[Sarah Gregory] Have there been other studies done on neurologic effects associated with COVID-19?

[Karima Benameur] So there have been reports and case series, the first of which came out of China, where they showed that up to a third of patients had neurologic complications. And the neurologic complications ranged between what you've heard about—you know, loss of taste and smell, to encephalopathy, to stroke, to your peripheral nerves being affected, to encephalitis. So, there's a wide range. But we do know that a third of patients do have neurologic effects related to COVID-19.

[Sarah Gregory] How would SARS-CoV-2 virus get into the nervous system?

[Karima Benameur] So, the data that we know...that we have, is based on previous viruses, such as the original SARS in 2003. For...for SARS-CoV-2 specifically, we actually don't know yet how it gets into the brain. The theory is that it can get into the brain either by direct invasion; so once it gets into your nasal cavity, it can actually travel up to...to the olfactory nerve—so, your...your nerve of...smell—and from there, get into the brain. That's been shown in animal studies. There's another theory also that it can get into the brain through the blood. And so, the short answer is that for SARS-CoV-2 specifically, we do not know. And what we do know—in humans, anyway—what we do know is based on animal studies as well as the previous SARS epidemic.

[Sarah Gregory] Tell us about your study. How many patients were there, and what were you looking for? Were there significant aspects of it? What were they?

[Karima Benameur] So, I'm a neurohospitalist, meaning that I'm a neurologist practicing in the hospital only. And so because of that, all patients that we reported were inpatients that were admitted to the hospital. And in this case specifically, they were admitted to the Emory University Hospital – Midtown campus. The paper talks about three patients, those were the three patients that we saw with encephalitis, and since then, we have identified three more

patients with that. The way we went about this is that...I, as a neurologist, get consulted when other physicians get an inkling that something brain-related is going on. And so, if a patient is acting confused, or if a patient looks like they're having a seizure, or you know, if their exam shows neurologic findings, that's how we neurologists get involved. In these particular patients, there were different manifestations. And so, some of them were having, you know, twitching episodes. Some of them were having signs on their exams their brainstems were not functioning. And so that's how we got involved.

[Sarah Gregory] Clinical, blood, neuroimaging, and cerebrospinal fluid testing were used to find out that these neurological problems were related to COVID-19. How did you go about this?

[Karima Benameur] Right, so that's a really good question. So when we had consulted on patients who are confused or encephalopathic, you know, the first thing that we would do was to perform a full neurological exam—so, that's your clinical part. And in the paper, we detail what our findings were in these patients. And what's interesting is that all three patients had what we would call “brainstem findings,” which is something that has been described in the previous SARS epidemic, so the SARS virus has a predilection for the brainstem. So from there, we got brain imaging using MRIs as well as blood markers and cerebrospinal fluid markers. And what we were trying to do was to not only confirm what we were finding on our clinical exam, but also study more in-depth what was going on in these patients, from a blood marker standpoint and from a cerebrospinal fluid standpoint.

[Sarah Gregory] What were the results? How are they associated with COVID-19?

[Karima Benameur] So, what was unique about our study was the identification of SARS-CoV-2 serology and inflammatory markers in the spinal fluid, which is evidence of direct CNS involvement by the SARS-CoV-2 virus. These measurements were done in my colleague William Hu's lab, who is the senior author on the paper. His lab is at the forefront of identifying diagnostic and prognostic biomarkers for various inflammatory diseases, including dementias and other inflammatory diseases. And...and so, it's important to know that inflammation is a common denominator for multiple diseases, whether they be due to viral infection or other.

In our case series, we found that these patients had elevated levels of what we call IGM, which is an acute marker, an acute antibody, that is formed in response to a particular virus or...or, you know, pathogen. All three of our patients had high levels of IGM against the SARS-CoV-2 virus and the sicker the patient, the higher the levels were. We also measured cytokine levels in the spinal fluid and compared them to healthy subjects as well as to...as to subjects with HIV who had neurologic involvement. So, that was our viral control. And what we found was that there were similarities between COVID and HIV when they do invade the brain, but there were also some unique biological footprints, if you will, to COVID, mainly that interleukin-8 and interleukin-10 were elevated in COVID patients, but not in HIV.

[Sarah Gregory] So, we do hear a lot about cytokine storms. What exactly are they?

[Karima Benameur] Cytokines are a diverse group of small proteins that are made and secreted by cells in the body for the purpose of signaling and communication between different cells. And so, you have different kinds of cytokines depending on what they do; you have the interleukins, the interferons, the chemokines, the tumor necrosis factor. In our study specifically, we measured interferons, interleukins, and tumor necrosis factor, in addition to other things that are detailed in the paper. So, the “cytokine storm” is a term that first came by from transplant studies, and then

from there it was kind of taken on by infectious disease studies, and it was really popularized by the avian flu epidemic. And what that means is that you kind of have a...an overwhelming response by the immune system to this pathogen that it's exposed to. So instead of having a measured response, you will have this quote-end-quote "storm" of cytokines. And, you know, what we tell patients is that the immune system kind of goes into overdrive, which in itself can cause damage to various structures in the body's organs.

[Sarah Gregory] In what ways is this important to public health and understanding COVID-19?

[Karima Benameur] I think it's really important because a lot of people think COVID-19 means, you know, lung injuries. You know, when you hear COVID-19, you think about shortness of breath and fever and cough. And the truth is that what we have seen is that it really affects multiple organs in the body. You know, I, as a neurologist, of course focus on the neurologic complications of COVID-19, which are...which are very important, right? Because we have even seen people who have recovered from COVID-19, but are still having chronic symptoms of having cognitive decline. For example, they say they can't think straight, or people are continuing to have headaches. So, there's still a lot of work to be done just to understand the chronic manifestations. But it's important for people to know that it affects not just your lungs, it affects your brain, your heart, your kidneys, your skin, actually. So it's really a widespread...or a disease with wide manifestations.

[Sarah Gregory] Well, tell us about your job at Emory and how you're involved with this virus, and also what it's like to continue practicing medicine in the middle of all of this?

[Karima Benameur] As I said before, I'm a neurohospitalist. So, I see patients who are admitted to the hospital. So, if you will, I see a skewed population—only patients who are sicker get admitted to the hospital. And so, I've seen patients who are in the intensive care unit, as well as patients who are just in the regular floors, all around the hospital, with neurologic manifestations. You know, practicing in the time or the era of COVID-19 has been really challenging but also really eye-opening—challenging in the way that, you know, we are dealing with a virus that can cause serious complications, including death. And so, you know, we as healthcare workers—you know, physicians, nurses, therapists, all kinds of healthcare workers—are exposed to this virus on a daily basis. And it kind of added a layer of anxiety where we have to, you know, put on the appropriate PPE before—PPE meaning, you know, the protective equipment, so, masks and shields and all that—before seeing a patient with COVID-19. And, you know, people worry about not only getting this disease but also carrying the virus to their loved ones and their families. It's really been eye-opening because we are at the forefront of discovering a new disease and studying it, and we kind of are learning as we go. And this is not something that, you know, physicians do on a regular basis in their practice, right? So, we are trained on various diseases and when we go in, we know what we're doing. And when you're faced with a new epidemic or pandemic, you are discovering as you go. And so, it's eye-opening, it's exciting, but also anxiety-inducing all in one.

[Sarah Gregory] I can imagine. What do you think the immediate future holds for us concerning this virus?

[Karima Benameur] A lot more to learn....you know, I really worry that we started having the numbers...seeing numbers go down and now we're seeing numbers increase in various states. And of course I worry about, you know, these people having...even though people think that, "oh, you know, 80% of people only get a mild course," I, of course, only see the ones who are

admitted to the hospital. And this virus can make people really, really sick. So I worry that the numbers are going back up, and I really hope that folks continue to social distance and wear their masks and do the appropriate things—you know, washing hands, sanitizing—to try to dampen the pandemic.

[Sarah Gregory] Well, thank you so much for taking the time to talk with me today, Dr. Benameur.

[Karima Benameur] Thank you, thanks for having me.

[Sarah Gregory] And thanks for joining me out there. You can read the September 2020 article, Encephalopathy and Encephalitis Associated with Cerebrospinal Fluid Cytokine Alterations and Coronavirus Disease, Atlanta, Georgia, USA, 2020, online at [cdc.gov/eid](https://www.cdc.gov/eid).

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

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