# Arkansas Department of Health

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**Neurologic Complications Associated with Novel Influenza A (H1N1) Virus Infection in Children - Dallas, Texas, May 2009,** *MMWR*, July 24, 2009 / 58(28);773-778

Neurologic complications, including seizures, encephalitis, encephalopathy, Reye syndrome, and other neurologic disorders, have been described previously in association with respiratory tract infection with seasonal influenza A or B viruses, but not with novel influenza A (H1N1) virus. On May 28, 2009, the Dallas County Department of Health and Human Services (DCHHS) notified CDC of four children with neurologic complications associated with novel influenza A (H1N1) virus infection admitted to hospitals in Dallas County, Texas, during May 18-28. Patients were aged 7-17 years and were admitted with signs of influenza-like illness (ILI) and seizures or altered mental status. Three of the four patients had abnormal electroencephalograms (EEGs). In all four patients, novel influenza A (H1N1) viral RNA was detected in nasopharyngeal specimens but not in cerebrospinal fluid (CSF). Antiviral therapy included oseltamivir (four patients) and rimantadine (three patients). All four patients recovered fully and had no neurologic sequelae at discharge. These findings indicate that, as with seasonal influenza, neurologic complications can occur after respiratory tract infection with novel influenza A (H1N1) virus. For children who have ILI accompanied by unexplained seizures or mental status changes, clinicians should consider acute seasonal influenza or novel influenza A (H1N1) virus infection in the differential diagnosis, send respiratory specimens for appropriate diagnostic testing, and promptly initiate empirical antiviral treatment, especially in hospitalized patients.

A patient with acute neurologic complications associated with novel influenza A (H1N1) virus infection was defined as having laboratory-confirmed novel influenza A (H1N1) virus infection of the respiratory tract associated with seizures, encephalopathy, or encephalitis within 5 days of ILI symptom onset, without evidence of an alternative etiology. Encephalopathy was defined as altered mental status lasting ≥24 hours. Encephalitis was defined as encephalopathy plus two or more of the following: fever ≥100.4°F (≥38.0°C), focal neurologic signs, CSF pleocytosis, EEG indicative of encephalitis, or abnormal neuroimaging indicative of infection or inflammation.

Patient A. On May 17, a previously healthy black male aged 17 years visited a community hospital emergency department after 1 day of fever reaching 102.6°F (39.2°C), cough, headache, dizziness, and weakness. Influenza A was diagnosed by EIA, and the patient was discharged home with a prescription for oseltamivir. The patient was admitted the next day to another community hospital because of increased generalized weakness, disorientation to place, and markedly slow and intermittent responsiveness to questions. On physical examination, the patient was noted to be confused and unable to provide history of his own illness. He also was unable to lift his arms above his shoulders or stand. He had taken 1 dose of oseltamivir the morning of admission. A computed tomography (CT) head scan revealed pan-sinusitis, CSF was normal. The patient received ceftriaxone for 2 days, which was discontinued when CSF bacterial cultures indicated no growth. He received oseltamivir throughout his hospital admission. His mental status returned to normal on day three. He was discharged on day four with no apparent sequelae and completed a 5-day total course of oseltamivir.

Patient B. On May 23, a previously healthy Hispanic male aged 10 years was taken to a Dallas community hospital via emergency medical services after a 3-minute generalized tonic-clonic seizure and subsequent postictal mental state. The seizure occurred after 4 days of fever reaching 104.0°F (40.0°C), cough, decreased appetite, and fatigue. His family reported that the patient had contact with another child with ILI symptoms before the patient's illness onset. Upon initial evaluation in the emergency department, the patient was afebrile. A chest radiograph revealed a left lower lobe infiltrate, and a CT head scan was normal except for an incidentally noted single punctuate calcification in left frontal cortex. Influenza A was detected in a nasopharyngeal swab specimen by EIA. Three hours later, the patient had a second 3-minute generalized seizure. Intravenous (IV) lorazepam and ceftriaxone were administered, and the patient was transferred to a Children's Medical Center of Dallas (CMCD) intensive-care unit.

On admission to CMCD, the patient was febrile, confused, and drowsy. He had difficulty answering questions and made frequent inappropriate attempts to get out of bed. CSF analysis was normal. He was administered IV fosphenytoin to prevent additional seizures, vancomycin and ceftriaxone for empirical treatment of bacterial pneumonia, supplemental oxygen via bilevel positive airway pressure for oxygen saturations <92%, and anticonvulsants. Over the ensuing 2 days, he had intermittent fevers reaching 102.0°F (38.9°C). On hospital day four, he had a prolonged partial complex seizure with focal onset (eye deviation to the right) and secondary generalization, lasting 30-40 minutes, which eventually was controlled by 4 doses of IV lorazepam and a bolus of IV fosphenytoin. Oseltamivir and rimantadine were initiated. Brain magnetic resonance imaging (MRI) with magnetic resonance angiography was normal, and an EEG was consistent with encephalopathy. His mental status returned slowly to baseline by hospital day seven, when he was discharged without apparent sequelae to continue levetiracetam, amoxicillin, and clindamycin, and complete a 5-day course of oseltamivir.

Patient C. On May 26, a white male aged 7 years with a history of a simple febrile seizure 1 year previously was taken to a Dallas community hospital via emergency medical services after a seizure and 2 days of cough, nasal congestion, and fatigue. On the day of admission, he had been found at home on the floor, with tonic movements of his upper and lower extremities lasting at least 2 minutes. On admission to the community hospital, he was noted to have postictal drowsiness and a temperature of 100.8°F (38.2°C). A diagnosis of influenza A was made by EIA. Blood tests, CSF, and a CT head scan were normal.

The patient was transferred the same day to CMCD, where he exhibited normal mental status and no fever or seizures. A brain MRI showed nonspecific white matter abnormalities not characteristic of infection or inflammation. Localized cerebral dysfunction was evident on EEG. Oseltamivir and rimantadine were started on hospital day one, and the patient was discharged on hospital day three without any neurologic sequelae, to complete a 5-day course of both antivirals and to continue levetiracetam until reassessment by neurologists in 3 months.

Patient D. On May 27, a black male aged 11 years with a history of asthma was taken to CMCD because of 1 day of fever and vomiting. A household contact, his grandmother, had an upper respiratory infection 3 days before his illness. One day before admission, he had a fever of 102.0°F (38.9°C), fatigue, headache, abdominal pain, and vomiting, and was given bismuth subsalicylate twice and one 81 mg aspirin. At CMCD, he was febrile. Neurologic examination revealed ataxia. Soon after admission, the patient had a seizure consisting of episodic eye rolling and tongue thrusting. An EIA test for influenza A was positive, and oseltamivir, rimantadine, cefotaxime, and acyclovir were initiated.

During the first 2 hospital days, the patient was disoriented, had visual hallucinations, had difficulty responding to questions and following commands, had slow speech, and required supplemental oxygen via facemask for mild hypoxia and hypopnea attributed to decreased respiratory drive associated with encephalopathy. Chest radiograph was normal. An EEG was consistent with encephalopathy, and a CT

head scan was normal. The patient's mental status returned to normal by hospital day four. He completed a 5-day course of oseltamivir.

Considering that clusters of influenza-associated encephalopathy in children have been reported during previous community outbreaks of seasonal influenza and that children appear to be infected with novel influenza A (H1N1) virus more frequently than adults, additional neurologic complications in children are likely to be reported as the pandemic continues. Clinicians should consider influenza associated encephalopathy in the differential diagnosis of children with ILI and seizures or mental status changes, and remain aware of the potential for severe neurologic sequelae associated with seasonal or novel influenza A (H1N1) virus infection.

For patients with respiratory illness and neurologic signs, diagnostic testing for possible etiologic pathogens associated with neurologic disease, including influenza viruses, is recommended. Health-care providers also should consider a diagnosis of Reye syndrome in patients with viral illness and altered mental status. Although one of the patients described in this report, patient D, received a salicylate-containing product and aspirin, no evidence of Reye syndrome was observed. Salicylates and salicylate-containing products should not be administered to children with influenza or other viral infections because of the increased risk for developing Reye syndrome.

Antiviral treatment should be initiated as soon as possible for any hospitalized patient with neurologic symptoms and suspected seasonal influenza or novel influenza A (H1N1) virus infection. Although respiratory specimens should be obtained for appropriate diagnostic testing before administering antiviral agents, clinicians should not wait for the results before beginning treatment. Antiviral medications have been shown to decrease the risk for complications from influenza; however, the effectiveness of antiviral treatment to prevent influenza-associated encephalopathy sequelae is unknown. Clinicians also should send respiratory specimens for appropriate diagnostic testing. Although no vaccination against novel influenza A (H1N1) virus is available currently, CDC recommends that all children aged >6 months receive annual seasonal influenza vaccination to prevent illness and complications from infection with seasonal influenza virus strains.

If you have any questions please feel free to contact Dr. Sandy Snow at 501-661-2169 or fax to 501-661-2300 or e-mail to Sandra.snow@arkansas.gov