
Influenza-Associated Encephalopathy and Encephalitis in Children

February 28, 2025

SITUATION

Public health is investigating reports of pediatric influenza-associated encephalopathy and encephalitis (IAE), including four deaths nationally from acute necrotizing encephalopathy (ANE), a severe form of IAE. There is currently no national surveillance for IAE or ANE, so it is not known whether reported cases are within or above expected ranges. However, Centers for Disease Control and Prevention (CDC) has requested that local public health be notified about these conditions.

BACKGROUND

This year, [CDC estimates](#) that at least 29 million illnesses, 370,000 hospitalizations, and 16,000 deaths have occurred due to seasonal Influenza to date, including 68 pediatric deaths. According to California Department of Public Health (CDPH), influenza now accounts for [over 2%](#) of all deaths and [16 pediatric deaths](#) statewide.

An [MMWR published this week](#) provides the following guidance around clinical management of influenza-associated encephalopathy and encephalitis (IAE):

“[P]rompt recognition and intervention are crucial, including neurocritical supportive care for patients with increased intracranial pressure and management of multiorgan failure. Although there are currently no international evidence-based guidelines for standardized clinical management of patients with IAE, high-dose pulse methylprednisolone, plasma exchange, therapeutic hypothermia, and immune therapy such as gamma globulin, anakinra (an interleukin-1 receptor antagonist), and tocilizumab (an interleukin-6 receptor blocker) have been used. In one study, use of the nonsteroidal anti-inflammatory drug diclofenac sodium (but not acetaminophen) was associated with increased mortality in IAE cases.”

Recently, there have been reports of Acute Necrotizing Encephalitis (ANE), a devastating neurologic condition that can arise following influenza and other infections, in the pediatric population. Affected individuals typically present with rapid changes in consciousness, focal neurological deficits, and seizures. Neuroimaging reveals symmetric, bilateral deep gray matter lesions, often involving the thalami, with evidence of necrosis and/or hemorrhage.

ACTIONS REQUESTED OF CLINICIANS

1. At every opportunity, strongly recommend and administer influenza vaccine to all patients at least 6 months of age.
2. Initiate early antiviral treatment for patients of any age who are at increased risk for influenza-associated complications.
3. Consider IAE or ANE in pediatric patients who present with persistent fever and altered mental status. CSF may show normal WBCs with elevated protein. Providers should:
 - a. Test for influenza. Retain and submit positive specimens to Alameda County Public Health Laboratory for subtyping and sequencing.
 - b. Hold serum and CSF for possible further testing.
 - c. **Voluntarily report all suspected or confirmed IAE or ANE cases that have occurred since October 1, 2024 and meet the following criteria to Alameda County Public Health at (510) 267-3250:**
 - 1) Age <18 years
 - 2) Admitted to an acute care hospital or pronounced dead in an emergency department between October 1, 2024, and May 30, 2025
 - 3) Laboratory-confirmed influenza virus infection within 14 days preceding hospital presentation, during hospitalization, or in respiratory specimens collected post-mortem
 - 4) Documented neurologic abnormalities (meets one or more of the following):
 - a) Diagnosis of encephalopathy or encephalitis
 - b) Neurologic signs or symptoms including but not limited to seizures, altered mental status, delirium, decreased level of consciousness, lethargy, hallucinations, or personality changes lasting >24 hours
 - c) Neuroimaging abnormalities such as brain edema, brain inflammation, or brain lesions
 - d) Electroencephalogram abnormalities
 - e) Abnormal brain autopsy findings, if available, for children who died
 - d. Report laboratory-confirmed influenza-associated fatal pediatric cases (<18 years) to Alameda County Public Health at acuteecd@acgov.org as soon as possible.

RESOURCES

- <https://promedmail.org/promed-post/?id=8722003>
- [Reports of Encephalopathy Among Children with Influenza-Associated Mortality — United States, 2010–11 Through 2024–25 Influenza Seasons](#)
- [Severe A\(H1N1\)pdm09 influenza acute encephalopathy outbreak in children in Tuscany, Italy, December 2023 to January 2024](#)
- [Influenza-Associated Deaths among Children in the United States, 2003–2004](#)