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HEALTH ADVISORY

Pediatric Influenza-Associated Encephalopathy and Encephalitis (IAE)

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This advisory is intended for emergency medicine and urgent care clinicians, intensivists, neurologists, infectious disease specialists, primary care, internal medicine, family practice, pediatric, and OB/GYN. Please distribute as appropriate.

Situational update:

The Centers for Disease Control and Prevention (CDC), the California Department of Public Health (CDPH), other states and several local health departments in California are currently investigating reports of **pediatric cases of influenza-associated encephalopathy and encephalitis (IAE)**, including fatal cases from **acute necrotizing encephalopathy (ANE), a severe form of IAE.** ANE is a devastating neurologic condition that can arise following a variety of systemic infections, including influenza and other viral infections. Affected individuals typically present with rapid changes in consciousness, focal neurological deficits, and seizures.

There is currently no statewide or national surveillance for IAE or ANE, and although there appears to be an increase in such cases this season, it is not known whether reported cases are within or above expected ranges. CDC and CDPH have requested that clinicians report such cases to their local public health Departments.

Background:

Although seasonal influenza activity is decreasing, it remains elevated compared to previous seasons, with high numbers of flu-related medical visits, hospitalizations, and deaths and CDC expects several more weeks of flu activity. This 2024-2025 flu season is classified as a high severity season overall and for all age groups (children, adults, older adults) and is the first high severity season since 2017-2018.

CDC estimates that there have been at least 40 million illnesses, 520,000 hospitalizations, and 22,000 deaths from flu so far this season. As of March 1, 2025, there have been 114 pediatric deaths across the United States, 18 in California and 1 in San Mateo County.

On February 27, 2025, CDC published a Morbidity and Mortality Weekly Report (MMWR) with the following guidance around the clinical management of IAE:

"Progression to severe neurologic impairment and death from IAE can occur rapidly after onset of influenza symptoms; thus, prompt recognition and intervention are crucial, including neurocritical supportive care for patients with increased intracranial pressure and management of multiorgan failure. Early initiation of antiviral treatment is recommended for children at increased risk for influenza-associated complications, although whether antiviral treatment is beneficial for management of IAE is unknown. Notably, one study reported that oseltamivir treatment was associated with a reduced risk for neuropsychiatric events among patients with influenza. 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."

Actions requested of clinicians:

- Continue to recommend and offer influenza vaccination for all patients aged 6 months and older. It is not too late to vaccinate as seasonal influenza can circulate through late spring.
- Initiate early antiviral treatment for all patients with influenza who are at increased risk for influenza-associated complications.
- Consider IAE or ANE in patients who present with persistent fever and altered mental status. CSF is almost always negative for influenza in these cases and may show normal WBCs with elevated protein.
    - Test for influenza and retain positive specimens so they can be sent to the San Mateo County Public Health Laboratory for subtyping and sequencing.
    - Hold serum and CSF for possible further testing.
    - **Please report to the San Mateo County Communicable Disease Control Program all suspected or confirmed IAE or ANE cases that have occurred since October 1, 2024, and meet the following criteria:**
        1. Age <21 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 the 14 days preceding hospital presentation, during hospitalization, or in respiratory specimens collected post-mortem.
        4. Documented neurologic abnormalities (meeting 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 die.

Clinical consultation on known or suspected IAE/ANE cases in California is available from Stanford University pediatric neurologists who are working with a network of pediatric neurologists across the United States to study ANE. For information on how to obtain a consult, please contact the San Mateo County Communicable Disease Control Program.

Resources:

- 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
- Weekly US Influenza Surveillance Report: Key Updates for Week 9, ending March 1, 2025 | FluView | CDC

The Communicable Disease Control Program is available to help meet the reporting needs of, and answer questions for, San Mateo County clinicians. To report a disease or outbreak, please call 650-573-2346, Monday through Friday, 8:00 am to 5:00 pm, or fax a Confidential Morbidity Report (CMR) to 650-573-2919. You may download an electronic copy of the CMR at smchealth.org/cmr. Web-based reporting via CalREDIE is also available and accounts may be requested at https://calrediehelp.powerappsportals.us/. Non-urgent questions and/or general inquiries may be directed to SMCCDControl@smcgov.org.

Categories of urgency levels:

Health Alert: conveys the highest level of importance; warrants immediate action or attention.

Health Advisory: provides important information for a specific incident or situation; may not require immediate action.

Health Update: provides information regarding an incident or situation; unlikely to require immediate attention.