

Influenza-Associated Pediatric Mortality

Case Definition

A pediatric influenza-associated death is defined for surveillance purposes as a death resulting from a clinically compatible illness that was confirmed to be influenza by an appropriate laboratory or rapid diagnostic test in a person aged <18 years.

A death should not be reported if:

1. There is no laboratory confirmation of influenza virus infection.
2. The influenza illness is followed by full recovery to baseline health status prior to death.
3. The death occurs in a person 18 years or older.
4. After review and consultation there is an alternative agreed upon cause of death.

Laboratory criteria for diagnosis

Laboratory testing for influenza virus infection may be done on pre- or post-mortem clinical specimens, and include identification of influenza A or B virus infections by a positive result by at least one of the following:

- Commercial rapid influenza diagnostic testing of respiratory specimens;
- Influenza virus isolation in tissue cell culture from respiratory specimens;
- Direct or indirect fluorescent antibody staining of respiratory specimens;
- Enzyme immunoassay (EIA) testing of respiratory specimens;
- Reverse-transcriptase polymerase chain reaction (RT-PCR) testing of respiratory specimens;
- Immunohistochemistry (IHC) staining for influenza viral antigens in respiratory tract tissue from autopsy specimens

Case classification

Confirmed: A death meeting the clinical case definition that is laboratory confirmed.

Laboratory confirmation is required as part of the case definition; therefore, all deaths reported in the *MMWR* will be classified as confirmed. However, data on deaths meeting the clinical case definition but pending laboratory confirmation may be entered in the reporting system and listed as “**Unclassified.**”

Cases entered into the reporting system cannot be deleted. Therefore cases entered with laboratory results pending that are determined to not be influenza-related should be classified as “**Not a Case.**” Cases initially classified as confirmed but that are later determined to not be influenza-related should also be reclassified as “**Not a Case.**”

Influenza-Associated Pediatric Mortality Reporting Instructions

This document is to guide state and local health department staff in completing the case report form and the use of the CDC Pediatric Influenza-Associated Death Reporting System found on the Secure Access Administrative System (SAMS). In order to report cases within this system, each person who will be entering data from the state or local health department will need to access to SAMS. To obtain access to a SAMS account, please email Rosy Dhara (RDhara@cdc.gov) and Lenee Blanton (LBlanton@cdc.gov).

STATE USE ONLY Section (case report form only)

This section at the top of the form should be used by your state health office to record personal identifiers such as name and address of patient. Do not send this information to the Centers for Disease Control and Prevention (CDC). The web-based reporting system will not have data entry fields for this information.

Patient Demographics

1. State: state of residence of patient
 - States are responsible for reporting their residents, regardless of the location of death. If a patient dies outside their state of residence, the state where the death occurs should make arrangements to transfer any data regarding the case to the patient's state of residence, who should then report the case to CDC. This is a required field in the reporting system and is automatically populated in the web-based report.
2. County: county of residence of patient (required field)
3. State ID: the state assigned unique identifier (required field).
4. CDC ID: the CDC case ID automatically assigned by the web-based reporting system.
5. Age: The age of the patient at the time of death. Age may be entered as days, months, or years. All cases should be <18 years old.
6. Date of birth
7. Sex
8. Ethnicity
9. Race

Death Information

10. Date of illness onset: earliest date of symptom onset associated with influenza illness
11. Date of death (required field).
12. Autopsy performed
- 13a. Cardiac/respiratory arrest occurred outside of hospital
- 13b. Location of death: if other, please specify location in text field
- 13c. Admission date if the death occurred in the hospital

CDC Laboratory Specimens

- 14a. Were pathology specimens sent to CDC's Infectious Diseases Pathology Branch (please provide the laboratory ID number if known)
- 14b. Were influenza isolates or original clinical material sent to CDC's Influenza Division (please provide laboratory ID number if known)?

Influenza Testing

15. The purpose of the influenza testing section is to collect diagnostic information. Multiple testing methods may be recorded, and both negative and positive results can be entered. All confirmed cases are required to have at least one positive diagnostic test for influenza along with a corresponding specimen collection date. Result values are specific to the test type that is listed. The web-based reporting system will require a specimen collection date for every test type entered.
 - a. Commercial rapid diagnostic test

- b. Viral culture
- c. Fluorescent antibody (IFA or DFA)
- d. Enzyme immunoassay (EIA)
- e. RT-PCR
- f. Immunohistochemistry (IHC)

Culture confirmation of bacterial pathogens from STERILE (Invasive) SITES

- 16a. Was a specimen collected for bacterial culture from a normally sterile site (e.g. blood, cerebrospinal fluid [CSF], tissue, or pleural fluid)?
- Specimens collected greater than 24 hours after death are **NOT** sterile
 - The purpose of this question is to collect data on bacterial infections that may have been complicating factors of the influenza illness and potentially led to death. It is important to include information about bacterial organisms that were cultured from normally sterile sites.
 - A normally sterile site is blood, cerebrospinal fluid (CSF), pleural fluid, peritoneal fluid, pericardial fluid, bone, joint fluid, or internal body site (lung, lymph node, brain, heart, liver, spleen, vitreous fluid, kidney, pancreas, or ovary).
 - *Pleural fluid*: includes "chest fluid", thoracentesis fluid.
 - *Peritoneal fluid*: includes abdominal fluid, ascites.
 - *Joint*: includes synovial fluid; fluid, needle aspirate or culture of any specific joint (knee, ankle, elbow, hip, wrist).
 - *Bone*: includes bone marrow
 - *Muscle*: includes tissue or biopsy that is surgically obtained (considered an acceptable sterile site for GAS only)
 - *Internal Body Site*: specimen obtained from surgery or aspirate from lung, lymph node, brain, heart, liver, spleen, vitreous fluid, kidney, pancreas, or ovary.
- 16b. If yes, please indicate the site from which the specimen was obtained and the result (if more than one specimen type is positive and more than one organism cultured from each specimen type in the comments section)
- If other specimen type is selected, please specify in text field
- 16c. If positive, the organism cultured
- Select any of the species listed or select other and indicate the species isolated
 - If reporting another viral co-infection, please do so in section 18b (Clinical Diagnosis and Complications)

Culture confirmation of bacterial pathogens from NON-STERILE SITES

- 16d. Were other respiratory specimens collected for bacterial culture (e.g. sputum, ET tube aspirate)?
- **The following are respiratory sites:** sputum and endotracheal aspirate. While these are non-sterile sites, they can indicate real bacterial infections with pathogens such as *S. aureus* and may be the only indication for a related pneumonia.
- 16e. If yes, please indicate the site from which the specimen was obtained and the result (if more than one specimen type is positive and more than one organism cultured from each specimen type in the comments section)
- If other specimen type is selected, please specify in text field
- 16f. If positive, the organism cultured
- Select any of the species listed or select other and indicate the species isolated

- If reporting another viral co-infection, please do so in section 18b (Clinical Diagnosis and Complications)

Pathology confirmation of bacterial pathogens

16g. Was a specimen (e.g. fixed lung tissue) collected from an autopsy for testing of bacterial pathogens by a local or state pathologist. (If pathology results are available from CDC it is not necessary to input those results here, however please make sure to complete section 14 “CDC Laboratory Specimens)

- If yes, please indicate the results of these tests in the comments section at the end of the form

Medical Care

17. Did the patient require mechanical ventilation?

- For patients admitted to the ICU, this will most often be recorded in the ICU notes. References to vent settings, oscillator, HFOV, or HI-FI are typically associated with mechanical ventilation. Do not include cases in which the patient experienced cardio-respiratory arrest and was intubated during an unsuccessful resuscitative effort outside the hospital or in transit to the hospital.

Clinical Diagnoses and Complications

18a. Did complications occur during the acute illness?

18b. If yes, check all complications that occurred during the acute illness.

- Complications are usually stated in the general hospital chart. Additionally, hospital physicians may be able to provide information regarding a patient’s hospital course.
- Acute Respiratory Disease Syndrome (ARDS)
- Another viral co-infection – specify diagnosis if available.
- Bronchiolitis
- Cardiomyopathy/myocarditis
- Croup
- Encephalopathy/encephalitis
- Hemorrhagic pneumonia/pneumonitis
- Pneumonia (Chest X-Ray confirmed)
- Reye syndrome
- Seizures
- Sepsis
- Shock
- Other
 - Please specify if there is a complication that occurred during the acute illness that is not available for selection

19a. Did the child have any medical conditions that existed before the state of acute illness?

19b. If yes, check all medical conditions that existed before the start of the acute illness:

- Previous medical conditions are often listed on the hospital admission note or in the general hospital chart. Additionally, hospital physicians may be able to provide information regarding a patient’s previous medical conditions.
- Asthma/reactive airway disease

- Cancer (diagnosis and/or treatment began in previous 12 months) (specify)
 - Includes both solid tumors and hematologic malignancies. If the patient has complete cure, do not check. Examples include acute myelogenous leukemia (AML), acute lymphocytic leukemia (ALL), and lymphoma.
- Cardiac disease/congenital heart disease (specify)
 - Examples include includes ventriculoseptal defect (VSD), Tetralogy of Fallot, transposition of the great arteries, atrial septal defect (ASD), pulmonary stenosis, hypoplastic left ventricle syndrome, aortic stenosis, mitral regurgitation, and coarctation of the aorta.
- Cerebral palsy
- Chromosomal abnormality/genetic syndrome (specify)
 - Record any history of chromosomal abnormalities on the medical chart. Examples include trisomy 21 (Down Syndrome) or trisomy 18 (Edwards syndrome).
- Chronic pulmonary disease (specify)
 - Specify any underlying chronic pulmonary disease that existed before the acute illness, other than asthma/reactive airway disease and cystic fibrosis. Examples include chronic aspiration pneumonia, bronchopulmonary dysplasia (BPD), "chronic lung disease", and interstitial lung disease.
- Cystic fibrosis
- Diabetes mellitus
 - Includes either type I *or* type II (both “insulin-dependent” and “adult-onset”). Also includes glucose intolerance and new-onset diabetes. Do not include patients noted as “pre-diabetic”.
- Hemoglobinopathy
 - Examples include sickle cell disease, hemoglobin SS, hemoglobin SC, hemoglobin S-beta thalassemia, beta thalassemia, and alpha thalassemia. Do NOT include sickle cell trait or thalassemia trait (also known as thalassemia minor).
- History of febrile seizures
 - Include history of seizures associated **only** with fever; also known as febrile convulsions. Patients with a history of febrile seizures do not typically require anti-seizure medication.
- Immunosuppressive condition (specify)
 - Includes HIV infection, immunosuppressive therapy, and immunoglobulin deficiency.
- Endocrine disorder (specify)
 - Examples include congenital adrenal hyperplasia, hypothyroidism, hyperthyroidism, adrenal insufficiency/Cushing syndrome, and pituitary abnormalities.
- Mitochondrial disorder (specify)
 - Examples include Pearson syndrome and Myoclonic Epilepsy with Ragged Red Fibers (MERRF).
- Moderate to severe developmental delay
- Neuromuscular disorder (specify)
 - Examples include muscular dystrophy and spinal muscular atrophy.
- Obesity
 - Childhood obesity is defined for children ≥ 2 years as BMI –for-age percentile $\geq 95^{\text{th}}$. Morbid obesity is not defined for children.
- Other Neurological Disorder (specify)

- Include conditions that affect muscles of breathing or the ability to swallow (swallowing disorders/dysfunctions). Examples include static encephalopathy and hypoxic ischemic encephalopathy.
- Premature at birth (specify gestational age in weeks)
 - Preterm birth is defined as the birth of a baby of less than 37 weeks gestational age. Indicate gestational age for premature births in number of *completed* weeks. If gestational age is available as weeks and days, record exact age in weeks only; do not round up. For example, if the infant was 26 weeks, 6 days at delivery (26_6), enter 26 weeks for gestational age.
- Pregnant (specify gestational age in weeks)
 - Patient was pregnant at the time of hospitalization and/or death. Specify gestational age in weeks.
- Renal disease (specify)
 - This does not include *acute* renal failure or renal insufficiency. Includes end stage renal disease, chronic renal failure from any cause, nephrotic syndrome, renal tubular acidosis, glomerulonephritis, and polycystic kidney disease
- Seizure disorder
 - Includes seizure disorders other than febrile seizures. Include any seizure condition (e.g, epilepsy), if it requires routine anti-seizure medication.
- Skin or soft tissue infection
- Other
 - Please specify if there is an underlying condition that is not available for selection.

Medication and Therapy History

20a. Was the patient receiving any of the following therapies *prior* to illness onset? (check all that apply)

- Antiviral prophylaxis
- Chemotherapy or radiation therapy
- Chronic aspirin therapy
- Steroids by mouth or injection
- Other immunosuppressive therapy (specify)

20b. Did the patient receive any of the following after illness onset? (check all that apply)

- Antibiotic therapy (specify)
- Antiviral therapy (specify)

Influenza vaccine history

21. Did the patient receive any influenza vaccine during the current season (before illness)?

22. If YES, please specify the influenza vaccine received before illness onset:

- Inactivated influenza vaccine (IIV3) [*injected*]
- Quadrivalent inactivated influenza vaccine (IIV4) [*injected*]
- Live-attenuated vaccine (LAIV) [*nasal spray*]
- Unknown

23. If YES, how many doses did the patient receive and what was the timing of each dose? (Enter dates of vaccination if available)

- Children receive either one or two doses of influenza vaccine depending on their age. If the child received only 1 dose, then select 1 dose ONLY. If the child received two doses, select 2 doses. Only one of these two selections can be made in the web-based reporting system.

- For each selection indicate if the last dose was given more than or equal to 14 days, or less than 14 days, before the patient reported influenza symptoms.

23b. If the patient received two doses of influenza vaccine during the current season, please specify the SECOND influenza vaccine received before illness onset:

- Inactivated influenza vaccine (IIV3) [*injected*]
- Quadrivalent inactivated influenza vaccine (IIV4) [*injected*]
- Live-attenuated vaccine (LAIV) [*nasal spray*]
- Unknown

24. Did the patient receive any influenza vaccine in previous seasons?

24a. If YES, and the patient was ≤ 8 years of age at the time of death, did they receive 2 doses of vaccine during a previous season?

Comments

The comments field is available to reporters to leave additional information regarding the patient's history that the state feels is important to share with CDC.

Submitting Information

The person submitting the form, their contact phone number, email, and date submitted will be automatically populated in the web-based reporting system with the information corresponding to the person entering the information. The date submitted will be considered the date reported by the web-based system.

Case Investigation Closed:

When all data that is available for the patient has been collected and recorded on the Influenza-Associated Pediatric Mortality Case Report Form, this option allows state and local health departments to indicate that no additional information will be submitted to CDC.