

Influenza-Associated Pediatric Mortality

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BASIC EPIDEMIOLOGY

Infectious Agent

Influenza A, B or C virus

Transmission

Transmission occurs via droplet spread. After a person infected with influenza coughs, sneezes, or talks, influenza viruses contained in the respiratory droplets travel through the air; other persons nearby can become infected if these droplets land in their noses or mouths. These droplets can also contaminate surfaces, and people can become infected when they touch an object or a surface on which these droplets have landed and then touch their noses or mouths. Transmission may also occur by direct contact, such as kissing.

Incubation Period

The incubation period is 1 to 4 days with most infections occurring within 2 days of exposure to an infected individual.

Communicability

Influenza is easily transmitted from person to person. Infected persons can start shedding virus up to 24 hours before the onset of symptoms. Shedding of the virus is greatest during the first 3 days of illness. The duration of virus shedding may be longer in young children and immunocompromised persons. Additionally, some persons who become infected with influenza remain asymptomatic.

Clinical Illness

Symptoms of influenza may include fever, cough, sore throat, myalgia (muscle aches), headaches and fatigue. Among children, otitis media, nausea, vomiting and diarrhea are also commonly reported. Influenza is usually a self-limiting infection, but in people with chronic medical conditions such as heart or lung disease, it can lead to pneumonia and other life-threatening complications.

Severity

An estimated 23,607 (range: 3,349-48,614) deaths (all ages) associated with influenza occur every year in the United States.

DEFINITIONS

Clinical Case Definition

An 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. There should be no period of complete recovery between the illness and death. Influenza-associated deaths in all persons aged <18 years should be reported.

- A death should not be reported if there is
 - No laboratory confirmation of influenza virus infection,
 - The influenza illness is followed by full recovery to baseline health status prior to death,
 - The death occurs in a person 18 years of age or older, or
 - After review and consultation there is an alternative agreed upon cause of death which is unrelated to an infectious process.
 - For example, a child with a positive influenza test whose death clearly resulted from trauma after a car accident would not qualify as a case. However, a child with a respiratory illness and a positive influenza test whose death is attributed to another infectious cause such as staphylococcal pneumonia would still qualify as a case.

Laboratory Confirmation

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

- Influenza virus isolation in tissue cell culture from respiratory specimens
- Reverse-transcriptase polymerase chain reaction (RT-PCR) testing of respiratory specimens
- Immunofluorescent antibody staining (direct or indirect) of respiratory specimens
- Rapid influenza diagnostic testing of respiratory specimens
- Immunohistochemical (IHC) staining for influenza viral antigens in respiratory tract tissue from autopsy specimens
- Four-fold rise in influenza hemagglutination inhibition (HI) antibody titer in paired acute and convalescent sera

Case Classifications

- **Confirmed:** A death meeting the clinical case definition that is laboratory confirmed
- **Probable:** No probable case definition

SURVEILLANCE AND CASE INVESTIGATION

Case Investigation

Local and regional health departments should investigate all reports of suspected influenza-associated death in any person under 18 years of age. Please use the Influenza-Associated Pediatric Mortality Case Report Form available on the DSHS website at <http://www.dshs.state.tx.us/idcu/investigation/>. Please use the most recent version of the form (the form is updated annually, usually in September before the coming flu season).

Case Investigation Checklist

- Confirm that laboratory results meet the case definition.
- Review medical records or speak to an infection preventionist or physician to verify case definition, underlying health conditions and course of illness.
- Notify the State Influenza Surveillance Coordinator in DSHS EAIDB about the case under investigation as soon as enough information is available to determine that the case meets case definition.

- Complete the Influenza-Associated Pediatric Mortality Case Report Form using medical records and information from healthcare providers, and by interviewing the case's parent/guardian or surrogate to identify vaccination status and risk factors.
 - Sources of vaccination status include parent/guardian, school, primary care provider and ImmTrac. All sources of vaccination history should be explored before deciding that vaccination status is unknown.
 - If multiple attempts were made to contact the parent/guardian or surrogate and attempts were unsuccessful, please fill out the case investigation form with as much information as possible and indicate the reasons for missing information (e.g., "lost to follow-up – parent did not return call; multiple messages left").
- Ensure that any available (pre- or post-mortem) respiratory specimens and autopsy specimens are forwarded to the DSHS lab for influenza testing.
- If the case is associated with an outbreak, see the Managing Special Situations section.
- Fax the completed Influenza-Associated Pediatric Mortality Case Report Form to DSHS.
 - The initial report should be submitted within 2 weeks of death.
 - The final completed report should be submitted upon conclusion of the investigation.
- All confirmed case investigations must be entered and submitted for notification in the NEDSS Base System (NBS).
- Copies of the death certificate and autopsy report should be faxed to DSHS when they become available. Copies of the medical records (admission report, history and physical, progress notes, laboratory results, radiology reports, discharge summary, etc.) are also appreciated.

Control Measures

- Provide education on influenza as needed:
 - Get vaccinated for influenza every year.
 - Wash hands frequently with soap and water, especially after coughing or sneezing.
 - Use alcohol-based hand sanitizers when facilities are not available for hand washing.
 - Cover coughs and sneezes with disposable tissues or your arm/sleeve.
 - Avoid touching your eyes, nose or mouth.
 - Avoid close contact with people who are sick.
 - When you are sick, limit contact with others and stay home until fever free for 24 hours without the use of fever-reducing medications.
 - Take antiviral medications if prescribed by your doctor.
 - The Texas Medical Board recently changed its rules (Texas Administrative Code, Title 22, Part 9, Chapter 190, Subchapter B, §190.8) regarding the prescribing of prophylaxis for close contacts of patients with certain infectious diseases. Physicians can now prescribe antiviral medications to contacts of influenza cases without first medically evaluating the contact.
- Recommend that anyone with risk factors experiencing symptoms or anyone with severe illness be evaluated by a healthcare provider.
- See the [Texas Influenza Surveillance Handbook](#) for additional influenza control measures.

School/Daycare Exclusion Criteria

Children with influenza are required to be excluded from school and daycare for at least 24 hours after fever has subsided without the use of fever suppressing medications. It is recommended that adults with influenza not return to work for at least 24 hours after fever has subsided without the use of fever suppressing medications.

MANAGING SPECIAL SITUATIONS

Outbreaks

Influenza-associated pediatric deaths may result in high levels of media and public attention. If the death is linked to an influenza outbreak, then the outbreak investigation may also be subject to additional media or public attention. If an outbreak of influenza is suspected, notify DSHS EAIDB at **(800) 252-8239** or **(512) 776-7676**.

The local/regional health department should:

- Work with the facility to ensure that staff and students/residents get hand hygiene and respiratory etiquette education.
- Recommend that staff with influenza be restricted from working until 24 hours after fever has subsided without the use of fever suppressing medications.
- Recommend that anyone with risk factors experiencing symptoms or anyone with severe illness be evaluated by a healthcare provider.
- See the Texas Influenza Surveillance Handbook for more information on control measures and responding to influenza outbreaks.

REPORTING AND DATA ENTRY REQUIREMENTS

Provider, School, Child-Care Facility, and General Public Reporting Requirements

Confirmed and clinically suspected cases are required to be reported **within 1 work day** to the local or regional health department or to DSHS EAIDB at **(800) 252-8239** or **(512) 776-7676**.

Local and Regional Reporting and Follow-up Responsibilities

Local and regional health departments should:

- Notify DSHS EAIDB of the case by phone or e-mail as soon as enough information is collected to confirm a case.
- Enter the case into NBS and submit an NBS notification on all **confirmed** cases within 30 days of receiving a report of a confirmed case.
 - Please refer to the *NBS Data Entry Guidelines* for disease-specific entry rules.
 - A notification can be sent as soon as the case criteria have been met. Additional information from the investigation may be entered upon completion of the investigation.
- **Fax an investigation form (may be incomplete) within 2 weeks of death.**
 - Document any reasons for delays in reporting the death (e.g., found during death certificate review, delayed reporting the health department, etc.).
- Fax a completed investigation form upon conclusion of the investigation.
 - Investigation forms may be faxed to **512-776-7616**.

When an outbreak of influenza or an influenza-like illness is investigated, local and regional health departments should:

- Report outbreaks within 24 hours of identification to the regional DSHS office or to EAIDB at **512-776-7676**.
- Submit a completed **Respiratory Disease Outbreak Summary Form** at the conclusion of the outbreak investigation.
 - Fax a copy to the DSHS regional office and/or to EAIDB at 512-776-7676.
 - The Respiratory Disease Outbreak Summary Form is available at <http://www.dshs.state.tx.us/idcu/investigation/>.

LABORATORY PROCEDURES

Specimens for influenza testing **should** be submitted to the DSHS Laboratory (or a Texas Laboratory Response Network [LRN] laboratory) for all influenza-associated pediatric mortality case. It is especially important to submit specimens if influenza was suspected but not confirmed or only confirmed with a rapid influenza test.

If available, respiratory specimens collected pre- or post-mortem (e.g., nasopharyngeal swabs, throat swabs, lower respiratory tract specimens, etc.), and post-mortem (autopsy) specimens should be submitted for influenza testing. The DSHS Austin Laboratory and the Texas Laboratory Response Network (LRN) laboratories can perform influenza PCR testing on respiratory specimens; post-mortem tissue specimen testing is performed by the CDC Pathology Laboratory.

Specimen Collection

Pre- or Post-Mortem Respiratory Specimens/Swabs

- Follow the specimen collection instructions in the current influenza season's DSHS Influenza Laboratory Surveillance Protocol. The protocol is available by request from DSHS EAIDB or from the regional influenza surveillance coordinator.
- A nasopharyngeal swab is the preferred specimen type. Other respiratory specimens may be accepted as described in the current protocol.
- Refrigerate (2°–8 °C) or freeze (-70°C) specimen vials immediately after collection.

Post-mortem tissue specimens/slides collected during autopsy

- CDC can test post-mortem specimens collected during an autopsy for influenza, other viruses (upon request), and bacterial co-infections.
- Contact EAIDB at (800) 252-8239 or (512) 776-7676 for instructions on post-mortem autopsy specimen collection and submission.

Submission Form (if submitting specimen(s) to DSHS Austin)

Pre- or Post-Mortem Respiratory Specimens/Swabs

- Use the DSHS Laboratory G-2V Specimen Submission Form for specimen submission. On the form, under the Virology section, check the box for “Influenza surveillance {Influenza real-time RT-PCR}”. In the blank space to the left of “Influenza surveillance {Influenza real-time RT-PCR}”, write “pediatric flu death”.

Section 4. VIROLOGY	
<input type="checkbox"/> Electron Microscopy	<input checked="" type="checkbox"/> Influenza surveillance {Influenza real-time RT-PCR}
<input type="checkbox"/> Culture: Reference {Virus ID}	Vaccine received: <input type="checkbox"/> Yes <input type="checkbox"/> No
Virus suspected: _____	Date vaccine received: _____
Submitted on (cell type): _____	Travel history (if known): _____
<input type="checkbox"/> Chikungunya, real time RT-PCR	<input type="checkbox"/> Measles, real-time RT-PCR
Date of onset: _____	<input type="checkbox"/> Mumps, real-time RT-PCR
Travel history: _____	<input type="checkbox"/> MERS Coronavirus (Novel coronavirus)
*** Information required prior to testing. ***	**** Prior authorization required. ****
Performed only if specimen is collected within 5 days or less of symptom onset.	Call Infectious Disease (512) 776-7676 for authorization
<input type="checkbox"/> Dengue, real time RT-PCR	<input type="checkbox"/> Viral isolation, clinical {Comprehensive cell culture}
Date of onset: _____	Virus suspected: _____
Travel history: _____	<input type="checkbox"/> Other: _____
*** Information required prior to testing. ***	
Performed only if specimen is collected within 5 days or less of symptom onset.	

Pediatric flu death

- Indicate the patient's flu vaccination status for the current season and the date of vaccination, if known.
- If applicable, indicate the patient's travel history and/or animal contact history.
- Make sure the patient's name and date of birth on the form exactly match what is written on the specimen tube.
- Make sure to fill in the date and time of collection in addition to the patient demographics on the form.

Post-mortem tissue specimens/slides collected during autopsy

- Contact EAIDB at (800) 252-8239 or (512) 776-7676 for instructions on post-mortem autopsy specimen collection and submission.

Specimen Shipping

Pre- or Post-Mortem Respiratory Specimens/Swabs

- Transport temperature: Store the specimen at 2°-8°C if the specimen will be received at the laboratory within 72 hours of collection; ship the specimen on cold or freezer packs. Otherwise, the specimen must be stored frozen (-70°C) and shipped on dry ice.
- Ensure that the specimen is triple-contained and that the outer shipping container is properly labeled for "Biological Substance, Category B" shipments.
- Ship specimens for overnight delivery.
- DO NOT mail specimens on a Friday or the day before a holiday unless special arrangements have been made in advance with the DSHS or LRN Laboratory.
- If shipping specimens to DSHS Austin, ship specimens to:

Laboratory Services Section, MC-1947
Texas Department of State Health Services
Attn. Walter Douglass (512) 776-7569
1100 West 49th Street
Austin, TX 78756-3199

Post-mortem tissue specimens/slides collected during autopsy

- Contact EAIDB at (800) 252-8239 or (512) 776-7676 for instructions on post-mortem autopsy specimen collection and submission.

Common Causes for Rejection

- There is a discrepancy between the patient name on the specimen tube and the name on submission form.
- The specimen is not shipped in viral transport medium or the medium is expired.
- The specimen is received more than 72 hours after collection (if refrigerated).
- The specimen is received at ambient temperature.

UPDATES

- Basic Epidemiology: minor changes to Transmission, Communicability, Clinical Illness, and Severity
- Laboratory Procedures: changes made to Submission Form instructions to reflect form updates; references to “wet ice” removed in Specimen Shipping instructions