

Influenza-Related Pediatric Mortality Investigation and Reporting: Guidance for Medical Examiners, Pathologists and Healthcare Providers

Michigan Department of Health and Human Services (MDHHS) Division of Communicable Disease

Immediately contact the MDHHS Division of Communicable Disease (517-335-8165; after hours 517-335-9030) or your local health department to report suspect or confirmed cases.

Reporting Rationale

- Pediatric deaths due to influenza are a key component of state and national influenza surveillance
- The Centers for Disease Control and Prevention (CDC) and the Council of State and Territorial Epidemiologists (CSTE) have listed pediatric mortality associated with influenza infection as a nationally reportable condition
- Nationally, over 1000 influenza-associated pediatric mortalities have been reported since 2004
- MDHHS also requests that any unexplained pediatric death with evidence of an infectious process be reported. These cases are of public health interest and investigations lead to a better understanding of fatal disease agents and processes.

Case Definitions

Lab-confirmed: Death in a patient <18 years of age associated with a laboratory-confirmed influenza infection via one of the following test methods:

- Rapid antigen test
- Polymerase chain reaction (RT-PCR)
- Viral culture
- Direct or indirect fluorescence assay (DFA/IFA)
- 4-fold antibody titer rise in acute and convalescent sera

Suspect: Death in a patient <18 years of age with an influenza-like illness (fever >100°F with cough and/or sore throat) or other symptoms consistent with a viral respiratory illness, without a recovery to baseline health between illness and death

- A negative influenza test should not preclude further case investigation
- Attention should be paid to cases presenting as secondary bacterial co-infection due to a preceding primary influenza-like illness
- MDHHS encourages inquiries on cases that do not fit the above definitions but have noteworthy clinical presentation, lab results or pathology

Reporting and Investigation Procedures

1. To report a suspect or confirmed influenza-associated pediatric mortality, or an unexplained pediatric mortality, immediately contact the MDHHS Division of Communicable Disease at 517-335-8165 (after hours at 517-335-9030) or your local health department.
2. MDHHS and/or the local health department will request relevant medical and laboratory records for review. This documentation will most often include hospital records and autopsy reports from the medical examiner/pathologist and other medical staff.
3. MDHHS and the local health department will work with healthcare providers, laboratories, and the medical examiner/pathologist to coordinate submission of representative premortem and postmortem samples to the MDHHS Bureau of Laboratories (see Specimen Collection/Submission section on the following page).
4. Specimens will be tested at MDHHS and/or forwarded to the CDC. CDC testing may take several weeks to months to obtain final results. Results will be sent to both the medical examiner/pathologist and the local health department. There is no charge for MDHHS or CDC influenza testing services.

Specimen Collection/Submission

All specimens should be sent directly to MDHHS Bureau of Laboratories*

1. *Premortem and Postmortem specimens for PCR or viral culture confirmation at MDHHS*

- Premortem clinical influenza specimens (e.g. rapid test or PCR specimens, viral cultures)
- Non-fixed postmortem specimens (e.g. nasopharyngeal or tracheal swabs or fresh lung tissue)
- Shipping for these specimens requires refrigeration or freezing at -70°C and shipment on dry ice

2. *Postmortem specimens for testing by immunohistochemistry (IHC)*

- Viral antigens may be focal and sparsely distributed in patients with influenza. Larger airways have the highest yield for detection of influenza viruses by CDC IHC staining methods. Additional representative tissues, especially those showing significant pathology that may be related to influenza infection (e.g. myocarditis, encephalitis, rhabdomyolysis), should also be submitted.

Optimal tissues to collect for all cases are:

- Central (hilar) lung with segmental bronchi
- Right and left primary bronchi
- Trachea (proximal and distal)
- Representative pulmonary parenchyma from right and left lung

Additional tissues may include:

- Myocardium from the right and left ventricle
- CNS including cerebral cortex, basal ganglia, pons, medulla, and cerebellum
- Skeletal muscle

- The above tissues can be submitted in any or all of the following preparations:
 - Fixed, unprocessed tissues in 10% neutral buffered formalin
 - Tissue blocks containing formalin-fixed, paraffin-embedded specimens
 - Unstained sections cut at 3 microns, placed on charged glass slides (10 slides per specimen)
- A minimum of 8 tissue blocks or fixed tissue samples representing a sample of the above sites should be submitted if available.
- The above samples should be shipped at room temperature

3. Unexplained pediatric deaths with no evidence of influenza infection may require different samples, which will be decided on a case-by-case basis.

4. Additional materials to include with specimen shipment to MDHHS:

- Autopsy report (preliminary or final if available)
- Cover letter – include the following items:
 - Brief patient clinical history
 - Patient lab results (viral and bacterial testing), influenza vaccination status and travel history
 - Your name, title, mailing address, phone and fax numbers, and email address

5. *All shipping must be done in consultation with the MDHHS Division of Communicable Disease. MDHHS can assist with identifying shipping services.

Contact the MDHHS Division of Communicable Disease (517-335-8165; after hours 517-335-9030) or your local health department for any questions, case consultation or investigation coordination.