MIS-C Mortality Investigation and Reporting
Guidance for Medical Examiners, Pathologists and Healthcare Providers

Multisystem Inflammatory Syndrome in Children (MIS-C) is required to be reported in Michigan (Michigan Communicable Disease Rules 325.171-325). Immediately contact the MDHHS Division of Communicable Disease at 517-335-8165 (after-hours: 517-335-9030) or your local health department to report suspect or confirmed cases MIS-C. The Centers for Disease Control and Prevention (CDC) recommends consideration of MIS-C in any pediatric death with evidence of SARS CoV-2 infection.

Multisystem Inflammatory Syndrome in Children (MIS-C) Case Definition

- <21 years of age presenting with fever*, laboratory evidence of inflammation**, and evidence of clinically severe illness requiring hospitalization, with multisystem (≥2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic, or neurological); AND
- No alternative plausible diagnoses; AND
- Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or exposure to a suspected or confirmed COVID-19 case within four weeks prior to symptom onset.

**Fever ≥38.0°C for ≥24 hours, or report of subjective fever lasting ≥24 hours.*
***Including, but not limited to, one or more of the following: an elevated C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), fibrinogen, procalcitonin, d-dimer, ferritin, lactic acid dehydrogenase (LDH), or interleukin 6 (IL-6), elevated neutrophils, reduced lymphocytes and low albumin.*

- A negative SARS-CoV-2 test should not preclude further case investigation.
- 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 suspected or confirmed MIS-C-associated pediatric mortality, or an unexplained pediatric mortality with clinical suspicion of MIS-C, immediately contact the MDHHS Division of Communicable Disease at 517-335-8165 (after-hours: 517-335-9030) or local health department.
2. MDHHS and/or the local health department will request relevant medical and laboratory records for review. This will most often include hospital records and autopsy reports.
3. If indicated, MDHHS and the local health department will work with healthcare providers and the medical examiner/pathologist to coordinate submission of representative antemortem and postmortem samples to the MDHHS Bureau of Laboratories.
4. Specimens will be tested at MDHHS and/or forwarded to the CDC. Testing at CDC may take several weeks to obtain final results. Results will be sent to both the medical examiner/pathologist and the local health department. There is no charge for SARS-CoV-2 testing services at MDHHS or CDC.

Specimen Collection/Submission

If clinical or pathologic findings indicate the need for COVID-19 testing*, the following specimens if collected should be retained for possible submission.

1. Antemortem and postmortem specimens for SARS-CoV-2 testing at MDHHS.
    - Premortem respiratory specimens (e.g., nasopharyngeal swab in VTM (viral transport media), throat swab in VTM; tracheal/endotracheal aspirates; bronchial/bronchoalveolar fluid, sputum)*.
    - Non-fixed postmortem specimens (nasopharyngeal swab in VTM, nasal swab in VTM, nasal wash/aspirate, throat swab in VTM, tracheal swab in VTM, lung swab from each lung in VTM)*.
    - Serum specimen for antibody testing.

**Shipping these specimens requires refrigeration or freezing at -70°C and shipment on dry ice*.

2. Postmortem specimens for SARS-CoV-2 molecular and immunohistochemical testing at CDC
    - Formalin-fixed (wet) tissues or formalin-fixed, paraffin-embedded (FFPE) tissue blocks from lung and upper airways.

      A minimum of two respiratory tissue blocks is required. As viral antigens and nucleic acids may be distributed focally, chances of detection are enhanced when a minimum of three blocks of lung and one block of large airway (trachea or mainstem bronchus) are submitted for evaluation.

    - If involvement of one or more other organs is suggested by clinical history or laboratory findings prior to death, representative fixed samples of these tissues may be considered to better evaluate extrapulmonary complications of COVID-19 and optimize assessment for coinfections or alternative infectious etiologies.

***CDC recommends professional judgment to determine if a decedent had signs and symptoms compatible with COVID-19 and whether postmortem testing is necessary. Epidemiologic factors may also help guide decisions about testing such as contact with a known COVID-19 patient, being part of a cluster of respiratory illness, and community levels of COVID-19 transmission.*

Implementing proper biosafety and infection control practices is critical when collecting specimens. Postmortem activities should be conducted with a focus on avoiding aerosol generating procedures and ensuring that appropriate engineering controls and personal protective equipment (PPE) are used. Please refer to Interim Laboratory Biosafety Guidelines for Handling and Processing Specimens Associated with Coronavirus Disease 2019 (COVID-19) for additional information.

Specimen submission and testing requires pre-approval by MDHHS.

All shipping must be done in consultation with the MDHHS Division of Communicable Disease. Please contact MDHHS at 517-335-8165 for assistance identifying shipping services.

MDHHS
Michigan Department of Health & Human Services