Continued Vigilance for Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with COVID-19

Summary

Healthcare providers should continue to be vigilant for cases of multisystem inflammatory syndrome in children (MIS-C) in anyone <21 years of age.

Typical presentation includes:

- Persistent fever, abdominal pain, vomiting, diarrhea, skin rash, mucocutaneous lesions and, in severe cases, hypotension and shock,
- Elevated laboratory markers of inflammation, and in a majority of patients laboratory markers of damage to the heart.

However, a documented previous COVID-19 infection is often absent from the patient’s history, particularly as some individuals who develop MIS-C may not show any symptoms at the time of their initial infection. Additionally, symptoms of MIS-C may begin weeks after a patient is infected with COVID-19 and may be vague or frequently missed. Some patients may also develop myocarditis, cardiac dysfunction, and acute kidney injury. Thus, MIS-C should be considered as a differential diagnose in patients:

- Aged 0-20 years,
- Who have had a fever for more than a day,
- With symptoms involving ≥2 organ systems.

This HAN provides current information regarding the MIS-C case definition and reporting of MIS-C cases to DHEC.

Background

On May 15, 2020, DHEC distributed a Health Alert Network (HAN) message regarding initial reports of multisystem inflammatory syndrome in children (MIS-C) associated with SARS-CoV-2 infection, the virus that causes COVID-19, and recommended that healthcare providers report MIS-C cases to DHEC. On July 12, 2020, DHEC announced the first confirmed case of MIS-C in South Carolina. On January 29, 2021, DHEC announced the first confirmed death in a patient with MIS-C. DHEC also began posting MIS-C case counts by region to the DHEC website and updates these numbers weekly. For more information, visit the DHEC MIS-C web page.
Identification of MIS-C Cases

Given the upper limit of the age range for MIS-C cases, some patients with MIS-C may present to non-pediatric healthcare providers including providers in outpatient settings and emergency departments. Additionally, MIS-C should be considered in any pediatric death with evidence of SARS-CoV-2 infection. See the MIS-C case definition listed below for more information about identifying MIS-C cases.

MIS-C Case Definition

- An individual aged <21 years 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 the 4 weeks prior to the onset of symptoms.

*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

Note: Some individuals may meet full or partial criteria for Kawasaki disease but should be reported if they meet the case definition for MIS-C.

Clinical Presentation and Evaluation

It’s important to note that symptoms of MIS-C may begin weeks after a patient is infected with COVID-19 and may be vague or frequently missed. A previous COVID-19 infection is often absent from the patient’s history, particularly as some individuals who develop MIS-C may not show any symptoms at the time of their initial infection. Additionally, the patient may have been infected from an asymptomatic contact and, in some cases, the patient and their caregivers may not even know they have been infected. Not all patients will have the same signs and symptoms, and some patients may have symptoms not included in the list below. Some patients may also develop myocarditis, cardiac dysfunction, and acute kidney injury.

Patients with MIS-C usually present with:

- Persistent fever, abdominal pain, vomiting, diarrhea, skin rash, mucocutaneous lesions and, in severe cases, hypotension and shock,
- Elevated laboratory markers of inflammation (e.g., CRP, ferritin), and in a majority of patients laboratory markers of damage to the heart (e.g., troponin; B-type natriuretic peptide (BNP) or proBNP)

Consider MIS-C as a differential diagnose if the patient:

- Is between 0-20 years of age,
- Has had a fever for more than a day,
- Is having symptoms involving ≥2 organ systems.

Testing of suspected MIS-C cases should include:
• Tests that will identify laboratory evidence of inflammation as listed in the MIS-C case definition above,*
• SARS-CoV-2 by PCR or antigen test,
• Where feasible, SARS-CoV-2 serologic testing is suggested, regardless of the presence or absence of positive results from PCR or antigen testing. Any serologic testing should be performed prior to administering intravenous immunoglobulin (IVIG) or any other exogenous antibody treatments.

*Measuring inflammatory markers may help establish MIS-C as the diagnosis. And, although recommended, COVID-19 viral tests (PCR and antigen) may be negative. Therefore, as listed above, serologic testing should be done where feasible.

Visit the CDC website for more information about treatment of MIS-C including clinical guidance from the American College of Rheumatology.

Reporting MIS-C Cases

Healthcare providers should report suspected MIS-C cases among patients younger than 21 years of age meeting the MIS-C criteria described in the case definition above to the regional health department in which the patient resides. For contact information for the regional health departments, please see the table below.

After an MIS-C case has been reported, DHEC will work with the healthcare provider to complete a MIS-C case report form (CRF) for each patient meeting the MIS-C case definition. When classifying MIS-C cases for billing purposes, use the ICD-10 code, M35.81. For additional questions about how to report, please contact DHEC at MISC@dhec.sc.gov.

Resources for Additional Information

DHEC MIS-C case counts by region: https://scdhec.gov/covid19/mis-c-covid-19-variants
CDC MIS-C web page: https://www.cdc.gov/mis-c/
MIS-C Case Report Form

• Fillable PDF version of MIS-C Case Report Form: https://www.cdc.gov/mis-c/pdfs/hcp/mis-c-form-fillable.pdf
• Printable PDF version of MIS-C Case Report Form: https://www.cdc.gov/mis-c/pdfs/hcp/mis-c-form-printable.pdf
• Instructions for the MIS-C Case Report Form: https://www.cdc.gov/mis-c/pdfs/hcp/mis-c-form-instructions.pdf
  o Note: DHEC will enter the information for the CDC MIS ID, health department ID, and CDC NCOV ID.


DHEC contact information for reportable diseases and reporting requirements

Reporting of MIS-C is consistent with South Carolina Law requiring the reporting of diseases and conditions to your state or local public health department. (State Law # 44-29-10 and Regulation # 61-20) as per the DHEC 2021 List of Reportable Conditions available at: https://www.scdhec.gov/sites/default/files/Library/CR-009025.pdf

Federal HIPAA legislation allows disclosure of protected health information, without consent of the individual, to public health authorities to collect and receive such information for the purpose of preventing or controlling disease. (HIPAA 45 CFR §164.512).

### Regional Public Health Offices – 2021
Mail or call reports to the Epidemiology Office in each Public Health Region

**MAIL TO:**

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<tr>
<th>Lowcountry</th>
<th>Midlands</th>
<th>Pee Dee</th>
<th>Upstate</th>
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| 4050 Bridge View Drive, Suite 600  
N. Charleston, SC 29405  
Fax: (843) 953-0051 | 2000 Hampton Street  
Columbia, SC 29204  
Fax: (803) 576-2993 | 1931 Industrial Park Road  
Conway, SC 29526  
Fax: (843) 915-6506 | 200 University Ridge  
Greenville, SC 29602  
Fax: (864) 282-4373 |

**CALL TO:**

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<th>Lowcountry</th>
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| Aiken, Barnwell, Chester, Edgefield, Fairfield, Kershaw, Lancaster, Lexington, Newberry, Richland, Saluda, York  
Office: (888) 801-1046  
Nights/Weekends: (888) 801-1046 | Aiken, Barnwell, Chester, Edgefield, Fairfield, Kershaw, Lancaster, Lexington, Newberry, Richland, Saluda, York  
Office: (888) 801-1046  
Nights/Weekends: (888) 801-1046 | Clarendon, Chesterfield, Darlington, Dillon, Florence, Georgetown, Horry, Lee, Marion, Marlboro, Sumter, Williamsburg  
Office: (843) 915-8886  
Nights/Weekends: (843) 915-8845 | Abbeville, Anderson, Cherokee, Greeneville, Greenwood, Laurens, McCormick, Oconee, Pickens, Spartanburg, Union  
Office: (864) 372-3133  
Nights/Weekends: (864) 423-6648 |

For information on reportable conditions, see https://www.scdhec.gov/ReportableConditions

**DHEC Bureau of Communicable Disease Prevention & Control**
Division of Acute Disease Epidemiology  
2100 Bull St · Columbia, SC 29201  
Phone: (803) 898-0861  
Fax: (803) 898-0897  
Nights / Weekends: 1-888-847-0902

Categories of Health Alert messages:

- **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 updated information regarding an incident or situation; unlikely to require immediate action.
- **Info Service** Provides general information that is not necessarily considered to be of an emergent nature.