PENNSYLVANIA DEPARTMENT OF HEALTH
2022 – PAHAN –636– 04-15 - UPD
Update: Multisystem Inflammatory Syndrome in Children (MIS-C) and in Adults (MIS-A)

DATE:	4/15/2022
TO:	Health Alert Network
FROM:	Keara Klinepeter, Acting Secretary of Health
SUBJECT:	**UPDATE: Multisystem Inflammatory Syndrome in Children (MIS-C) and in Adults (MIS-A)**
DISTRIBUTION:	Statewide
LOCATION:	n/a
STREET ADDRESS:	n/a
COUNTY:	n/a
MUNICIPALITY:	n/a
ZIP CODE:	n/a

This transmission is a Health Update: Provides updated information regarding an incident or situation; unlikely to require immediate action.

HOSPITALS: PLEASE SHARE WITH ALL MEDICAL, PEDIATRIC, NURSING, AND LABORATORY STAFF IN YOUR HOSPITAL**; EMS COUNCILS:** PLEASE DISTRIBUTE AS APPROPRIATE; **FQHCs:** PLEASE DISTRIBUTE AS APPROPRIATE **LOCAL HEALTH JURISDICTIONS**: PLEASE DISTRIBUTE AS APPROPRIATE; **PROFESSIONAL ORGANIZATIONS:** PLEASE DISTRIBUTE TO YOUR MEMBERSHIP

- Multisystem inflammatory syndrome (MIS) is a rare but serious condition associated with COVID-19 and can affect children (MIS-C) and adults (MIS-A).
- Although MIS-C and MIS-A are similar in clinical presentation, their case definitions differ. MIS-A also has more likely severe outcomes.
- As of March 28, 2022, there are a total of 7,880 MIS-C cases and 66 MIS-C deaths reported to the Centers for Disease Control and Prevention (CDC). Pennsylvania has reported 248 cases.
- Healthcare providers should continue to promote COVID-19 vaccination with the mRNA vaccines for people 5 years of age and older to prevent severe COVID-19 complications, including MIS.
- For patients with MIS who are considering starting the COVID-19 vaccination series, a consultation with clinical team and specialists in infectious diseases, rheumatology, and/or cardiology is strongly encouraged.
- Healthcare providers must report suspect cases of MIS-A and MIS-C by faxing the included case report form to 717-772-6975 or to your local health department or by securely emailing the form to ra-dhcovidcontact@pa.gov

This guidance is based on available information about COVID-19 and subject to change as additional information becomes available. This HAN **replaces** PA HAN 529, 557 & 572.

Background and Clinical Information

Multisystem inflammatory syndrome (MIS) is a rare but serious condition that occurs after an infection with COVID-19. It can affect both children (MIS-C) and adults (MIS-A). MIS-C is more commonly recognized and reported than MIS-A. Case definitions and clinical

presentations for MIS-C and MIS-A differ slightly but both have the commonality of a dysregulated immune response to COVID-19.

Patients with MIS-C usually present with persistent fever, abdominal pain, vomiting, diarrhea, skin rash, mucocutaneous lesions and, in severe cases, with hypotension and shock. They have elevated laboratory markers of inflammation (e.g., CRP, ferritin), and in the majority of patients laboratory markers of damage to the heart (e.g., troponin; B-type natriuretic peptide (BNP) or proBNP). Some patients develop myocarditis, cardiac dysfunction, and acute kidney injury. There is a broad presentation in both symptoms and severity of symptoms. Many cases of MIS-C present 2–8 weeks after mild to asymptomatic infections with COVID-19 and, in some cases, the child and their caregivers may not even know they had been infected with COVID-19.

Case reports suggest that the presentation of Multisystem Inflammatory Syndrome in adults (MIS-A) may be more complicated than in children, with heterogeneity of clinical signs and symptoms. Patients with MIS-A typically require intensive care and can have fatal outcomes. Severe outcomes might be more likely for MIS-A because of differences in the immune systems of adults compared with children, as well as the higher likelihood of underlying medical conditions in adults.

A recent study reported that the mRNA vaccines are highly effective in preventing severe COVID-19-related complications in children aged 12-18 years, including MIS-C. Healthcare providers should encourage patients to take actions to prevent infection from COVID-19, especially including promotion of COVID-19 vaccination with the mRNA vaccines for people 5 years of age and older.

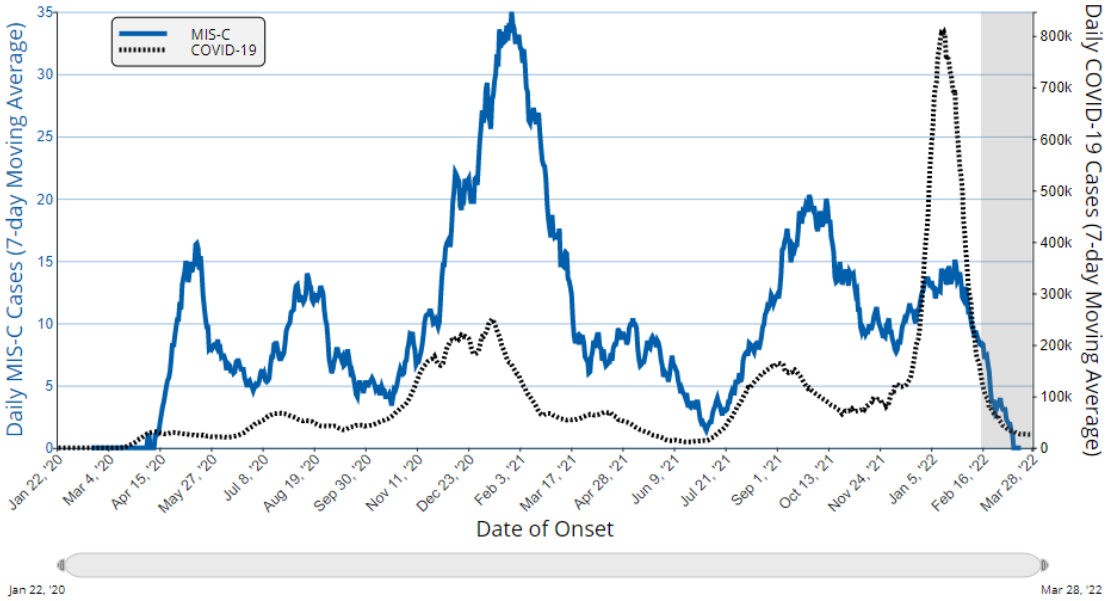
Epidemiology

Since mid-May 2020, the CDC has been tracking MIS-C and MIS-A case reports from state and local health departments. Nationally, there are a total of 7,880 MIS-C patients meeting case definition reported to CDC from 55 U.S. jurisdictions (including 50 states, New York city, Puerto Rico, Guam, US Virgin Islands, and Washington DC). Pennsylvania has reported 248 cases.

Summary of the available data from the 7,880 reported patients with MIS-C

- The median age was 9 years. Half of the cases were between the age of 5 and 13 years.
- 57% were Hispanic/Latino or Black.
- 98% had a positive test result for SARS CoV-2. The remaining had COVID-19 exposure.
- 61% were male.

Fig 1. Daily MIS-C cases and COVID-19 cases reported to CDC (7-day moving average)



https://covid.cdc.gov/covid-data-tracker/#mis-national-surveillance

The grayed-out area on the right side of Fig 1 represents the most recent 6 weeks of data, for which reporting of MIS-C cases is still incomplete. The actual number of MIS-C cases during this period is likely larger, and these numbers are expected to increase as additional case reports are incorporated.

National case counts for MIS-A are currently not available and Pennsylvania has reported <5 cases to the CDC.

MIS Case Reporting

Healthcare providers must report suspect cases of MIS-C and MIS-A by faxing the included case report form to 717-772-6975, or to your local health department, or by securely emailing the form to ra-dhcovidcontact@pa.gov. Case report forms should be fully completed with particular attention to **race and ethnicity** and **vaccination** information, as appropriate.

COVID-19 vaccination and MIS patients

Clinical guidance for MIS patients who have not received COVID-19 vaccination:

For patients with MIS who are considering starting the COVID-19 vaccination series, a consultation with clinical team and specialists in infectious diseases, rheumatology, and/or cardiology is strongly encouraged. There are limited data on the safety of COVID-19 vaccines in people who had had MIS-C or MIS-A.

Clinical guidance for patients who developed MIS post a COVID-19 vaccine:

For patients with MIS or similar clinical illness after COVID-19 vaccination, referral to a specialist in infectious diseases, rheumatology, and/or cardiology should be considered. Assessment should include testing for both current and prior COVID-19 . A positive anti-nucleocapsid antibody test can be used to indicate a prior COVID-19 case in a vaccinated person, but a positive anti-spike protein antibody test cannot, because a positive result can be due to prior vaccination or COVID-19. A discussion between the patients, their guardian(s), and their clinical team is strongly encouraged to assist with decisions about subsequent vaccine doses. For complicated situations, a consultation from the Clinical Immunization Safety Assessment COVIDvax Project may be requested.

All clinical illnesses consistent with MIS or similar illnesses occurring after receiving COVID-19 vaccines should be reported to the Vaccine Adverse Events Reporting System (VAERS). Additionally, vaccine providers should provide the VAERS ID and date of submission to the health department by emailing ra-dhcovidcontact@pa.gov.

If you have any questions, please call PA DOH at 1-877-PA-HEALTH (1-877-724-3258) or your local health department.

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.

This information is current as of April 15,2022 but may be modified in the future.

U.S. DEPARTMENT OF
HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL
AND PREVENTION
ATLANTA, GA 30329

Multisystem Inflammatory Syndrome Associated with COVID-19 Case Report Form

Patient First Name: **Last Name:** **Patient/Parent/Guardian Telephone:**

Patient Address: **City:** **State: PA** **Zip:**

Abstractor Name: **Facility Name:** **Telephone:** **Abstraction Date:**

SECTION 1 – INCLUSION CRITERIA

1.1 ☐ Age < 21 years old, OR ☐ ≥ 21 years old, AND

1.2 ☐ Fever >38.0°C for ≥24 hours, or report of subjective fever lasting ≥24 hours, AND

1.3 ☐ Laboratory markers of inflammation (including, but not limited to one or more; 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, AND

1.4 ☐ Evidence of clinically severe illness requiring hospitalization, with multisystem (≥2) organ involvement *(check all applicable below)*: AND

- **1.4.1** ☐ Cardiac (e.g. shock, elevated troponin, BNP, abnormal echocardiogram, arrhythmia)
- **1.4.2** ☐ Renal (e.g. acute kidney injury or renal failure)
- **1.4.3** ☐ Respiratory (e.g. pneumonia, ARDS, pulmonary embolism)
- **1.4.4** ☐ Hematologic (e.g. elevated D-dimers, thrombophilia, or thrombocytopenia)
- **1.4.5** ☐ Gastrointestinal (e.g. elevated bilirubin, elevated liver enzymes, or diarrhea)
- **1.4.6** ☐ Dermatologic, (e.g. rash, mucocutaneous lesions)
- **1.4.7** ☐ Neurological, (e.g. CVA, aseptic meningitis, encephalopathy)

1.5 ☐ No alternative plausible diagnosis; AND

1.6 ☐ Positive for current or recent SARS-COV-2 infection by (check all applicable below): OR

- **1.6.1** ☐ RT-PCR
- **1.6.2** ☐ Serology
- **1.6.3** ☐ Antigen test

1.7 ☐ COVID-19 exposure within the 4 weeks prior to the onset of symptoms

- **1.7.1** If yes, date of first exposure within the 4 weeks prior : *(MM/DD/YYYY)*: _____ ☐ Unknown

SECTION 2 – PATIENT DEMOGRAPHICS

2.1 **State of Residence:** _____

2.2 **Patient zip code**/postal code *(primary residence)*: _____

2.3 **Date of birth** *(MM/DD/YYYY)*: _____

2.4 **Sex:** ○ Male ○ Female

2.5 **Ethnicity:** ○ Hispanic or Latino ○ Not Hispanic or Latino ○ Refused or Unknown

2.6 **Race** *(mark all that apply, selecting more than one option as necessary)*:

- **2.6.1** ☐ White
- **2.6.2** ☐ Black or African American
- **2.6.3** ☐ American Indian
- **2.6.4** ☐ Alaska Native or Aboriginal Canadian
- **2.6.5** ☐ Native Hawaiian
- **2.6.6** ☐ Other Pacific Islander
- **2.6.7** ☐ Asian
- **2.6.8** ☐ Other
- **2.6.9** ☐ Refused or Don't know

2.7 **Height:** _____ inches

2.8 **Weight:** _____ lbs

2.9 **BMI:** _____

Comorbidities:

2.10.1	Immunosuppressive disorder/malignancy	○ Yes	○ No
2.10.2	Obesity	○ Yes	○ No
2. 10.3	Type 1 diabetes	○ Yes	○ No
2. 10.4	Type 2 diabetes	○ Yes	○ No
2. 10.5	Seizures	○ Yes	○ No
2. 10.6	Congenital heart disease	○ Yes	○ No
2. 10.7	Sickle cell disease	○ Yes	○ No
2. 10.8	Chronic lung disease	○ Yes	○ No
2. 10.9	Other congenital malformations	○ Yes	○ No

2. 10.10 Other *(specify)*:

_____

2.11 Hospital admission date *(MM/DD/YYYY)*: _____

- **2.11.1** Number of days in the hospital: _____

2.12 If admitted to the ICU, admission date *(MM/DD/YYYY)*: _____

- **2.12.1** Number of days in the ICU: _____

2.13 **Patient outcome:** ○ Died ○ Discharged ○ Still admitted

- **2.13.2** Hospital discharge or death date *(MM/DD/YYYY)*: _____

SECTION 3 – CLINICAL SIGNS AND SYMPTOMS

3.1 Did the patient have preceding COVID-like illness? ○ Yes ○ No

3.1.1 Date of symptom onset *(MM/DD/YYYY)*: _____

3.2 Date of symptom onset of MIS *(MM/DD/YYYY)*: _____

3.3. Fever ≥ 38.0°C: ○ Yes ○ No

3.3.1 Date of fever onset *(MM/DD/YYYY)*: _____

3.3.2 Highest Temperature: _____ °C

3.3.3 Number of days febrile: _____

Signs and symptoms ***during present illness***

3.4.1	**Cardiac**			
3.4.1.1	Shock	○ Yes	○ No	
3.4.1.2	Elevated troponin	○ Yes	○ No	
3.4.1.3	Elevated BNP or NT-proBNP	○ Yes	○ No	
3.4.2	**Renal**			
3.4.2.1	Acute kidney injury	○ Yes	○ No	
3.4.2.2	Renal failure	○ Yes	○ No	
3.4.3	**Respiratory**			
3.4.3.1	Cough	○ Yes	○ No	
3.4.3.2	Shortness of breath	○ Yes	○ No	
3.4.3.3	Chest pain/tightness	○ Yes	○ No	
3.4.3.4	Pneumonia	○ Yes	○ No	
3.4.3.5	ARDS	○ Yes	○ No	
3.4.3.6	Pulmonary embolism	○ Yes	○ No	
3.4.4	**Hematologic**			
3.4.4.1	Elevated D-dimers	○ Yes	○ No	
3.4.4.2	Thrombophilia	○ Yes	○ No	
3.4.4.3	Thrombocytopenia	○ Yes	○ No	
3.4.5	**Gastrointestinal**			
3.4.5.1	Abdominal pain	○ Yes	○ No	
3.4.5.2	Vomiting	○ Yes	○ No	
3.4.5.3	Diarrhea	○ Yes	○ No	
3.4.5.4	Elevated bilirubin	○ Yes	○ No	
3.4.5.5	Elevated liver enzymes	○ Yes	○ No	
3.4.6	**Dermatologic**			
3.4.6.1	Rash	○ Yes	○ No	
3.4.6.2	Mucocutaneous lesions	○ Yes	○ No	
3.4.7	**Neurological**			
3.4.7.1	Headache	○ Yes	○ No	
3.4.7.2	Altered mental state	○ Yes	○ No	
3.4.7.3	Syncope/near syncope	○ Yes	○ No	
3.4.7.5	Meningitis	○ Yes	○ No	
3.4.7.6	Encephalopathy	○ Yes	○ No	
3.4.8	**Other**			
3.4.8.1	Neck pain	○ Yes	○ No	
3.4.8.2	Myalgia	○ Yes	○ No	
3.4.8.3	Conjunctival injection	○ Yes	○ No	
3.4.8.4	Periorbital edema	○ Yes	○ No	
3.4.8.5	Cervical lymphadenopathy >1.5 cm diameter	○ Yes	○ No	

SECTION 4 – COMPLICATIONS

4.1	**Arrhythmia**	○ Yes	○ No
	If yes:		
4.1.1	Ventricular arrhythmia:	○ Yes	○ No
4.1.2	Supraventricular arrhythmia:	○ Yes	○ No
4.1.3	Other arrhythmia *(specify)*: _____	○ Yes	○ No
4.2	Congestive heart failure	○ Yes	○ No
4.3	Myocarditis	○ Yes	○ No
4.4	Pericarditis	○ Yes	○ No
4.5	Liver failure	○ Yes	○ No
4.6	Deep vein thrombosis or PE	○ Yes	○ No
4.7	ARDS	○ Yes	○ No
4.8	Pneumonia	○ Yes	○ No
4.9	CVA or stroke	○ Yes	○ No
4.10	Encephalitis or aseptic meningitis	○ Yes	○ No
4.11	Shock	○ Yes	○ No
4.12	Hypotension	○ Yes	○ No

SECTION 5 – TREATMENTS

5.1	Low flow nasal cannula	○ Yes	○ No
5.2	High flow nasal cannula	○ Yes	○ No
5.3	Non-invasive ventilation	○ Yes	○ No
5.4	Intubation	○ Yes	○ No
5.5	Mechanical ventilation	○ Yes	○ No
5.6	ECMO	○ Yes	○ No
5.7	Vasoactive medications (e.g. epinephrine, milrinone, norepinephrine, or vasopressin) *(specify)*: _____	○ Yes	○ No
5.8	Steroids	○ Yes	○ No
5.9	Immune modulators (e.g. anakinra, tocilizumab) *(specify)*: _____	○ Yes	○ No
5.10	Antiplatelets (e.g. aspirin, clopidogrel) *(specify)*: _____	○ Yes	○ No
5.11	Anticoagulation (e.g. heparin, enoxaparin, warfarin) *(specify)*: _____	○ Yes	○ No
5.12	Dialysis	○ Yes	○ No
5.13	First IVIG	○ Yes	○ No
5.14	Second IVIG	○ Yes	○ No

SECTION 6 – STUDIES

6.1 Blood Test Results

6.1.1	Fibrinogen	Highest value: _____	units: _____	○ Low	○ Normal	○ High
6.1.2	CRP	Highest value: _____	units: _____	○ Low	○ Normal	○ High
6.1.3	Ferritin	Highest value: _____	units: _____	○ Low	○ Normal	○ High
6.1.4	Troponin	Highest value: _____	units: _____	○ Low	○ Normal	○ High
6.1.5	BNP	Highest value: _____	units: _____	○ Low	○ Normal	○ High
6.1.6	NT-proBNP	Highest value: _____	units: _____	○ Low	○ Normal	○ High
6.1.7	D-dimer	Highest value: _____	units: _____	○ Low	○ Normal	○ High
6.1.8	IL-6	Highest value: _____	units: _____	○ Low	○ Normal	○ High

6.1.9	Serum White blood count	Highest value: _____	Lowest value: _____	units: _____
6.1.10	Platelets	Highest value: _____	Lowest value: _____	units: _____
6.1.11	Neutrophils	Highest value: _____	Lowest value: _____	units: _____
6.1.12	Lymphocytes	Highest value: _____	Lowest value: _____	units: _____
6.1.13	Bands	Highest value: _____	Lowest value: _____	units: _____

6.2 CSF Studies

6.2.1	White blood count	Highest value: _____	Lowest value: _____	units: _____
6.2.2	Protein	Highest value: _____	Lowest value: _____	units: _____
6.2.3	Glucose	Highest value: _____	Lowest value: _____	units: _____

6.3 Urinalysis

6.3.1	Urine White blood count	Highest value: _____	Lowest value: _____	units: _____

6.4 Echocardiogram (check if seen on ANY echocardiogram)

- **6.4.1** ☐ Not done
- **6.4.2** ☐ Normal results
- **6.4.3** ☐ Coronary artery aneurysms
  - **6.4.3.1** Max coronary artery Z-score: _____
- **6.4.4** ☐ Coronary artery dilatation
- **6.4.5** ☐ Cardiac dysfunction (decreased function), specify type:
  - **6.4.5.1** ☐ left ventricular dysfunction
  - **6.4.5.2** ☐ right ventricular dysfunction
- **6.4.6** ☐ Pericardial effusion
- **6.4.7** ☐ Pleural effusion
- **6.4.8** ☐ Mitral regurgitation, specify type: ○ mild ○ moderate ○ severe
- **6.4.9** ☐ Other *(specify)*: _____

6.5 Date of first test showing coronary artery aneurysm or dilatation *(MM/DD/YYYY)*: _____

6.6 Abdominal imaging ☐ Ultrasound ☐ CT ☐ Not done

- **6.6.1** ☐ Normal
- **6.6.2** ☐ Mesenteric lymphadenopathy
- **6.6.3** ☐ Free fluid
- **6.6.4** ☐ Other *(specify)*: _____

6.7 Chest imaging ☐ Chest x-ray ☐ CT ☐ Not done

- **6.7.1** ☐ Normal
- **6.7.2** ☐ Pneumonia
- **6.7.3** ☐ Atelectasis
- **6.7.4** ☐ Pleural effusion
- **6.7.5** ☐ Other *(specify)*: _____

SARS-COV-2 testing

6.8 RT-PCR: ○ Positive ○ Negative ○ Not done
6.8.1 If performed, date *(MM/DD/YYYY)*: _____

6.9 Antigen: ○ Positive ○ Negative ○ Not done
6.9.1 If performed, date *(MM/DD/YYYY)*: _____

6.10 IgG: ○ Positive ○ Negative ○ Not done
6.10.1 If performed, date *(MM/DD/YYYY)*: _____

6.11 IgM: ○ Positive ○ Negative ○ Not done
6.11.1 If performed, date *(MM/DD/YYYY)*: _____

6.12 IgA: ○ Positive ○ Negative ○ Not done
6.12.1 If performed, date *(MM/DD/YYYY)*: _____

SECTION 7 COVID-19 VACCINE INFORMATION

7.1 **Has the patient received a COVID-19 vaccine?** ○ Yes ○ No ○ Unknown

7.2 **If yes, how many doses?** ○ 1 dose ○ 2 doses ○ 3 doses ○ 4 doses ○ Unknown

7.2.1 Date Dose 1 *(MM/DD/YYYY)*: _____ Vaccine Manufacturer ○ Pfizer ○ Moderna ○ J & J/ Janssen ○ Other, (*specify*)

7.2.2 Date Dose 2 *(MM/DD/YYYY)*: _____ Vaccine Manufacturer ○ Pfizer ○ Moderna ○ J & J/Janssen ○ Other, (*specify*)

7.2.3 Date Dose 3 *(MM/DD/YYYY)*: _____ Vaccine Manufacturer ○ Pfizer ○ Moderna ○ J & J/Janssen ○ Other, (*specify*)

7.2.4 Date Dose 4 (MM/DD/YYYY): _____ Vaccine Manufacturer ○ Pfizer ○ Moderna ○ J & J/ Janssen ○ Other, (*specify*)

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