



Nebraska Department of Health and Human Services
HEALTH ALERT NETWORK
Update



TO: Healthcare Providers, Infection Control, Hospitals, Labs, and Public Health
FROM: Gary Anthon, MD
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RE: Multisystem Inflammatory Syndrome in Children and Adults & Monoclonal Antibody
Therapy Indications
DATE: April 22, 2021

MIS-C & MIS-A

As the state works to vaccinate Nebraskans, clinicians should continue monitoring for signs and symptoms of a rare complication of SARS-CoV-2 infection called multisystem inflammatory syndrome (MIS). MIS was first identified in children but has recently been reported among adults. Multisystem inflammatory syndrome in children (MIS-C) and multisystem inflammatory syndrome in adults (MIS-A) are severe clinical syndromes affecting multiple organ systems, frequently requiring intensive care support, which **manifest days to weeks** after SARS-CoV-2 infection. Signs and symptoms of MIS-C and MIS-A are nonspecific and might include fever, hypotension, hypoxia, altered mental status, lethargy, dyspnea, chest pain or pressure, abdominal pain, nausea, vomiting, diarrhea, or neck pain.

Both MIS-C and MIS-A have been reported among Nebraska residents. Nationally, 2,617 cases of MIS-C and 33 deaths attributed to MIS-C have been reported to the CDC. In Nebraska, 41 cases of MIS-C (and 0 deaths) have been reported to the Department of Health and Human Services (DHHS). Less is known about MIS-A than MIS-C and counts are not yet formalized. A case series published in October, 2020 described 27 cases of MIS-A in the United States and the United Kingdom. Three of the cases died. A majority of these patients belonged to racial and ethnic minority groups (<https://www.cdc.gov/mmwr/volumes/69/wr/mm6940e1.htm>). As surveillance efforts for MIS evolve nationally and here in our state, clinicians are encouraged to report suspected cases to local or state health departments (www.dhhs.ne.gov/lhd).

Rapid identification of MIS is critical because early administration of appropriate therapy is crucial to slow the progression of serious manifestations (e.g., cardiac involvement) and to prevent death. Hospitalization and a multidisciplinary healthcare approach, including infectious disease, rheumatology, or critical care clinicians, might produce the best outcomes. Treatment usually includes intravenous immunoglobulin, corticosteroids, interleukin-6 inhibitors, and other immunosuppressive agents.

Physicians should consider MIS-C or MIS-A in patients that meet CDC's case definition. Currently, there is not a standard, national case definition for MIS-A, so the case definition for MIS-C is also being applied to individuals aged 21 years and older. Per [CDC's Health Alert](#), the case definition for MIS-C includes:

- 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, hematologic, 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 COVID-19 exposure 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

- Some individuals may fulfill full or partial criteria for Kawasaki disease but should be reported if they meet the case definition for MIS-C
- Consider MIS-C in any pediatric death with evidence of SARS-CoV-2 infection
- Patients presenting without a recently positive SARS-CoV-2 test and without known exposure, might require serologic testing to suggest SARS-CoV-2 infection and meet the case definition.
- For more information on the evaluation of MIS-C please visit: <https://www.cdc.gov/mis-c/hcp/>.

Monoclonal Antibody Therapy Updates

Patients, including younger patients, with mild to moderate symptoms of COVID-19 infection might be eligible to receive monoclonal antibody therapies, such as bamlanivimab-etesevimab or casirivimab-imdevimab. Given emerging resistance to bamlanivimab when used as monotherapy, it should now ONLY be given in combination with etesevimab. This treatment is a single intravenous (IV) infusion of often less than one hour that has been shown to decrease the risk of being hospitalized.

Eligibility criteria for receiving monoclonal antibodies include:

1. Mild-moderate symptoms for 10 days or less, but the earlier received the better the chance of preventing hospitalization
2. Not yet requiring use of oxygen and not yet hospitalized for COVID-19
3. Fall into at least one of the below categories:
 - Be 65 years of age or older
 - Be 55 years of age or older WITH heart disease, high blood pressure, or chronic lung disease
 - Be 18 years of age or older WITH diabetes, chronic kidney disease, a condition that weakens the immune system, taking medications that weaken the immune system, or obesity with a BMI of 35 or higher
 - Be 12-17 years of age WITH heart disease, sickle cell disease, chronic lung disease (including asthma), a developmental condition like cerebral palsy, requiring chronic use of a medical device like a tracheostomy or dialysis, or obesity with a BMI higher than the 85th percentile

Health care providers seeking these therapies for assisted living, nursing home, or long-term care facility patients, should complete a questionnaire at this link:

<https://redcap.nebraskamed.com/surveys/?s=74H88YD3RE>. Staff from Nebraska's Infection Control Assessment and Promotion Program (ICAP) will respond within 24 hours to assist in arranging for infusion of monoclonal antibody therapy. For patients outside of long term care/skilled nursing facilities, providers should engage with their affiliated health care system or the nearest hospital. These parties can assist in arranging for infusion. For assistance in identifying locations in Nebraska capable of administering monoclonal antibodies, please go to: <https://covid.infusioncenter.org>. Institutions interested in administering COVID-19 monoclonal antibodies, or who need resupply, can find details here: <https://www.phe.gov/emergency/events/COVID19/investigation-MCM/Pages/direct-order-process-covid19-mAb.aspx>.