MIS-C and Pediatric Hepatitis of Unknown Origin Updates

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June 2022
Multisystem Inflammatory Disorder Case Definitions

➢ MIS-C (“children” – <21 years)
  • Fever
  • Laboratory evidence of inflammation
  • Clinically severe illness requiring hospitalization
  • Multisystem (>2) organ involvement
  • No alternative plausible diagnosis
  • Current or recent COVID-19 infection
    o By history, current positive swab or antibody testing

➢ MIS-A (“adults” – 21 or older)
  • Hospitalized ≥24 hours, or died, and meets the following clinical and laboratory criteria without a more likely alternative diagnosis
  • Clinical Evidence
    o Fever within 3 days before or after hospital admission AND
    o At least 3 of the primary and secondary criteria, one of which must be primary
    o Primary criteria
      ▪ Severe cardiac illness
      ▪ Rash AND non-purulent conjunctivitis
    o Secondary
      ▪ New-onset neurologic signs and symptoms
      ▪ Shock or hypotension not attributable to medical therapy
      ▪ Abdominal pain, vomiting, or diarrhea
      ▪ Thrombocytopenia (platelet count <150,000/ microliter)
  • Lab Evidence
    o Laboratory evidence of inflammation AND SARS-CoV-2 infection
CDC handout “when to consider MIS-C”

https://www.cdc.gov/mis/MIS-C/hcp/provider-resources/symptoms.pdf
Who is getting MIS-C?

- US data: 8525 Cases, 69 deaths
- No group appears to be spared but:
  - 61% male
  - 38% Black and 26% Non-white Hispanic (overrepresented in both total US population and COVID infected population)
- Median age 9 years
Kentucky MIS-C cases over time

*Figure 1: Multisystem Inflammatory Syndrome in Children (MIS-C) by Month of Onset, Kentucky, April 1, 2020 – June 08, 2022 (N=125) *

*Case counts are preliminary and subject to change; Cases with missing MIS-C onset date were excluded*
Current KY MIS-C Demographics

- 125 cases that meet case definition (6/9/22)
  - Increases in numbers are both new cases and reviewing historic cases/catching up
- Median age = 10 years
- 61% male
- MIS-C: 56% White/20% Black
- COVID 19 infections 78% White/7% Black
- KY Statewide is 87% White and 8% Black
- Over-representation of Black children in MIS-C population compared to total population and compared to the COVID-19 infected population
Does vaccination prevent MIS-C?

Figure 8: MIS-C Cases by Age and Vaccination Status, Kentucky April 1, 2020** - June 08, 2022 (N=125)
Vaccination status:

- Patients were matched to KYIR records by name and date of birth. KYIR data through June 6, 2022 was matched for this summary update.
- Five of 125 (4.0%) patients received at least one documented dose of a COVID vaccination before MIS-C onset
  - 4 of 125 (3.2%) patients received 2 documented doses of a COVID vaccination before MIS-C onset
  - 1 of 125 (0.8%) patients received one documented dose of a COVID vaccination before MIS-C onset
- 15 of 125 (12.0%) patients were eligible* to receive at least 1 dose of vaccination at time of MIS-C onset. Of those eligible to receive COVID vaccination prior to MIS-C onset, 10 were unvaccinated.
- 27 of 125 (21.6%) received at least one documented dose of a COVID vaccination after MIS-C onset
- Layered protection to prevent COVID 19 infections is the only known method to prevent subsequent MIS-C.
Is preventing MIS-C worth it?

• Most kids with COVID 19 do not get MIS-C.

• Less than 1% of MIS-C patients die.

• BUT if the patient does develop MIS-C:
  • 6.2 day average hospitalization for MIS-C patients in KY
  • 63% require ICU care, 10% are intubated on a ventilator

• No current evidence that having had MIS-C confers better future immunity or that vaccination is not beneficial for those with MIS-C (but not a well-researched topic).
  • Several month immune system “boost” may be present due to the treatment for MIS-C that includes infusions of pooled donor immunoglobulin (IVIG).
  • Indications from some early research that patient may be more prone to other autoimmune diseases but unsure if that is a predisposition or an outcome.

• Next step: looking at severity of MIS-C when vaccinated.
  • Mild, Moderate, Severe definitions
Pediatric Acute Hepatitis of Unknown Etiology

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June 2022
Situation:

• **Summary**
The Centers for Disease Control and Prevention (CDC) issued Health Alert Network (HAN) Health Update April 21 2022 to provide clinicians and public health authorities with information about an epidemiologic investigation of pediatric cases of hepatitis of unknown etiology in the United States. This investigation focuses on collecting information to describe the epidemiology, etiology, clinical presentation, severity, and risk factors related to illness and to identify any relationship between adenovirus infection or other factors and hepatitis. In the original cohorts, more than half tested positive for adenovirus with more than 90% hospitalized, 14% with liver transplants, and five deaths under investigation*. Because this investigation is ongoing and includes reviewing cases of hepatitis of unknown cause with onset since October 2021, patients under investigation are not limited to current or newly diagnosed pediatric hepatitis illnesses.

• As of June 6, 2022, CDC and state partners are investigating 275 children with hepatitis of unknown origin across 39 states and territories.
Background:

- **Working PUI definition:** Child less than 10 years of age with clinical picture of hepatitis and lab values AST or ALT > 500, adenovirus positive by any testing *or no other cause found*.

- Numbers are evolving daily with weekly updates by CDC. Kentucky has reported 6 PUI (one historic and 5 since the HAN was sent, all recovered without transplant).
Background:

- Pediatric hepatitis can be caused by many things.
  - Part of work up is ruling out things like Hepatitis A, B, C and toxin exposure
  - Not all cases of pediatric hepatitis will fit

- Adenovirus infection is also common.
  - Fecal-oral route transmission and can cause GI or respiratory symptoms
  - Specific type in this case may be adenovirus 41
  - Many places can do some testing for adenovirus (respiratory swab, fecal test or serum) but most places cannot determine type
Background:

• The connection between adenovirus infection and this manifestation of hepatitis is still uncertain, but under investigation.
  • Adenovirus found in about half of the reported cases nationwide (only 2/6 in KY).
  • This does NOT appear to be a new virus or mutation thus far
  • Adenovirus has NOT been seen in the liver biopsies taken
• We need to identify PUIs and get samples to correct labs to determine if there is a biological connection.
  • Sample handling is a little unusual…
    • Local testing recommended
    • Frozen whole blood samples to go through the state lab to the CDC designated typing lab once the PUI/case has a case number assigned
    • Other samples may be requested “if available”—such as swabs, fecal samples and biopsies.
These data were posted on June 8, 2022 and reflect data from October 1, 2021. Reported PUIs are preliminary and subject to change as more data become available. Data will be updated weekly.

Assessment and Recommendations:

• LHD nurses should remain aware of this evolving situation.
• LHD nurses and regional epis should work together to identify, refer and complete paperwork on PUIs.
  • KDPH ID Branch available to help walk through info and real-time management (aka Call me or email me.)
• We do not know yet where this will lead.
  • Clinicians are also receiving updated guidelines on a rolling basis
• Be aware that KY residents may be out of state when diagnosed or treated.
• KDPH resources are available to help.
  • Dr Hodge is the designated CDC point of contact
  • Rachel Zinner in the State Lab can coordinate specimen transfers
  • Amanda Hunt will be managing REDcap database
Child < 10 years old with Hepatitis (AST or ALT > 500) identified. Routine work up does not reveal a cause.

Clinician contacts local or state public health with concern of PUI for pediatric hepatitis of unknown origin.

State and local work together to determine if case meets definition, complete PUI paperwork. Regional EPI or LHD from case home county/jurisdiction to help with investigation form.

PUI paperwork submitted to CDC by KDPH and put in REDCap database. Update REDCap with new results or outcomes information as it occurs.*

Determine what lab samples are available. Send these to DLS for processing to CDC typing lab. Regional EPIs needed to help coordinate this step regardless of patient treatment location.
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