DATE
May 13, 2022

SUBJECT
Updated Recommendations for Adenovirus Testing and Reporting of Children with Acute Hepatitis of Unknown Etiology

INSTRUCTIONS

DISTRIBUTE to your local HAN contacts. This HAN is intended for general sharing of information.
- Time for Forwarding: As Soon As Possible
- Please forward to DPHHS at hhshan@mt.gov
- Remove this cover sheet before redistributing and replace it with your own

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.
- **Information Service**: passes along low level priority messages that do not fit other HAN categories and are for informational purposes only.

Please update your HAN contact information on the Montana Public Health Directory

For technical issues related to the HAN message contact the Emergency Preparedness Section at 1-406-444-0919

For LOCAL HEALTH DEPARTMENT reference only

DPHHS Subject Matter Resource for more information regarding this HAN, contact:

DPHHS CDCP Epidemiology Section
1-406-444-0273

Please ensure that DPHHS is included on your HAN distribution list.

hhshan@mt.gov

DPHHS HAN Website:
www.han.mt.gov
DATE
May 13, 2022

SUBJECT
Updated Recommendations for Adenovirus Testing and Reporting of Children with Acute Hepatitis of Unknown Etiology

BACKGROUND
CDC and state partners are investigating 109 children with hepatitis of unknown origin across 25 states and territories, more than half of whom have tested positive for adenovirus with more than 90% hospitalized, 14% with liver transplants, and five deaths under investigation. No patients matching this clinical picture in Montana have been reported to DPHHS at this time. Healthcare providers in MT who have treated a pediatric patient that meets the clinical criteria described below since October 2021 are requested to report the suspected case to your local health department. [https://dphhs.mt.gov/publichealth/FCSS/countytribalhealthdepts](https://dphhs.mt.gov/publichealth/FCSS/countytribalhealthdepts)

INFORMATION
See CDC HAN 465

RECOMMENDATIONS
Local health departments should notify the CDEpi section at DPHHS of suspect cases by calling 406-444-0273. Adenovirus testing should be considered for pediatric patients with hepatitis of unknown etiology. CDC recommends NAAT testing of multiple specimen types including whole blood, respiratory, stool, and liver tissue (if liver biopsy is clinically indicated). CDEpi and the Montana State Public Health Lab will work with local health departments and providers to coordinate testing of suspect cases.
Updated Recommendations for Adenovirus Testing and Reporting of Children with Acute Hepatitis of Unknown Etiology

Summary
The Centers for Disease Control and Prevention (CDC) is issuing this Health Alert Network (HAN) Health Update to provide clinicians and public health authorities with updated 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. As of May 5, 2022, CDC and state partners are investigating 109 children with hepatitis of unknown origin across 25 states and territories, more than half of whom have 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.

This HAN Health Update also provides updated recommendations for testing specimens from patients under investigation. It is an update to a HAN Health Advisory that CDC issued on April 21, 2022, that initially notified clinicians and public health authorities of children identified with hepatitis of unknown origin and adenovirus infection.

Background
A cluster of pediatric cases of hepatitis without an apparent etiology was identified and reported to CDC in November 2021. A possible association between pediatric hepatitis and adenovirus infection is under investigation after laboratory testing identified adenovirus infection in all nine patients in the initial cluster; the five specimens that could be typed were all adenovirus type 41. Investigators continue to examine the role of other possible causes and identify contributing factors.

Recommendations for Clinicians
- Clinicians should continue to follow standard practice for evaluating and managing patients with hepatitis of known and unknown etiology.
- Clinicians are recommended to consider adenovirus testing for patients with hepatitis of unknown etiology and to report such cases to their state or jurisdictional public health authorities.
- Because the potential relationship between adenovirus infection and hepatitis is still under investigation, clinicians should consider collecting the following specimen types if available from pediatric patients with hepatitis of unknown cause for adenovirus detection:
  - Blood specimen collected in Ethylenediaminetetraacetic Acid (EDTA) (whole blood, plasma, or serum); whole blood is preferred to plasma and serum
  - Respiratory specimen (nasopharyngeal swab, sputum, or bronchioalveolar lavage [BAL])
  - Stool specimen or rectal swab; a stool specimen is preferred to a rectal swab
  - Liver tissue, if a biopsy was clinically indicated, or if tissue from native liver explant or autopsy is available:
    - Formalin-fixed, paraffin embedded (FFPE) liver tissue
• Fresh liver tissue, frozen on dry ice or liquid nitrogen immediately or as soon as possible, and stored at ≤ -70°C

Nucleic acid amplification testing (NAAT), such as polymerase chain reaction (PCR), is preferred for adenovirus detection (currently not available for FFPE liver biopsy or native liver explant). Testing whole blood by PCR is more sensitive to and is preferred over testing plasma by PCR.

Where possible, clinical specimens should be tested locally to ensure timely results for patient care. For any diagnostic testing needs beyond the local capacity, CDC recommends that clinicians contact their state public health laboratory.

For More Information
- Expanded testing guidance: Clinical Guidance for Adenovirus Testing and Typing of Patients Under Investigation
- Information for state health departments and laboratories: Instructions for Adenovirus Diagnostic Testing, Typing and Submission
- Email ncirdvdgast@cdc.gov with additional questions

The Centers for Disease Control and Prevention (CDC) protects people's health and safety by preventing and controlling diseases and injuries; enhances health decisions by providing credible information on critical health issues; and promotes healthy living through strong partnerships with local, national, and international organizations.

Categories of Health Alert Network messages:
Health Alert Requires immediate action or attention; highest level of importance
Health Advisory May not require immediate action; provides important information for a specific incident or situation
Health Update Unlikely to require immediate action; provides updated information regarding an incident or situation
HAN Info Service Does not require immediate action; provides general public health information

# #This message was distributed to state and local health officers, state and local epidemiologists, state and local laboratory directors, public information officers, epidemiologists, HAN coordinators, and clinician organizations##