



MISSISSIPPI STATE DEPARTMENT OF HEALTH

**This is an official
MS Health Alert Network (HAN) Alert**

MESSAGE ID: MSHAN-20220421-00570-ALT (Health Alert)
RECIPIENTS: All Physicians, Hospitals, ERs, ICPs, NPs, PAs, and
Healthcare Providers – Statewide
Thursday, April 21, 2022
SUBJECT: Recommendations for Adenovirus Testing and
Reporting of Children with Acute Hepatitis of Unknown
Etiology

Dear Colleagues,

- The Centers for Disease Control and Prevention (CDC) released a Health Advisory to provide notification of a cluster of children with acute hepatitis and adenovirus infection.
- To date, 9 children in Alabama have been identified with acute hepatitis and adenovirus infection between October 2021 and February 2022. Five that were sequenced were positive for **Adenovirus type 41 infection**.
- Similar cases of pediatric hepatitis who tested negative for hepatitis viruses A, B, C, D and E have been identified in the U.K.; some with adenovirus.
- To date, no similar cases have been reported in Mississippi.

The Mississippi State Department of Health (MSDH) is asking physicians and providers to:

- Consider adenovirus testing in children with acute hepatitis of unknown etiology. PCR testing is preferable and can be performed on respiratory, blood or stool specimens.
- Report cases of children <10 years of age with elevated aspartate aminotransferase (AST) or alanine aminotransferase (ALT) (>500 U/L) who have an **unknown etiology** for their hepatitis (**with or without any adenovirus testing results and independent of the results**).
- Reports can be made to the MSDH Office of Epidemiology at 601-576-7725.

Please see below for the full CDC Advisory.

Regards,

Paul Byers, MD
State Epidemiologist



MISSISSIPPI STATE DEPARTMENT OF HEALTH

This is an official
CDC HEALTH ADVISORY

Distributed via the CDC Health Alert Network
April 21, 2022, 11:00 AM ET
CDCHAN-00462

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 Advisory to notify clinicians and public health authorities of a cluster of children identified with hepatitis and adenovirus infection. In November 2021, clinicians at a large children's hospital in Alabama notified CDC of five pediatric patients with significant liver injury, including three with acute liver failure, who also tested positive for adenovirus. All children were previously healthy. None had COVID-19. Case-finding efforts at this hospital identified four additional pediatric patients with hepatitis and adenovirus infection for a total of nine patients admitted from October 2021 through February 2022; all five that were sequenced had adenovirus type 41 infection identified. In two patients, plasma samples were negative for adenovirus by quantitative polymerase chain reaction (qPCR), but both patients were positive when retested using whole blood. Two patients required liver transplant; no patients died. A possible association between pediatric hepatitis and adenovirus infection is currently under investigation. Cases of pediatric hepatitis in children who tested negative for hepatitis viruses A, B, C, D, and E were reported earlier this month in the United Kingdom, including some with adenovirus infection [1].

This Health Advisory serves to notify US clinicians who may encounter pediatric patients with hepatitis of unknown etiology to consider adenovirus testing and to elicit reporting of such cases to state public health authorities and to CDC. Nucleic acid amplification testing (NAAT, e.g. PCR) is preferred for adenovirus detection and may be performed on respiratory specimens, stool or rectal swabs, or blood.

Background

Hepatitis is inflammation of the liver that can be caused by viral infections, alcohol use, toxins, medications, and certain other medical conditions. In the United States, the most common causes of viral hepatitis are hepatitis A, hepatitis B, and hepatitis C viruses [2]. Signs and symptoms of hepatitis include fever, fatigue, loss of appetite, nausea, vomiting, abdominal pain, dark urine, light-colored stools, joint pain, and jaundice [2]. Treatment of hepatitis depends on the underlying etiology.

Adenoviruses are double-stranded DNA viruses that spread by close personal contact, respiratory droplets, and fomites [3]. There are more than 50 types of immunologically distinct adenoviruses that can cause infections in humans. Adenoviruses most commonly cause respiratory illness but depending on the adenovirus type they can cause other illnesses such as gastroenteritis, conjunctivitis, cystitis, and, less commonly, neurological disease [3]. There is no specific treatment for adenovirus infections.

Adenovirus type 41 commonly causes pediatric acute gastroenteritis, which typically presents as diarrhea, vomiting, and fever; it can often be accompanied by respiratory symptoms [4]. While there have been case reports of hepatitis in immunocompromised children with adenovirus type 41 infection, adenovirus type 41 is not known to be a cause of hepatitis in otherwise healthy children [5, 6].

Recommendations

1. Clinicians should consider adenovirus testing in pediatric patients with hepatitis of unknown etiology. NAAT (e.g. PCR) is preferable and may be done on respiratory specimens, stool or rectal swabs, or blood.



2. Anecdotal reports suggest that testing whole blood by PCR may be more sensitive than testing plasma by PCR; therefore, testing of whole blood could be considered in those without an etiology who tested negative for adenovirus in plasma samples.

Request for Notification of Possible Cases

CDC is requesting notification from clinicians or state public health authorities of children <10 years of age with elevated aspartate aminotransferase (AST) or alanine aminotransferase (ALT) (>500 U/L) who have an unknown etiology for their hepatitis (with or without any adenovirus testing results, independent of the results) since October 1, 2021.

Please email CDC at ncirddvdgast@cdc.gov to notify of any cases meeting the above criteria or with any related questions.

If patients are still under medical care or have residual specimens available, please save and freeze them for possible additional testing and contact CDC at ncirddvdgast@cdc.gov for additional instructions.

For More Information

[Division of Viral Hepatitis | CDC](#)

[Adenovirus | CDC](#)

References

[1] World Health Organization. Acute hepatitis of unknown aetiology - the United Kingdom of Great Britain and Northern Ireland. Disease Outbreak News [Internet]. 2022 Apr 15; Available from:

<https://www.who.int/emergencies/disease-outbreak-news/item/acute-hepatitis-of-unknown-aetiology---the-united-kingdom-of-great-britain-and-northern-ireland>

[2] Hepatitis Webpage. Centers for Disease Control and Prevention. Available from:

<https://www.cdc.gov/hepatitis/abc/index.htm>

[3] Adenoviruses Webpage. Centers for Disease Control and Prevention. Available from:

<http://www.cdc.gov/adenovirus/index.html>

[4] Kang G. Viral Diarrhea. International Encyclopedia of Public Health [Internet]. Elsevier; 2017. P. 260-7.

Available from <https://www.sciencedirect.com/referencework/9780128037089/international-encyclopedia-of-public-health>

[5] Munoz FM, Piedra PA, Demmler GJ. Disseminated Adenovirus Disease in Immunocompromised and Immunocompetent Children. CLIN INFECT DIS. 1998. Nov;27(5):1194-200.

<https://doi.org/10.1086/514978>

[6] Peled N, Nakar C, Huberman H, Scherf E, Samra Z, Finkelstein Y, et al. Adenovirus Infection in Hospitalized Immunocompetent Children. Clin Pediatr (Phila). 2004 Apr;43(3):223-9.

<https://doi.org/10.1177/000992280404300303>

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.



Alerting Message Specification Settings

Originating Agency: Mississippi State Department of Health
Alerting Program: MS Health Alert Network (MS HAN)
Message Identifier: MSHAN-20220421-00570-ALT
Program (HAN) Type: Health Alert
Status (Type): Actual ()
Message Type: Alert
Reference: MSHAN-00570
Severity: Unknown
Acknowledgement: No
Sensitive: Not Sensitive
Message Expiration: Undetermined
Urgency: Undetermined
Delivery Time: 600 minutes

Definition of Alerting Vocabulary and Message Specification Settings

Originating Agency: A unique identifier for the agency originating the alert.

Alerting Program: The program sending the alert or engaging in alerts and communications using PHIN Communication and Alerting (PCA) as a vehicle for their delivery.

Message Identifier: A unique alert identifier that is generated upon alert activation (MSHAN-yyymmdd-hhmm-TTT (**ALT=Health Alert**, **ADV=Health Advisory**, **UPD=Health Update**, **MSG/INFO=Message/Info Service**)).

Program (HAN) Type: 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.

Health Info Service: Provides Message / Notification of general public health information; unlikely to require immediate action.

Status (Type):

- Actual: Communication or alert refers to a live event
- Exercise: Designated recipients must respond to the communication or alert
- Test: Communication or alert is related to a technical, system test and should be disregarded

Message Type:

- Alert: Indicates an original Alert
- Update: Indicates prior alert has been Updated and/or superseded
- Cancel: Indicates prior alert has been cancelled
- Error: Indicates prior alert has been retracted



Reference: For a communication or alert with a Message Type of “Update” or “Cancel”, this attribute contains the unique Message Identifier of the original communication or alert being updated or cancelled. “n/a” = Not Applicable.

Severity:

Extreme:	Extraordinary threat to life or property
Severe:	Significant threat to life or property
Moderate:	Possible threat to life or property
Minor:	Minimal threat to life or property
Unknown:	Unknown threat to life or property

Acknowledgement: Indicates whether an acknowledgement on the part of the recipient is required to confirm that the alert was received, and the timeframe in which a response is required (Yes or No).

Sensitive:

Sensitive:	Indicates the alert contains sensitive content
Not Sensitive:	Indicates non-sensitive content

Message Expiration: Undetermined.

Urgency: Undetermined. Responsive action should be taken immediately.

Delivery Time: Indicates the timeframe for delivery of the alert (15, 60, 1440, 4320 minutes (.25, 1, 24, 72 hours)).