



## This is an official CDC Health Advisory

Distributed via Health Alert Network  
April 21, 2022; 1:30 PM  
10513-CHA-04-21-2022-HEP

### **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](mailto: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](mailto:ncirddvdgast@cdc.gov) for additional instructions.

## Resources for Additional 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>

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

## DHEC contact information for reportable diseases and reporting requirements

Reporting of **acute viral hepatitis** is consistent with South Carolina Law requiring the reporting of diseases and conditions to your state or local public health department. (State Law # 44-29-10 and

Regulation # 61-20) as per the DHEC 2022 List of Reportable Conditions available at:  
<https://www.scdhec.gov/sites/default/files/Library/CR-009025.pdf>

Federal HIPAA legislation allows disclosure of protected health information, without consent of the individual, to public health authorities to collect and receive such information for the purpose of preventing or controlling disease. (HIPAA 45 CFR §164.512).

<b>Regional Public Health Offices – 2022</b>			
Mail or call reports to the Epidemiology Office in each Public Health Region			
<b>MAIL TO:</b>			
<b><u>Lowcountry</u></b> 4050 Bridge View Drive, Suite 600 N. Charleston, SC 29405 Fax: (843) 953-0051	<b><u>Midlands</u></b> 2000 Hampton Street Columbia, SC 29204 Fax: (803) 576-2993	<b><u>Pee Dee</u></b> 1931 Industrial Park Road Conway, SC 29526 Fax: (843) 915-6506	<b><u>Upstate</u></b> 352 Halton Road Greenville, SC 29607 Fax: (864) 282-4373
<b>CALL TO:</b>			
<b><u>Lowcountry</u></b> Allendale, Bamberg, Beaufort, Berkeley, Calhoun, Charleston, Colleton, Dorchester, Hampton, Jasper, Orangeburg  Office: (843) 441-1091 Nights/Weekends: (843) 441-1091	<b><u>Midlands</u></b> Aiken, Barnwell, Chester, Edgefield, Fairfield, Kershaw, Lancaster, Lexington, Newberry, Richland, Saluda, York  Office: (888) 801-1046 Nights/Weekends: (888) 801-1046	<b><u>Pee Dee</u></b> Clarendon, Chesterfield, Darlington, Dillon, Florence, Georgetown, Horry, Lee, Marion, Marlboro, Sumter, Williamsburg  Office: (843) 915-8886 Nights/Weekends: (843) 409-0695	<b><u>Upstate</u></b> Abbeville, Anderson, Cherokee, Greenville, Greenwood, Laurens, McCormick, Oconee, Pickens, Spartanburg, Union  Office: (864) 372-3133 Nights/Weekends: (864) 423-6648
<b>For information on reportable conditions, see</b> <a href="https://www.scdhec.gov/ReportableConditions">https://www.scdhec.gov/ReportableConditions</a>		<b><u>DHEC Bureau of Communicable Disease Prevention &amp; Control</u></b> <b>Division of Acute Disease Epidemiology</b> 2100 Bull St • Columbia, SC 29201 Phone: (803) 898-0861 • Fax: (803) 898-0897 Nights / Weekends: 1-888-847-0902	

Categories of Health Alert messages:

<b>Health Alert</b>	Conveys the highest level of importance; warrants immediate action or attention.
<b>Health Advisory</b>	Provides important information for a specific incident or situation; may not require immediate action.
<b>Health Update</b>	Provides updated information regarding an incident or situation; unlikely to require immediate action.
<b>Info Service</b>	Provides general information that is not necessarily considered to be of an emergent nature.