

**Center for Policy, Planning and Evaluation  
Division of Epidemiology–Disease Surveillance and Investigation**

May 3, 2022

**Health Notice for District of Columbia Health Care Providers**  
**CALL FOR CASES: Adenovirus Testing and Reporting of Children**  
**with Acute Hepatitis of Unknown Etiology****SUMMARY**

On April 21, 2022, the Centers for Disease Control and Prevention (CDC) published a health advisory alerting clinicians and public health authorities to a cluster of 9 children with hepatitis and adenovirus infection identified in Alabama<sup>1</sup>. CDC is investigating this association between pediatric hepatitis and adenovirus. The cases occurred between October 2021 and February 2022. A growing number of similar cases of pediatric hepatitis have been reported in Europe. As of April 29, 2022, there have been no reports of hepatitis and adenovirus infection among pediatric patients in the District of Columbia. CDC has issued recommendations for testing and reporting for pediatric cases of hepatitis of unknown etiology. Clinicians are instructed to report all such cases to DC Health to help local public health authorities and the CDC monitor occurrence as well as characterize factors associated with this illness. This health notice provides recommendations, reporting guidelines, and resources on hepatitis and adenovirus infection.

**BACKGROUND**

In November 2021, CDC was notified of a cluster of 5 children under the age of 10 with severe acute hepatitis and adenovirus infection, including 3 with acute liver failure. Cases occurred at a large children's hospital in Alabama. Case finding efforts identified 4 additional cases. All 9 cases tested positive for adenovirus and negative for SARS-CoV-2. Two patients required liver transplant. All cases were previously healthy. No deaths occurred. The 5 cases that were sequenced were positive for adenovirus type 41. In 2 of the 5 sequenced cases, plasma samples had tested negative for adenovirus by quantitative polymerase chain reaction (qPCR), and subsequent whole blood samples tested positive.

On April 5, 2022, the World Health Organization (WHO) was notified of 10 cases of severe acute hepatitis of unknown etiology in previously healthy children under the age of 10 in central Scotland.<sup>2</sup> Laboratory testing for Hepatitis A, B, C and E (and D as applicable) was negative in all cases. By April 8, 2022, 74 total cases had been identified throughout the United Kingdom.

As of May 3, 2022, at least 228 cases have been reported in 20 countries<sup>3</sup>. As of April 21, 2022, cases ranged in age from 1 month to 16 years old, with 17 children requiring liver transplant and at least 1 death reported in Europe. Worldwide, adenovirus has been detected in at least 74 cases, adenovirus type 41 in 18 cases, SARS-CoV-2 infection in 20 cases, and coinfection with adenovirus and SARS-CoV-2 in 19 cases<sup>4</sup>. No other epidemiological risk factors have been identified to date, including recent international travel. Further investigations are ongoing to understand the etiology of these cases.

Hepatitis is a disease of liver inflammation. Hepatitis has many causes including 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 virus. Signs and symptoms of hepatitis include fever, fatigue, loss of appetite, nausea, vomiting, abdominal pain, dark urine, light-colored stools, joint pain, and jaundice<sup>5</sup>. Treatment of hepatitis depends on the underlying etiology.

Adenoviruses are doubled-stranded DNA viruses that spread by close contact, respiratory droplets, and fomites<sup>3</sup>. There are more than 50 types of immunologically distinct adenoviruses that can cause infections in humans. Adenovirus infections are endemic in pediatric populations. Adenoviruses most commonly

cause respiratory illness but can cause other illnesses such as gastroenteritis, conjunctivitis, cystitis, and, less commonly, neurological disease. Adenovirus type 41 commonly causes pediatric acute gastroenteritis and has not previously been known to cause hepatitis in healthy children. There is no specific treatment for adenovirus infections<sup>6</sup>.

## **RECOMMENDATIONS**

- **CASE MANAGEMENT:** All children with elevated aspartate aminotransferase (AST) or alanine aminotransferase (ALT) greater than 500 U/ml should undergo appropriate clinical evaluation and workup. Testing for adenovirus should be considered for pediatric patients with hepatitis of unknown etiology.
- **CASE REPORTING:** DC Health is requesting notification from healthcare providers of children <10 years of age with elevated AST or ALT levels greater than 500 U/L who have an unknown etiology for their hepatitis (with or without adenovirus testing results and independent of results). Report cases immediately by submitting a [Notifiable Disease and Condition Case Report Form](#) online using the DC Reporting and Surveillance Center (DCRC), which can be found on our Infectious Diseases website ([dchealth.dc.gov/service/infectious-diseases](https://dchealth.dc.gov/service/infectious-diseases))
  - Submit clinical notes including laboratory test results for all patients when reporting cases. DC Health may reach out to obtain any additional information if needed.
- **LABORATORY TESTING:**
  - Nucleic acid amplification testing (NAAT e.g., PCR) is the preferred method of testing for adenovirus. NAAT testing may be performed on respiratory specimens, stool or rectal swabs, or blood.
  - Anecdotal reports suggest that whole blood testing may be more sensitive for adenovirus than plasma samples. Testing of whole blood could be considered for pediatric patients with hepatitis of unknown etiology who test negative for adenovirus with plasma samples.

**NOTE:** If assistance is needed for testing, please collect the necessary specimens, and submit them with the required [lab forms](#) to DC Public Health Lab via your normal route for specimen submission.

## **REFERENCES**

1. Centers for Disease Control and Prevention Health Alert Network, Recommendations for Adenovirus Testing and Reporting of Children with Acute Hepatitis of Unknown Etiology [emergency.cdc.gov/han/2022/han00462.asp](https://emergency.cdc.gov/han/2022/han00462.asp)
2. World Health Organization. Acute hepatitis of unknown aetiology – the United Kingdom of Great Britain and Northern Ireland. 2022 Apr 15; Available from: [who.int/emergencies/disease-outbreak-news/item/acute-hepatitis-of-unknown-aetiology---the-united-kingdom-of-great-britain-and-northern-ireland](https://who.int/emergencies/disease-outbreak-news/item/acute-hepatitis-of-unknown-aetiology---the-united-kingdom-of-great-britain-and-northern-ireland)
3. Reuters. At least 228 probable cases of child hepatitis so far: WHO. 2022 May 3; Available from [reuters.com/business/healthcare-pharmaceuticals/least-228-probable-cases-child-hepatitis-so-far-who-2022-05-03/](https://reuters.com/business/healthcare-pharmaceuticals/least-228-probable-cases-child-hepatitis-so-far-who-2022-05-03/)
4. World Health Organization. Multi-Country-Acute, severe hepatitis of unknown origin in children. 2022 Apr 23; Available from: [who.int/emergencies/disease-outbreak-news/item/2022-DON376](https://who.int/emergencies/disease-outbreak-news/item/2022-DON376)
5. Hepatitis Webpage. Centers for Disease Control and Prevention. Available from: [cdc.gov/hepatitis/abc/index.htm](https://cdc.gov/hepatitis/abc/index.htm)
6. Adenoviruses Webpage. Centers for Disease Control and Prevention. Available from: [cdc.gov/adenovirus/index.html](https://cdc.gov/adenovirus/index.html)

**Please contact the DC Health Division of Epidemiology–Disease Surveillance and Investigation at:**  
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