



Health Alert Network Message

22-14: Recommendations for Adenovirus Testing and Reporting of Children with Acute Hepatitis of Unknown Etiology

Origination Date:
April 22, 2022

Revision Dates (List All Revision Dates):

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

Summary

The Louisiana Department of Health (LDH) is requesting notification from clinicians 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. **Providers should notify LDH of suspect cases by calling the Infectious Disease Epidemiology Section (IEDpi) 24/7 clinician hotline: 800-256-2748.**

On Tuesday, April 21, the Centers for Disease Control and Prevention (CDC) issued a 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].

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 doubled-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].

Request for Notification of Possible Cases in Louisiana

LDH is requesting notification from clinicians of children <10 years of age with elevated AST or 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.

Providers should notify LDH of suspect cases by calling the Infectious Disease Epidemiology Section (IEDpi) 24/7 clinician hotline: 800-256-2748.

Testing 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 at the LDH laboratory if necessary. A stool sample in Cary-Blair should be collected for testing using the BioFire FilmArray® Gastrointestinal (GI) Panel. More detailed instructions can be found at [LDH lab Biofire GI Panel informational sheet](#).
2. If a stool specimen cannot be obtained, LDH will work with the clinician to facilitate other options for testing.
3. If patients are still under medical care or have residual specimens available, please contact IDEpi (800-256-2748) for further guidance.

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>