



COUNTY OF SAN LUIS OBISPO HEALTH AGENCY  
PUBLIC HEALTH DEPARTMENT

Penny Borenstein, MD, MPH *Health Officer/Public Health Director*

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## PROVIDER HEALTH ADVISORY

**Date:** April 22, 2022

**Contact:** Rick Rosen, MD, MPH, 805-781-5500, [frosen@co.slo.ca.us](mailto:frosen@co.slo.ca.us)

## Adenovirus Testing and Reporting of Children with Acute Hepatitis

The California Department of Public Health (CDPH) and the Centers for Disease Control and Prevention (CDC) have both issued an advisory to notify clinicians and public health authorities of a cluster of children identified with hepatitis and adenovirus infection. CDPH requests that clinicians who may encounter pediatric patients with hepatitis of unknown etiology:

- **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.
- **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, independent of the results) since October 1, 2021 to the County of San Luis Obispo Public Health Department. Reporting should occur within 24 hours of case identification.

### To test for adenovirus:

Submit specimens to the San Luis Obispo County Public Health Laboratory (SLOPHL):

- Be sure to include "Suspect Adenovirus 41" on requisition forms.
- **For whole blood specimens:**
  - Collect in EDTA.
- **For respiratory specimens (nasopharyngeal swabs):**
  - Refrigerate at 2-8 degrees Celsius.
  - Include test code 6310 (Respiratory PCR Panel) on requisition form.
- **For stool specimens:**
  - Store specimens in Cary-Blair Medium.
  - Keep specimens at room temperature.
  - Include test code 6500 (Gastro Pathogen PCR Panel) on requisition form.

### To report cases:

**Call the San Luis Obispo County Health Officer.** Call 805-781-5500 (M-F, 8 a.m.–5 p.m.) or 805-781-4553 (weekends and after hours).

### For more information:

Please see the attached CDPH advisory and the CDC advisory or visit:

<https://emergency.cdc.gov/han/2022/han00462.asp>.

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### Public Health Department

2191 Johnson Avenue | San Luis Obispo, CA 93401 | (P) 805-781-5500 | (F) 805-781-5543

[www.slopublichealth.org](http://www.slopublichealth.org)



TOMÁS J. ARAGÓN, M.D., Dr.P.H.  
Director and State Public Health Officer

State of California—Health and Human Services Agency  
California Department of Public Health



GAVIN NEWSOM  
Governor

**Health Advisory: Recommendations for Adenovirus Testing and Reporting of Children with Acute Hepatitis of Unknown Etiology**  
**April 21, 2022**

**Situation Summary**

The California Department of Public Health is issuing this advisory to notify clinicians of clusters of children identified with hepatitis and adenovirus infection, and to request reporting of cases to the clinician's [Local Health Department \(LHD\)](#).

[CDC issued a Health Advisory on April 21, 2022 regarding a cluster of children with hepatitis associated with adenovirus.](#) The cluster of cases occurred in Alabama, with illness onset from October 2021 to February 2022. Case-finding efforts have identified a total of nine patients; five 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. Since January 2022, [similar cases have been recognized in Europe](#). Many cases have tested positive for adenovirus.

**Reporting to Public Health**

CDPH requests that clinicians report cases of children meeting the following working case definition to their LHD's [communicable disease control program](#) within one business day.

- Children <10 years of age with elevated aspartate aminotransferase (AST) or alanine aminotransferase (ALT) (>500 U/L) AND
- who have an unknown etiology for their hepatitis (with or without any adenovirus testing results, independent of the results) since October 1, 2021

Other etiologies for acute hepatitis should also be considered and ruled out, including acute hepatitis A, B, and C as appropriate. CDPH will notify CDC of these cases.

**Testing Recommendations**

Clinicians should consider adenovirus testing in pediatric patients with hepatitis of unknown etiology. Specimens should be collected as soon as possible in the clinical course of illness. Adenovirus 40/41 may not be as readily detected by respiratory virus panel testing as other adenovirus types, therefore collection of stool and blood specimens is recommended in addition to standard respiratory specimens (e.g, nasopharyngeal swab). Of the adenovirus-



associated hepatitis cases in Alabama and Europe, no single specimen type was consistently positive.

Blood (collected in EDTA tubes) has been more sensitive in detection of adenovirus than serum. NAAT testing (e.g., PCR) is preferable and should be performed on respiratory, stool, and blood samples. At this time the role for adenovirus serology is unclear.

NOTE: Heparin should not be used as the blood anti-coagulant because it may interfere with PCR.

Depending on your facility, adenovirus testing can be performed either within facility or through a commercial lab. Clinical lab testing should include:

- Stool adenovirus 40/41 PCR (often included as GI panel PCR panel, e.g., Bio Fire) or EIA
- Respiratory viral panel that includes adenovirus detection
- Whole blood (collected in EDTA) adenovirus qualitative PCR. (This test is offered by ARUP laboratories and may be available at other commercial labs as well. Detection in whole blood is likely to be more sensitive than in serum.)

All positive adenovirus specimens from suspect cases should be sent to the State CDPH/VRDL for further characterization including typing and whole genome sequencing. CDPH will work closely with LHJs and clinical and commercial laboratories to have specimens forwarded to CDPH/VRDL; please email [VRDL.Mail@cdph.ca.gov](mailto:VRDL.Mail@cdph.ca.gov) or call 510-307-8585 for further information or guidance on specimen submission to CDPH/VRDL.

### **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. Signs and symptoms of hepatitis include fever, fatigue, loss of appetite, nausea, vomiting, abdominal pain, dark urine, light-colored stools, joint pain, and jaundice. Treatment of hepatitis depends on the underlying etiology.

Adenovirus type 41 commonly causes pediatric acute gastroenteritis, which typically presents as diarrhea, vomiting, and fever; it can often be accompanied by respiratory symptoms. 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.

### **For More Information**

[HAN: Recommendations for Adenovirus Testing and Reporting of Children with Acute Hepatitis of Unknown Etiology | CDC](#)

[Division of Viral Hepatitis | CDC](#)

[Adenovirus | CDC](#)

**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](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.

### **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.*

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**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, HAN coordinators, and clinician organizations##