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**PUBLIC HEALTH ADVISORY**  
**RECOMMENDATIONS FOR ADENOVIRUS TESTING AND REPORTING**  
**OF CHILDREN WITH ACUTE HEPATITIS OF UNKNOWN ETIOLOGY**  
**MAY 3, 2022**

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**Situation Update**

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.

**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.

**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 Riverside County Public Health lab who will forward them 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.

### **Reporting to Public Health**

Cases of children meeting the following working case definition should be reported to RUHS – Public Health within one business day by fax (951)358-5446 or CalREDIE for those who are enrolled.

- 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.

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