

**Communicable Disease Epidemiology
and Immunization Section**

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www.kingcounty.gov/health

Health Advisory: Recommendations for Adenovirus Testing and Reporting of Children with Acute Hepatitis of Unknown Etiology, May 17, 2022

Summary

The Centers for Disease Control and Prevention (CDC) issued a [Health Alert Network \(HAN\) Health Update](#) on May 11, 2022, to provide Healthcare providers with updated information about an epidemiologic investigation of pediatric cases of hepatitis of unknown etiology in the United States. This is an update to the [HAN Health Advisory issued by CDC on April 21, 2022](#). This investigation focuses on collecting information to describe the epidemiology, etiology, clinical presentation, severity, and risk factors related to illness and identify any relationship between adenovirus infection or other factors and acute hepatitis of unknown etiology in children.

Actions Requested

- **Immediately report suspected cases that meet CDC's current case criteria to Public Health Seattle & King County (PHSKC) at (206) 296-4774.**
 - Case definition
 - Children <10 years of age
 - Elevated Aspartate Aminotransferase (AST) or Alanine Aminotransferase (ALT) > 500 IU/L
 - Unknown etiology of acute hepatitis, with or without adenovirus testing results, since October 1, 2021
- Follow standard practice for evaluating and managing patients with hepatitis of known and unknown etiology.
- Consider [adenovirus testing](#) for patients with hepatitis of unknown etiology.
- Collect the following specimen types:
 - Blood specimen
 - Collect 1 mL of whole blood, serum, or plasma in a purple top EDTA tube (whole blood is preferred)
 - Submit to a Reference Lab (Quest Diagnostics or ARUP) able to perform adenovirus PCR testing using whole blood specimens in EDTA
 - Do NOT freeze whole blood for diagnostic PCR
 - Respiratory specimen
 - Collect nasopharyngeal (NP) swab in VTM/UTM, 1 ml of sputum, or bronchioalveolar lavage (BAL)
 - Stool specimen
 - Collect 1 gm of stool in a sterile container, or a rectal swab in VTM/UTM (stool is preferred to rectal swab)
 - Liver tissue, if a biopsy was clinically indicated, or if tissue from native liver explant or autopsy is available:
 - Formalin-fixed, paraffin-embedded (FFPE) liver tissue
 - Fresh liver tissue, frozen on dry ice or liquid nitrogen immediately or as soon as possible, and stored at $\leq -70^{\circ}\text{C}$

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Background

A cluster of pediatric cases of hepatitis without an apparent etiology was identified and reported to CDC in November 2021. A possible association between pediatric hepatitis and adenovirus infection is under investigation after laboratory testing identified adenovirus infection in all 9 patients in the initial cluster; the five specimens that could be typed were all adenovirus type 41. As of May 5, 2022, CDC and state partners are investigating 109 children with hepatitis of unknown origin across 25 states and territories, more than half of whom have tested positive for adenovirus, with more than 90% hospitalized, 14% with liver transplants, and five deaths under investigation. Because this investigation is ongoing and includes reviewing cases of hepatitis of unknown cause with onset since October 2021, patients under investigation are not limited to current or newly diagnosed pediatric hepatitis illnesses. Investigators continue to examine the role of other possible causes and identify contributing factors.

Globally, as of April 21, 2022, the World Health Organization (WHO) reported at least 169 cases of acute hepatitis of unknown origin from 11 countries (WHO case definition goes up to 16 years of age, as opposed to 10 years of age per CDC). Cases have been reported in the United Kingdom (114), Spain (13), Israel (12), Denmark (6), Ireland (<5), Netherlands (4), Italy (4), Norway (2), France (2), Romania (1), and Belgium (1). [Note: At that time, the US had only 9 reported cases which has since increased to 109 as noted above. It is likely that the number of cases overall, as well as number of countries affected, will increase once WHO updates their estimates soon.]

Resources

- Expanded testing guidance: [Clinical Guidance for Adenovirus Testing and Typing of Patients Under Investigation](#)
- Information for state health departments and laboratories: [Instructions for Adenovirus Diagnostic Testing, Typing, and Submission](#)
- Email ncirddvdgast@cdc.gov with additional questions
- [Acute hepatitis of unknown etiology](#): The United Kingdom of Great Britain and Northern Ireland-World Health Organization
- [Hepatitis Webpage](#): Centers for Disease Control and Prevention
- [Adenoviruses Webpage](#): Centers for Disease Control and Prevention.
- [International Encyclopedia of Public Health](#): Viral Diarrhea - Elsevier; 2017. P. 260-7
- [Adenovirus Infection in Hospitalized Immunocompetent Children](#): Clin Pediatr (Phila). 2004 Apr;43(3):223-9.
- [Disseminated Adenovirus Disease in Immunocompromised and Immunocompetent Children](#): CLIN INFECT DIS. 1998. Nov;27(5):1194-200.
- [Instructions for Adenovirus Diagnostic Testing, Typing, and Submission | CDC](#)
- [Adenovirus DNA by PCR, Qualitative, Body Fluid or Stool | MLabs \(umich.edu\)](#)
- [Adenovirus, Quantitative PCR | ARUP Laboratories Test Directory](#)
- [Adenovirus DNA, Qualitative, Real-Time PCR | Test Detail | Quest Diagnostics](#)