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Health Advisory

To: Healthcare Providers

From: David Canton, DO, MPH, JD, Health Officer (signed original on file)

Date: May 12, 2022

Re: **Updated** Recommendations for Adenovirus Testing and Reporting of Children with Acute Hepatitis of Unknown Etiology

The Centers for Disease Control and Prevention (CDC) is investigating pediatric cases of hepatitis of unknown etiology in the United States. This investigation focuses on collecting information to describe the epidemiology, etiology, clinical presentation, severity, and risk factors related to illness and to identify any relationship between adenovirus infection or other factors and hepatitis.

Background

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.

Recommendations for Clinicians

- Clinicians should continue to follow standard practice for evaluating and managing patients with hepatitis of known and unknown etiology.
- Clinicians are recommended to consider [adenovirus testing](#) for patients with hepatitis of unknown etiology and to report such cases to Butte County Department of Public Health.
- Because the potential relationship between adenovirus infection and hepatitis is still under investigation, clinicians should consider collecting the following specimen types if available from pediatric patients with hepatitis of unknown cause for adenovirus detection:
 - Blood specimen collected in Ethylenediaminetetraacetic Acid (EDTA) (whole blood, plasma, or serum); whole blood is preferred to plasma and serum)
 - Respiratory specimen (nasopharyngeal swab, sputum, or bronchioalveolar lavage [BAL])
 - Stool specimen or rectal swab; a stool specimen is preferred to a 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 $\leq -70^{\circ}\text{C}$

Nucleic acid amplification testing (NAAT), such as polymerase chain reaction (PCR), is preferred for adenovirus detection (currently not available for FFPE liver biopsy or native liver explant). Testing whole blood by PCR is more sensitive to and is preferred over testing plasma by PCR.

Reporting

Healthcare providers should report to BCPH **within one business day** cases meeting the following working case definition:

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

Please report to BCPH via [Confidentially Morbidity Report \(CMR\)](#) to be faxed to 530.538.5387 or submit electronically via CalREDIE. Report cases as new Hepatitis, non A-E disease condition.

Please contact BCPH's Infectious Disease Program at 530.552.3929 for further questions. For questions regarding submitting specimens to the BCPH lab, please call 530.891.2747.

Resources

Butte County Department of Public Health; [Report a Disease/Outbreak](#)

Centers For Disease Control and Prevention; [Updated Recommendations for Adenovirus Testing and Reporting of Children with Acute Hepatitis of Unknown Etiology \(5/11/22\)](#)

Centers for Disease Control and Prevention; [Recommendations for Adenovirus Testing and Reporting of Children with Acute Hepatitis of Unknown Etiology \(4/21/22\)](#)

National Center for Immunization and Respiratory Diseases; [Clinical Guidance for Adenovirus Testing and Typing of Patients Under Investigation](#)

National Center for Immunization and Respiratory Diseases [Instructions for Adenovirus Diagnostic Testing, Typing and Submission](#)

Categories of urgency levels:

Health Alert: conveys the highest level of importance; warrants immediate action or attention

Health Advisory: provides important information for a specific incident or situation; may not require immediate action

Health Update: provides updated information regarding an incident or situation; unlikely to require immediate action