



STATE OF HAWAII
DEPARTMENT OF HEALTH
P. O. BOX 3378
HONOLULU, HI 96801-3378

In reply, please refer to:
File:

May 6, 2022

Medical Advisory: Pediatric Hepatitis of Unknown Etiology

Dear Healthcare Providers:

The Hawaii Department of Health (HDOH) is investigating a case of hepatitis of unknown etiology in a child under 10 years of age. This case is still under investigation; however, typical infectious causes of hepatitis and medication toxicity have been ruled out. Adenoviral test results are currently pending.

As of [April 21, 2022](#), at least 169 cases of acute hepatitis of unknown origin in children have been reported from 11 countries. Cases have occurred in children ages 1 month to 16 years. Seventeen cases (10%) have required liver transplantation; at least one death has been reported.

Adenovirus has been detected in 74 cases (unknown how many tested); 18 have been identified as serotype 41F. A possible association between pediatric hepatitis and adenovirus infection is currently under investigation. 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. Adenovirus type 41 commonly causes pediatric acute gastroenteritis. While there have been case reports of hepatitis in immunocompromised children with adenovirus 41 infection, adenovirus type 41 is not known to be a cause of hepatitis in otherwise healthy children.

Case Definition:

- Children less than 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.

Clinical Guidance for Adenovirus Testing and Typing in Children with Acute Hepatitis of Unknown Etiology

- Standard diagnostic workup for acute hepatitis should be done
- CDC recommends including adenovirus testing in children with acute hepatitis of unknown cause
- Because the potential relationship between adenovirus and acute hepatitis is still under a national epidemiologic investigation, please consider collection and submission of the following specimen types (if available) for adenovirus detection:
 - Blood specimen collected in purple top EDTA tube (whole blood, plasma) or serum; whole blood is preferred to plasma
 - Respiratory specimen (nasopharyngeal swab in VTM/UTM, sputum, or bronchioalveolar lavage [BAL])

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- Stool specimen (or rectal swab in VTM/UTM); whenever possible, a stool specimen is preferred to a rectal swab
- If a liver biopsy has already been performed as clinically indicated, or from native liver explant or autopsy:
 - 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, e.g., PCR) is preferred for adenovirus detection (currently not available for FFPE liver biopsy or native liver explant). Testing whole blood by PCR may be more sensitive than testing plasma by PCR and is preferred.
- Please note: any clinical specimens that can be tested locally, should be, to ensure the most timely results for patient care.
- Any residual clinical specimens or aliquots that were **positive for adenovirus** and collected from pediatric cases with acute hepatitis should be kept frozen (use $\leq -70^{\circ}\text{C}$ if available) until adenovirus typing can be completed.

Report any clinically suspected cases of pediatric hepatitis **immediately**:

Oahu (Disease Reporting Line).....(808) 586-4586
Maui District Health Office.....(808) 984-8213
Kauai District Health Office.....(808) 241-3563
Big Island District Health Office (Hilo).....(808) 933-0912
Big Island District Health Office (Kona)(808) 322-4877
After hours on Oahu(808) 600-3625
After hours on neighbor islands(800) 360-2575 (toll free)

For more information, please see the following resources:

- Clinical Guidance for Adenovirus Testing and Typing of Patients Under Investigation: <https://www.cdc.gov/ncird/investigation/hepatitis-unknown-cause/hcp.html>
- Instructions for Adenovirus Diagnostic Testing, Typing, and Submission: <https://www.cdc.gov/ncird/investigation/hepatitis-unknown-cause/laboratories-testing-typing.html>
- CDC Health Advisory “[Recommendations for Adenovirus Testing and Reporting of Children with Acute Hepatitis of Unknown Etiology.](#)”
- MMWR, May 6, 2022 “[Acute Hepatitis and Adenovirus Infection Among Children – Alabama, October 2021 – February 2022](#)”
- WHO Multi-Country – Acute, severe hepatitis of unknown origin in children: <https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON376>
- AAP Red Book Online Guidance: Hepatitis Cases Possibly Associated with Adenoviral Infection: <https://publications.aap.org/redbook/resources/20171>

We appreciate your vigilance and assistance in identifying cases of pediatric hepatitis.

Sincerely,



Sarah K. Kemble, M.D.
State Epidemiologist