Yamhill County
Health and Human Services
Public Health

ALERT

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To: Health Care Providers in Yamhill County

From: Yamhill County Public Health

Date**: 4/25/22**

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

Phone number for follow-up: **(503) 434-7483**

State of Oregon
Health Alert Network

This is an official CDC HEALTH ADVISORY

Distributed via the CDC Health Alert Network

April 25, 2022, 1400

CDCHAN-00462

Summary

The Centers for Disease Control and Prevention (CDC) have issued a 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; none 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 clinicians who may encounter pediatric patients with hepatitis of unknown etiology to consider adenovirus testing and to elicit reporting of such cases to the **Oregon Health Authority on-call epidemiologist at 971-673-1111**. 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

Adenoviruses are doubled-stranded DNA viruses that spread by close personal contact, respiratory droplets, and fomites [2]. More than 50 types of immunologically distinct adenoviruses can infect 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 [2]. 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 [3]. While there have been case reports of hepatitis in immunocompromised children with adenovirus type 41 infection, adenovirus type 41 is not known to cause hepatitis in otherwise healthy children [4,5].

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.

Notification of Possible Cases

We ask that clinicians report to the Oregon Health Authority at 971-673-1111 children <10 years of age with elevated aspartate aminotransferase (AST) or alanine aminotransferase (ALT) (>500 U/L) of unknown etiology or with positive adenovirus testing results since October 1, 2021.

Submission of Specimens

If patients are still under medical care or have residual specimens available, first obtain approval for testing from the OHA Epidemiologist on call at 971-673-1111.

Submit specimens to the Oregon State Public Health Laboratory (OSPHL) as follows:

- Acceptable specimens include upper or lower respiratory tract specimens, eye swabs, stool, serum, plasma, whole blood, or pure culture isolate.

- Minimum sample volume is 0.50 mL.

- Refrigerate promptly after collection. If specimens can be shipped to OSPHL within 72 hours of collection, they should be kept refrigerated at 4°C and shipped with refrigerant (i.e., gel ice packs). If frozen, specimens should be stored at -70°C and shipped on dry ice. Do not store specimens for viral culture at -20°C.

- Specimens must be accompanied by a completed Virology/Immunology Test Request form, available at www.bitly.com/phl-forms.

- CDC will also accept fixed specimens from liver biopsy or autopsy. OHA epidemiologists will consult with CDC pathology for instructions on preparation and submission of specimens.

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] Adenoviruses Webpage. Centers for Disease Control and Prevention. Available from: http://www.cdc.gov/adenovirus/index.html

[3] 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

[4] 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

[5] 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.

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- Others within your organization.
- Professionals within your health, preparedness, and response affiliations.

Oregon 24/7 disease reporting: 971-673-1111