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Health Alert
Acute Non-Viral Hepatitis of Unknown Etiology Potentially
Associated with an Alkaline Water Product

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Key Messages

- Since November 2020, 16 probable cases and one suspect case of acute non-viral hepatitis of unknown etiology were reported to the Southern Nevada Health District (SNHD). One of the 16 probable cases resulted in a death. The U.S. Centers for Disease Control and Prevention (CDC), the U.S. Food and Drug Administration (FDA) and SNHD are investigating a potential link between these illnesses and the consumption of an alkaline water product (Real Water) and other possible etiologies.
- The California Department of Public Health (CDPH) has been notified of two California patients with similar illness potentially connected to Real Water alkaline water.
- Clinicians who become aware of cases similar to those described in this alert are asked to report them to their local health department. Local health departments should report new cases or direct any inquiries to toxoutbreak@cdph.ca.gov.

Current Situation

As of May 20, 2021, the [Southern Nevada Health District \(SNHD\)](#) has identified 16 probable cases (including one death) and one suspect case of acute non-viral hepatitis potentially linked to the consumption of an alkaline water product called “Real Water.” Five cases were initially identified in children from seven months to five years of age who were hospitalized between November 23 and December 3, 2020, with signs and symptoms of acute hepatitis but negative hepatitis viral panel results. SNHD subsequently identified 12 additional cases (11 probable cases and one suspect case that meets the clinical criteria but has not been tested for viral hepatitis) in adults from 32 to 71 years of age who were hospitalized. There has been one death of a female patient in her 60s who had underlying medical conditions.

Preliminary epidemiologic investigation has suggested that the only common link between the initial five cases is consumption of Real Water alkaline water. On March 24, 2021, Real Water, Inc. initiated a [recall](#) of all Real Water alkaline water. This product is available in 5-gallon, 3-gallon, 1-gallon, 1.5-liter, 1-liter, and 500-ml bottles, and as a 4-oz concentrate. Bottles and concentrate products are available for purchase online

and in stores nationwide.

The CDC and FDA are assisting the SNHD and other jurisdictions in investigating a potential link between these illnesses and the consumption of Real Water alkaline water or other possible etiologies, and issued a [health advisory](#) on March 31. Patients' signs and symptoms included vomiting, poor intake, and fatigue, and laboratory testing showed elevated hepatic transaminases, hyperbilirubinemia, coagulopathy, and a negative viral hepatitis serology panel. In some cases, adults and other children living in the same household as these patients reported similar but less severe symptoms.

The U.S. Food and Drug Administration (FDA) [advises](#) consumers, restaurants, and retailers not to drink, cook with, sell, or serve Real Water alkaline water until more information is known about the cause of the illnesses. Further, FDA advises that Real Water not be given to pets.

As of May 26, the California Department of Public Health (CDPH) has been notified of two potential illnesses associated with consumption of Real Water alkaline water and is investigating additional potential cases. Real Water alkaline water [was distributed](#) in California.

Information for Physicians and Hospitals

The CDC and CDPH have identified cases of acute non-viral hepatitis of unknown etiology potentially associated with consumption of Real Water alkaline water. While information to date from the preliminary epidemiologic investigation supports that there is a strong link between these cases of acute non-viral hepatitis and consumption of Real Water alkaline water, other etiologies are being evaluated.

Action Items for Physicians:

- 1) Have a high index of suspicion for non-viral hepatitis in your differential diagnosis of acute hepatitis in adults and children with compatible clinical findings.
- 2) Ask patients with suspected acute non-viral hepatitis about their exposure to Real Water alkaline water, as well as dietary and herbal supplements, and other possible etiologies.
 - Possible etiologies associated with acute non-viral hepatitis include exposure to medications, contaminated water or food, dietary and herbal supplements, traditional or home remedies, wild-growing mushrooms and plants, and chemicals such as metals, solvents, paint thinners, or pesticides.
- 3) Report all suspected cases to your local health department within 24 hours. An official from your local health department may interview the patient or family members, if appropriate.
- 4) Counsel your patients (or their caregivers and guardians) to stop drinking, cooking with, or using Real Water alkaline water until more is known about the cause of the illnesses per FDA recommendations.
- 5) Educate your patients on the signs and symptoms of acute hepatitis due to any cause, which may include fever, fatigue, decreased appetite, nausea, vomiting,

abdominal pain, dark urine, light-colored stools, joint pain, and yellow skin or eyes; and the importance of seeking medical care if they develop these symptoms.

Clinical Information on Acute Non-Viral Hepatitis of Unknown Etiology Potentially Associated with an Alkaline Water Product

Clinical course

The 17 patients identified by the SNHD (5 children aged 7 months to 5 years and 12 adults aged 32 to 71 years) presented for care with signs and symptoms of acute hepatitis. All five children and 11 adults tested negative for viral hepatitis and other infectious causes of acute hepatitis, and one adult has not been tested for viral hepatitis. One adult patient died; the other 16 patients ultimately recovered and were discharged home. All patients had been consuming Real Water alkaline water, and most continued to consume Real Water until hospitalization.

Symptoms

Commonly reported symptoms include:

- Vomiting
- Poor intake
- Fatigue

Laboratory findings

- Elevated hepatic transaminases
- Hyperbilirubinemia
- Coagulopathy
- Negative viral hepatitis serology panel

Diagnosis

Acute Non-Viral Hepatitis of Unknown Etiology Potentially Associated with an Alkaline Water Product is a clinical diagnosis of exclusion when infectious disease, chronic hepatic injury or illness, acetaminophen toxicity, sepsis, hypotensive shock, or other processes cannot explain the hepatitis in a patient that consumed Real Water alkaline water.

Treatment

Guidelines for treatment of Acute Non-Viral Hepatitis of Unknown Etiology Potentially Associated with an Alkaline Water Product are not yet available. The CDC recommends clinicians obtain early consultation with and/or referral to a gastroenterologist or infectious disease specialist for medical workup and management of patients with signs and symptoms of acute hepatitis.

Information for Local Health Departments

Background

Real Water alkaline water is distributed both as drinking water and as a concentrate nationwide including online sales and retail distribution. Real Water drinking water is sold in 1.5-liter, 1-liter, 500-ml, and 1-gallon ready-to-drink bottles, and 3-gallon and 5-gallon home and office delivery bottles. Real Water concentrate is sold as 4-oz bottles. Real Water alkaline water products have been sold in retail locations [throughout California](#).

Case Definition for Acute Non-Viral Hepatitis of Unknown Etiology Potentially Associated with an Alkaline Water Product

There is currently no definition of a confirmed case.

A probable case is defined as severe new-onset hepatitis of unknown etiology in a patient who visited a healthcare provider and meets all of the following criteria:

- Symptom onset on or after August 1, 2020
 - History of use of Real Water alkaline water within 30 days of illness onset
 - Having the following laboratory markers:
 - Aspartate transaminase (AST) or Alanine transaminase (ALT) > 4 times the upper limit of normal (ULN)
OR
 - Alkaline Phosphatase \geq 2 times the ULN
OR
 - AST or ALT above the reference range AND Total Bilirubin \geq 2 times ULN
 - A negative workup for infectious and any other explicative etiologies for hepatitis with:
 - Documentation of ALL of the following (required test results):
 - Hepatic imaging (i.e., ultrasound/doppler, CT scan, MRI) not consistent with alternative, explicative etiologies
 - Negative viral hepatitis panel (negative Hepatitis A IgM antibodies; negative Hepatitis B surface antigen and core antibody; negative anti-Hepatitis C Virus [HCV] antibody OR positive anti-HCV antibody with negative HCV RNA)
- AND
- No documentation of the following:
 - Hypotensive shock or septic episode within 14 days preceding onset of hepatitis
 - Acetaminophen hepatotoxicity
 - Pre-existing diagnosis of chronic liver disease (e.g., autoimmune hepatitis, primary biliary cirrhosis, primary sclerosing cholangitis, Wilson's disease, hemochromatosis, non-alcoholic fatty liver disease)
 - History of chronic alcohol use
 - Explicit documentation of another identified cause of the severe hepatitis as a

formal diagnosis in the discharge summary (e.g., hepatitis E, HSV, EBV, CMV, or another infectious or non-infectious cause)

A suspected case is defined as severe new-onset hepatitis of unknown etiology in a patient who visited a healthcare provider and meeting all of the following criteria:

- Symptom onset on or after August 1, 2020
- History of use of Real Water alkaline water within 30 days of illness onset
- Received a diagnosis of a liver-related illness that did not have a clear etiology, but for which medical record review has not been completed.

Suspected Cases

- Local health departments (LHDs) may use the “Case Screening Tool” attached as an Appendix to this Health Alert as a guide for the data to collect from reporting clinicians in order to determine if a potential case should be reported to CDPH and might require a follow-up interview and medical record review.
- LHDs are asked to report cases and direct inquiries to toxoutbreak@cdph.ca.gov. Please do not send protected health information (PHI) to toxoutbreak@cdph.ca.gov.
- Upon reporting a case to toxoutbreak@cdph.ca.gov, you will be contacted by a member of the CDPH staff and provided with a link to a standardized patient interview. We ask that a member of the LHD staff complete the questionnaire with the patient or family member. If the LHD is unable to do so, CDPH staff can provide assistance.
- LHDs are asked to obtain medical records related to the patient’s illness.
- After conducting the interview and if CDPH staff determine that the patient meets the case definition, please report the case to Linda Gilchrist, FDA Consumer Complaint Coordinator (Linda.Gilchrist@fda.hhs.gov), including patient name and contact information.
- The FDA will follow up with the patient, if needed, to collect any leftover Real Water from the patient. LHDs will have the option of signing an Information Sharing Agreement with the FDA to allow CDPH to share FDA Real Water testing results with the LHD.

CASE SCREENING TOOL: Acute Non-Viral Hepatitis of Unknown Etiology Potentially Associated with an Alkaline Water Product

This tool should be used by health departments for all calls or reports related to the investigation of acute non-viral hepatitis of unknown etiology associated with Real Water use. The purpose of this form is to determine whether to report to the California Department of Public Health (CDPH) an illness identified by the local health department through one of the following means:

- A report from a clinician (e.g., in response to the California Health Alert Network posting)
- A notification from the U.S. Food and Drug Administration (FDA) of a report submitted to FDA
- A report from an individual in the community

	Yes	No	Don't know
1) Did the person report receiving, or was the person reported by a healthcare provider as receiving, a diagnosis of a liver-related illness that did not have a clear etiology?			
2) Was the onset of illness on or after August 1, 2020?			
3) Did the person visit a healthcare provider because of the illness (or have lab results indicating a clinician visit)?			
4) Did the person ever consume Real Water?			
5) Did the person indicate that the illness started after they consumed Real Water?			

If the report came from the **person themselves** or **FDA**:

- If the answers to all of the questions above are “Yes,” then **contact** toxoutbreak@cdph.ca.gov. Please do not send PHI to toxoutbreak@cdph.ca.gov.
- If the answers to any of the questions above are “No” or “Don’t know,” **no follow up** is needed.

If the report came from a **clinician**:

- If the answers to questions 1, 2, and 3 are all “Yes,” and the answers to questions 4 and 5 are either “Yes” or “Don’t know,” **contact** toxoutbreak@cdph.ca.gov. Please do not send PHI to toxoutbreak@cdph.ca.gov.
- If the answers to questions 1, 2, and 3 are all “Yes,” and the answer to either question 4 or 5 is “No,” **no follow up** is needed.
- If the answers to questions 1, 2, or 3 are “No” or “Don’t know,” **no follow up** is needed

