# An Emerging and Deadly Waterborne Virus: Human Enterovirus 68

By Kelly A. Reynolds, MSPH, Ph.D.

Is it the flu or isn't it? Despite its distinctive symptomology and seasonal predictability, not all diagnoses of the flu may indeed be the flu. An emerging virus is on the scene and water is a possible source of transmission. Enterovirus 68 looks like the flu and feels like the flu but the influenza vaccine won't protect you—advanced water treatment, however, may.

## A new virus?

Human enterovirus 68 (HEV68) is making headlines in the US and around the world as a new, emergent pathogen. Given that sporadic cases of the virus have been reported since the early 1960s, some experts believe it is misleading to designate HEV68 as a new pathogen.[1] Fifty years ago, the virus was first recognized as the causative agent of pneumonia in four California children. HEV68 is known to be unique among the enterovirus group, having genetic characteristics of both enteroviruses and rhinoviruses (causative agent of the common cold). Increased application of genetic identification methods has improved diagnostics, and the recognition of HEV68 as an environmental contaminant and causative agent of respiratory disease. In the last two years, something seems to have changed with the virus. Clusters of cases are now being reported in the US, Asia and Europe. These clusters of respiratory disease associated with HEV68 have resulted in a range of symptoms from mild to severe respiratory illness and death.

## What are enteroviruses?

Enteroviruses are the most widely studied group of human viruses. Famous members of the group include poliovirus, coxsackievirus and echovirus. Extensive study has resulted in the availability of culture methods for isolation and detection of enteroviruses along with a plethora of genetic information. Genetic information has been used to track changes in related viruses, and enable researches to see new combinations of viruses or the evolution of new virus strains that can lead to an increase of infections or severity of illness.

The Enterovirus genus is further divided into different serotypes based on significant genetic differences. There are at least 69 enterovirus genus serotypes: poliovirus types 1-3, coxsakievirus types A1-24; B1-6, echovirus types 1-33, and enteroviruses types 68-71. Different groups of enteroviruses are associated with a wide range of diseases including: polio, meningitis and hand-foot-and-mouth disease. Worldwide outbreaks of enterovirus meningitis and hand-foot-and-mouth disease are frequently documented, primarily in children. The higher susceptibility in children is likely due to a lack of immunity from previous exposures and also to poorer hygiene habits.

Humans are commonly infected with enteroviruses. Most infections, however, are asymptomatic. This means that many of us do not even know we are infected. Even without symptoms of illness, infected individuals can still shed millions of the microscopic viruses in their feces and pass the virus onto others. As few as one to 10 enteroviruses are known to cause disease in humans.[2]

## HEV 68 increasing incidence

Several tracking systems are in place in the US to monitor enterovirus prevalence and incidence in the population. The National Enterovirus Surveillance System has collected information on enterovirus isolates in the United States since 1961 but reported only sporadic cases from 1987 to 2002.[3] In 2003, however, 11 cases were recorded, the highest number in a single year since surveillance was initiated. To assist states with identification of disease-causing agents, the Centers for Disease Control and Prevention (CDC) Unexplained Respiratory Disease Outbreak network (http://emergency.cdc.gov/urdo) receives isolates from clinical cases and provides laboratory diagnostics and outbreak reporting. Recently, the CDC published a report of six worldwide clusters of HEV68 respiratory illness from 2008-2010.[4] In this report, the CDC stated that HEV68 is an increasingly recognized etiological agent of respiratory illness and that clinicians should be alert to recognize and report cases of HEV68 in order to further elicit the impact of this virus in the population.

In the recent cluster of cases, three infections were fatal, two in the Philippines and one in Japan. In the Philippines' outbreak of 2008-2009, more than 800 children hospitalized with pneumonia were tested for HEV68; 2.6 percent (21 patients) were positive for the virus, which started in late October, peaked in early December, and continued through March. The majority of infected patients were less than four years old. Japan's HEV68 cluster began in 2010 with 120 cases identified that year—a dramatic increase above the normal rate of 10 cases per year. In this region, infections were documented from July through October. While infections appear to be more common in immunocompromised persons, during this outbreak, a previously healthy four-year-old boy died from HEV68 infection complications.

In the US, Georgia, Pennsylvania and Arizona reported increased HEV68 cases. Recognition of the virus in these states may be due in part to a more aggressive diagnostics approach using genetic analysis technologies to characterize enterovirus types in patients. Those found to have HEV68 included three over 50 years old, two of whom were immunocompromised. Pennsylvania health authorities noticed a doubling in the number of respiratory disease cases in the fall of 2009. More than 40 percent (28/66) of the patients tested positive for HEV68. Half of those (15/28) were under the age of four. Although no one died in this outbreak, 15 people were hospitalized in intensive care units. The case cluster in Arizona during the fall of 2010 was noted in a rural setting where respiratory illness was up to 43 percent of hospital admissions (compared to the normal 17 percent). Samples analyzed by the Arizona Department of Health Services failed to yield an identified agent; however, of the seven samples sent to the CDC, HEV68 was found in five.

Increased levels of enterovirus disease commonly occur in late summer to early fall in temperate climates and tend to

cycle with illness peaks every three to five years. As noted in recent disease clusters, HEV68 cycles extend beyond the typical enterovirus seasonality as was seen with the new H1N1 influenza strain that extended influenza seasonality.

Complications from enterovirus infection are known to include other co-infections, such as with *Cryptococcus* and *Streptococcus* bacteria. The wide range of symptomology and variety of enterovirus types has complicated documentation of their true disease burden. Like other viruses, HEV68 causes fever and cough, wheezing, asthma exacerbation and central nervous system disease. Without specific testing, HEV68 infections are likely confused with rhinovirus or influenza infections.

## Water treatment solutions

Similar to other virus infections, treatment of HEV68 illness is primarily supportive therapy, which includes keeping the patient comfortable and hydrated. Effective enterovirus antiviral medications are not yet available for post-infection treatment. Although a vaccine is available for prevention of poliovirus infections and progress in being made on the development of a vaccine for enterovirus 71, which causes hand-foot-and-mouth disease, there is currently no vaccine for HEV68. Thus, prevention of exposure is the most effective way to reduce your risk. As a respiratory virus, HEV68 is likely spread via the inhalation route. Exposure to contaminated aerosols from infected persons and water sources are possible routes of transmission. As with other enteroviruses, contaminated surfaces may also play a role where viruses are picked up from surfaces by hands and transmitted to mucous membranes. Swimming and ingestion of contaminated food or water have also been shown to transmit enteroviruses to humans.

Few waterborne outbreaks of enteroviruses have been reported and the role of water in the spread of HEV68 is not known. Data collected on other enteroviruses indicate that enteroviruses are frequently found in finished tapwater sources.[5, 6] One study found that the virus prevalence rate in drinking water was 16 percent. Enteroviruses are able to survive for long periods of time in water. Although more resistant than fecal bacteria, they are generally susceptible to chorination, ozone and ultraviolet light radiation typical of drinking water treatment.[7] The frequent isolation of enteroviruses from treated drinking water, however, brings into question the validity of the current bacterial (i.e., coliform bacteria or *E. coli*) monitoring protocol for determining the quality of drinking water supplies.[8] When applied properly, conventional drinking water treatment is highly effective against enterovirsues. Failures in treatment or distribution system recontamination events, however, can lead to increased exposure to waterborne viruses.[9] In addition, many water supplies in the US and worldwide are not treated, including private groundwater sources. POU and POE water treatment systems designed to remove viral contaminants are viable options for reducing exposure to HEV68 and other human pathogens. Combined treatment systems that utilize filtration and disinfection (i.e., chlorine, ozone or UV light) are the most effective microbial purifiers.

## Conclusions

Without a doubt, we now have better methods for the detection of enteroviruses and the distinction between HEV68 and other respiratory pathogens but detection improvements alone cannot explain the increased prevalence of respiratory illness in the populations. Emerging viruses and mutating microbes contribute to changing disease incidences that are difficult to predict. POU/POE systems offer protection to consumers that municipal water treatment systems simply cannot guarantee.

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