

# Amid Ebola preparation, an EV-D68 outbreak

**Karen Lusky**

[Labs ramp up for Ebola patients, specimens](#)

**December 2014—In addition to preparing for Ebola patients,** many clinical laboratories and hospitals in recent months faced outbreaks of respiratory illness caused by enterovirus D68 among children.

“EV-D68 infections may be associated with severe acute respiratory illness, viral pneumonia, and severe reactive airway disease,” says Susan Novak, PhD, D(ABMM), director of microbiology at Kaiser Permanente Regional Reference Laboratories in Southern California. Focal limb weakness has also been reported as possibly related to EV-D68, she adds.



**Dr. Novak**

What’s interesting about EV-D68, says infectious disease physician Jose Romero, MD, “is that most of the children infected with the virus don’t have fever.” Also, according to reports from the Centers for Disease Control and Prevention, “approximately 60 percent to 70 percent of children have an underlying pulmonary problem like asthma or wheezing,” adds Dr. Romero, section chief of pediatric infectious diseases at Arkansas Children’s Hospital and professor of pediatrics at the University of Arkansas for Medical Sciences.

Susan Gerber, MD, the team lead for respiratory viruses in the CDC’s Division of Viral Diseases, says the CDC began in late August investigating reports of increased numbers of respiratory illnesses in some hospitals and U.S. jurisdictions. “That became the impetus for the MMWR report that came out in early September [which] looked at severe respiratory illnesses in Kansas City and Chicago,” she says (MMWR Morb Mortal Wkly Rep. 2014;63[36]:798–799).

Children’s Mercy Hospital in Kansas City, Mo., was the first to get the CDC on the virus’ trail, according to Rangaraj Selvarangan, BVSc, PhD, D(ABMM), director of the clinical microbiology laboratory. He says the laboratory uses the BioFire FilmArray Respiratory Panel, which detects enterovirus (EV)/rhinovirus (RhV). In mid-August, the laboratory began seeing an uptick in such detections.



**Dr.  
Selvarangan**

At about the same time, Dr. Selvarangan received an email from an emergency room physician who reported

caring for several children in the prior 24 hours whose respiratory distress seemed out of proportion to their histories. "Most of them did not have fever. One child was in the intensive care unit," he says. In addition, all of the children responded to asthma medications, even though they didn't all have a history of asthma.

So he contacted the CDC and sent the agency a batch of 22 nasopharyngeal specimens. All but three turned out to be EV-D68. "It only got worse from that time point. We started seeing lots more kids attending the emergency room and needing hospitalization. A good portion of them ended up in the pediatric intensive care unit."

The outbreak's peak seemed to occur near the end of August. "From Aug. 4 to Oct. 30, we had 1,057 EV/RhV detections," Dr. Selvarangan says. Around the first week in November, the detections were back to expected levels for that time of year.

As part of research on the outbreak, the lab has tested specimens from about 100 children who were hospitalized in the pediatric intensive care unit from Aug. 5 to Sept. 15, and it expects the majority to be positive for EV-D68, Dr. Selvarangan says.

Different groups in the hospital are interested, too, in studying the outbreak. "The hospitalist group wants to describe the illness in the hospitalized children and their management. And then we certainly want to take a closer look at the children who needed intensive care, mechanical ventilation, albuterol inhalation, and oxygen supplementation," in order to understand why.

As for lessons learned, Dr. Selvarangan advises laboratories using multiplex viral detection to monitor trends to identify changes and to communicate with their physicians. "First recognize an outbreak and then prepare for the changes that it will bring in terms of patient management."

Richard B. Thomson Jr., PhD, D(ABMM), says he thinks it was public health authorities who alerted him that EV-D68 was causing respiratory illness in the Chicago area. "That's when the [laboratory and pediatricians] had some conversations about what we could do and what our test could tell them," says Dr. Thomson, division head of clinical laboratories at NorthShore University Health System in Chicago's northern suburbs. "Then we started testing aggressively and found a lot of positives" for enterovirus. "I don't know how many were D68 and how many were other enteroviruses," he says. To identify enterovirus, NorthShore uses a PCR test developed in-house.

By mid-October, the laboratory was "basically not getting any more positive enterovirus results," Dr. Thomson says.

The Cleveland Clinic has been able to meet the increased clinical demand for EV-D68 testing by using the FDA-approved Cepheid Xpert EV test, says Gary W. Procop, MD, MS, an infectious disease pathologist and microbiologist. "This required preparation and obtaining additional instrumentation to assure adequate testing capacity."

Detecting enterovirus helps "nail down the diagnosis," if you also do testing to exclude other possible illnesses, such as influenza, that might be treatable with specific antiviral therapy, Dr. Procop says. He stresses the importance of recognizing "the cross-reactivity between enterovirus and rhinovirus when using multiplex assays that contain rhinovirus as part of the panel. When such a panel is performed without assessing for enterovirus, the clinician could be misled by the positive rhinovirus result, which is actually a false-positive."

Although there's no licensed treatment for EV-D68 infection, says Dr. Romero, a drug called pleconaril has shown activity against enteroviruses in a number of trials. "What I understand from colleagues is that pleconaril has no activity specifically against enterovirus D68, but there are other related compounds that are currently either in the investigational stage or can be acquired by compassionate release that may have activity," he says. "But the drug would have to be specifically tested for activity against EV-D68 to be certain."

Could the EV-D68 virus wreak more havoc next year? The answer isn't clear, Dr. Gerber says. "So I think that's something we are certainly going to look at closely, but different enterovirus types may circulate to varying degrees each year, usually from summer through fall."

Dr. Romero notes that enteroviruses “tend to cause epidemics for a year or so and then go away. It’s very possible we won’t see it again next year to this degree.”

If it does return, the CDC will be able to test for it more quickly. On Oct. 14, Dr. Gerber says, the agency began using a rapid real-time assay that it developed to detect EV-D68. “It’s much like the real-time assays that can detect other viral pathogens as opposed to a longer assay that includes sequencing.”

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