Enterovirus Infections

L. Pasquinelli

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In Brief

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L. Pasquinelli, MD
Eastern Virginia Medical School
Norfolk, Va.

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Enterovirus infections are common infections in infants and children. They are often referred to as "summer viruses" because of their increased prevalence in the warmer months (May through October) in the temperate northern hemisphere, but they may be found throughout the year in the tropics. These single-stranded RNA viruses belong to the *Picornaviridae* family and include polioviruses, coxsackieviruses, and echoviruses.

Most cases involve children younger than 5 years of age due to their lack of prior exposure, but all age groups are at risk for infection. Humans are the only known natural hosts, and fecal-oral is the most common route of transmission. Once exposed, the virus enters the body via the oral or respiratory route, where it replicates in the lymph nodes of the respiratory or gastrointestinal system. An initial minor viremia results in spread to secondary sites, with subsequent viral replication at distant sites that may include the heart, liver, and skin. Infection of the central nervous system (CNS) is usually the result of a second major viremia. As antibodies develop, the viremia ends, and the patient's clinical recovery begins.

Most patients infected with enteroviruses become mildly ill and recover completely, but some develop serious illness, rarely suffering a fatal outcome. In general, enteroviral infections manifest as febrile illness, viral exanthem, vomiting, diarrhea, and malaise. Manifestations associated with specific viral agents include hemorrhagic conjunctivitis, pharyngitis, pleurodynia, herpangina, hand-foot-and-mouth disease, paralysis, hepatitis, myocarditis, pericarditis, encephalitis, aseptic meningitis, and multiorgan failure.

Neonates are at high risk for developing a severe disseminated infection. Infection can occur during birth or be acquired from an infected clinician. The clinical presentation often is difficult to differentiate from that of a bacterial cause. Severe manifestations may include hepatitis, pneumonitis, meningitis, encephalitis, disseminated intravascular coagulation, and multiorgan failure.

Poliovirus infection has nearly been eliminated from the wild due to vaccination. When recognized, poliovirus infection presents as three clinical syndromes: 1) abortive poliomyelitis, 2) aseptic meningitis, and 3) paralytic poliomyelitis. Clinical manifestations of abortive poliomyelitis may include fever, headache, sore throat, malaise, nausea, and vomiting without CNS involvement. Paralytic poliomyelitis begins as a minor febrile illness followed by a short asymptomatic period of 2 to 3 days, then sudden onset of a flaccid paralysis with no significant sensory loss. Lower motor neuron damage from infection may result in temporary or permanent flaccid paralysis.

Confirmation of enteroviral infection may be necessary in some clinical situations. Viral culture, polymerase chain reaction (PCR), and serologic diagnosis are three laboratory methods for identifying the causative organism. Viral culture of stool (not rectal swab), throat, blood, cerebrospinal fluid (CSF), or tissue can be obtained. The highest rates of positive culture come from cultures of stool and throat, with isolation from CSF being infrequent. The time required for growth in culture can make this method less appealing. PCR, a molecular method that uses nucleic acid probes where sequences are common to all enterovirus serotypes, can be accomplished with a small sample, and results can be available in less than 5 to 24 hours. PCR examination of CSF is 100% sensitive and 97% specific for detection of enterovirus. Unfortunately, this method is not widely available. Serologic diagnosis is based on a fourfold increase in neutralizing antibody titer. However, due to variations in individual titers and the number of enterovirus serotypes, this technique is difficult and impractical.

Treatment of enteroviral infection usually is supportive, although antiviral drug treatments that target enteroviral replication are under investigation. Pleconaril, an antiviral that prevents viral uncoating and attachment to host cells,

has shown beneficial effects in clinical trials, but its clinical applicability to treatment of enteroviral infection remains under investigation. Immune globulin intravenous (IGIV) may be of benefit for immunodeficient patients who have persistent enterovirus infection.

To prevent spread of infection, contact precautions should be used while patients are hospitalized. The benefits of hand washing should be stressed, particularly after diaper changes.

Comment: Enteroviruses are common causes of pediatric illness and hospitalization. (1)(2) In hospitalized patients, diagnostic testing by PCR has been associated with decreased intravenous antibiotic use, ancillary testing, and hospital length of stay. (3)(4)(5) In addition, identification of enteroviral illness allows for appropriate patient isolation, especially in the neonatal intensive care unit and, in certain situations, allows directed antiviral therapy. (6)(7)(8) Since one enterovirus PCR was withdrawn from the market, access to PCR testing in the United States has been limited. However, recent improvements in PCR technology, including development of multiplex assays and real-time PCR, have made this technology faster, more efficient, and more affordable. (9)(10)(11) Undoubtedly, this will allow more clinical laboratories to offer PCR testing in the future. In addition, some laboratories might opt for enhanced cell cultures by using shell-vial technology combined with monoclonal antibody testing for enteroviruses. These enhanced cultures can yield results in 48 hours compared with the usual 8 to 10 days required for traditional viral culture. (12) Diagnosing enteroviral disease can improve patient care significantly. Pediatricians and others who care for children should work closely with their clinical microbiology laboratories to assure that rapid testing for enterovirus is available.

Carrie Byington, MD
University of Utah
Salt Lake City, Utah

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