Enteroviruses

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Pediatrics in Review 2003;24;358

In Brief

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Prevention of Poliomyelitis: Recommendations for Use of Only Inactivated Poliovirus Vaccine for Routine Immunization. Committee on Infectious Diseases. American Academy of Pediatrics. *Pediatrics*. 1999;104: 1404–1406

The Role of Viruses in Human Diabetes. Hyoty H, Taylor K. *Diabetologia*. 2002;45:1353–1361

Treatment of Potentially Life-threatening Enterovirus Infections With Pleconaril. Rotbart H. *Clin Infect Dis*. 2001;32:228–235

The single-stranded RNA enteroviruses traditionally have been classified into three major groups: the 3 polioviruses, 29 coxsackieviruses, and 31 echoviruses. The coxsackieviruses have been subdivided further into groups A (23 types) and B (6 types). More recently discovered enteroviruses are not inserted into the classification scheme; instead, enteroviral type numbers are assigned to them. Of the 10 to 15 million symptomatic enteroviral infections that occur in the United States each year, 15 serotypes account for 90% or more of all reported isolates.

Infection with enteroviruses is distributed equally throughout the year in tropical climates. In contrast, in the United States and other temperate regions, the incidence of enteroviral infections peaks in the summer and fall. The viruses are transmitted primarily from person to person by the fecal-oral route, and fecal shedding of virus can continue for several weeks after infection. Respiratory and perinatal transmission also occur. Respiratory shedding is more limited than fecal shedding. Enteroviruses may survive on environmental surfaces long enough to allow transmission by fomites. Attack rates are highest among infants and young children, in tropical climates, in communities populated by lower socioeconomic groups, and in areas that have poor sanitation. Many enteroviral infections affect neonates more severely than older children, particularly coxsackie B infections.

Although the most common manifestation of enteroviral infection is a nonspecific febrile illness, other presentations may involve almost any organ system. Not surprisingly, "entero"virus can cause vomiting, diarrhea, and abdominal pain as well as hepatitis and pancreatitis. The respiratory tract can be affected with pharyngitis, rhinosinusitis, stomatitis, herpangina, pneumonia, or pleurodynia and the heart with myocarditis or pericarditis. Meningitis, encephalitis, and paralysis are neurologic manifestations of infection, and the skin may be involved with both enanthems and exanthems, including hand-foot-mouth disease (HFMD). Gross hematuria and even the hemolytic-uremic syndrome have been associated with enteroviral infection, as has a distinctive acute hemorrhagic conjunctivitis (AHC). Reports suggest an association between enteroviral infection and type 1 diabetes mellitus, but a causal relationship has not been established. The following enteroviral serotypes are associated with specific clinical presentations: group A coxsackieviruses with encephalitis, HFMD, and AHC; group B coxsackieviruses with neonatal myocarditis, pleurodynia, herpangina, and meningitis; echoviruses, particularly type 11, with meningitis and neonatal hepatitis; enterovirus 70 with AHC; and enterovirus 71 with HFMD and myelitis.

Thanks to the effectiveness of vaccination, infections caused by wild poliovirus have been eliminated in the United States since 1979. In 1994, the World Health Organization declared that polio had been eradicated from the western hemisphere. The oral vaccine (OPV), made from live virus, causes about one case of paralytic poliomyelitis for every 2.4 million doses administered, but vaccine-related illness has declined since 1997, when the Centers for Disease Control and Prevention and the American Academy of Pediatrics jointly recommended that OPV give way to vaccination with inactivated poliovirus (IPV). In contrast to the success of vaccination in industrialized countries, poliomyelitis remains a devastating disease in many regions of the developing world.

As many as 90% to 95% of poliovirus infections are asymptomatic, and most symptomatic infections, so-called "abortive poliomyelitis," manifest as nonspecific, self-limited viral illnesses. Only 1% to 2% of infected people develop neurologic disease, either nonparalytic poliomyelitis that is similar to aseptic meningitis, or the asymmetric flaccid paralysis that characterizes paralytic poliomyelitis. With paralytic poliomyelitis, there may be spinal, bulbar, or combined spinobulbar involvement.

Enteroviral infections are diagnosed clinically, but laboratory confirmation can be useful for surveillance, during epidemics, and when diagnosis is uncertain. Acute and convalescent serologies documenting a fourfold rise in antienteroviral antibody titers are diagnostic of recent infection. However, the gold standard for diagnosis is isolation

of the organism. Newer methods, such as polymerase chain reaction assay and sequencing studies, have improved the ability to diagnose infection and serotype the responsible enterovirus. Depending on the clinical picture, samples for identification of virus can be obtained from cerebrospinal fluid, a stool specimen or rectal swab, a nasopharyngeal swab, or urine.

No specific therapy is available against enteroviruses; supportive care is the rule. Intravenous immune globulin containing antienteroviral antibodies has been used to treat severe illness, particularly in neonates. Pleconaril has activity against the viral capsid protein and has shown promise in limiting the morbidity and mortality of nonpolio enteroviral infections. Public health efforts to eradicate poliomyelitis throughout the world by 2005 proceed, but universal vaccination continues to be hampered by political and economic instability.

The prognosis for most nonpolio enteroviral infections is excellent. Neonates and children who have underlying health conditions are most susceptible to severe morbidity and mortality.

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Comment: Poliomyelitis is one of the oldest diseases known—pictorial evidence traces it back at least to ancient Egypt. As has been true of other viral illnesses, its epidemiology remained obscure for so long because most infections (>90%) are inapparent. We used to think that Epstein-Barr virus (EBV) infection, characterized by infectious mononucleosis, primarily affected adolescents and young adults. With the availability of serologic testing, we learned that EBV infection is common among very young children, particularly in poor and crowded conditions, but it manifests with a nondescript clinical appearance. The same is true of polio. In poor and crowded conditions, infection strikes younger children, and for reasons not understood, infants and toddlers are less likely than older children to develop paralytic disease. Also not fully understood is the postpolio syndrome of worsening weakness and pain that strikes adults who were infected as children after many years of apparent clinical stability.

Henry M. Adam, MD
Editor, In Brief

More Lessons for the Clinician

Index of Suspicion Case 3 in the May 2003 issue (pp. 171–179) concerned a patient who had a deep vein thrombosis (DVT). The discussion listed a palpable cord as a sign of DVT. Dr. Abel Guerra pointed out that a palpable cord may be present in cases of superficial vein thrombosis, but thickening of a deep vein would not be palpable because of the location of the affected vessel. Author Dr. Ulfat Shaikh agrees with this correction.

Dr. Jaime Bimstein shared his experience and that of his colleagues in Mexico with the treatment of ascariasis, the subject of Case 3 in the June 2003 issue (pp. 207–212). Dr. Bimstein's comments were discussed with author Dr. Echzona Ezeanolue and Dr. Ellen Wald, a consultant in infectious disease. Both agreed that we should share these comments, which can be summarized as follows:

- Retreatment with piperazine 2 weeks after initial treatment with that drug is appropriate to ensure eradication of any parasites that may have been in the phase of extraintestinal migration when the first dose was given. Piperazine works in the lumen of the gut and, therefore, will not eradicate extraintestinal parasites.
- Counting the ova in the stool will predict the worm burden and provide clues to prognosis.
- In Mexico, piperazine is preferred to mebendazole because the latter leads to erratic migration of the parasites more often than does piperazine. Dr. Wald adds, "Piperazine paralyzes the worm, thereby facilitating elimination through defecation. Piperazine is low in cost and is particularly helpful when the worm burden is very high and intestinal obstruction is partial or complete."

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