



CONTAGIOUS COMMENTS

Department of Epidemiology

Enteroviruses

Ubiquitous and Diverse Pathogens

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Epidemiology: Enterovirus (EV) infections have a worldwide distribution and are common causes of illness in neonates, infants, and children, with a lower frequency in adolescents and adults. They are most prevalent during the summer and early fall in temperate regions, but cases can occur at any time of the year. Multiple EVs may circulate in the community at one time. For example, in Colorado in 2003, the two most prevalent serotypes were echovirus 30 (67%) and EV 71 (13%); echoviruses 7, 9, 13, and 18, as well as coxsackieviruses A9, B1, B2, and B5, were also present. Most concerning were the eight cases of EV 71 (subgroup C), as this small outbreak caused severe disease in three patients (including one death from neurogenic cardiopulmonary collapse). First isolated in 1969 in California, and since then detected in many parts of the world, EV 71 has caused extensive outbreaks of severe disease in the Far East - especially in Taiwan. There, in 1998 alone, ~129,500 cases occurred, including 78 deaths from neurogenic cardiopulmonary complications.

Virology: EVs are small single-stranded RNA viruses, belonging to the family Picornaviridae. There are at least 62 types, which, with the exception of EV types 68-71, are traditionally classified into subgroups: poliovirus, coxsackievirus group A (CA), coxsackievirus group B (CB), and Echovirus (Echo).

Pathogenesis & Immunity: Enteroviruses get their name, not because they primarily cause enteric disease, but rather because they grow in the GI tract. Disease occurs when viral replication is not contained in the reticuloendothelial system, and major viremia permits tropism to target organs, which - depending on serotype - include the CNS, heart, liver, pancreas, kidneys, muscle, and skin. Damage is mediated by both local necrosis and host inflammatory response. Protective immunity, for which humoral immunity plays a major role, is serotype-specific.

Clinical Syndromes: As shown in the Table, EV infections have protean clinical manifestations. Most clinical syndromes can be caused by more than one type of EV. Furthermore, one type of EV can cause more than one syndrome.

Diagnosis: Most cases of EV are mild, and therefore do not necessarily require virologic testing. In fact, some exanthems and enanthems (e.g., HFMD) are quite characteristic and can be diagnosed on clinical grounds. However, if the diagnosis is not clear, virologic testing may be warranted, and in the case of severe illness, or the possible index case of potentially severe epidemic disease, an etiologic diagnosis is important. EV diagnosis in hospitalized children may reduce unnecessary testing and therapies and reduce hospital costs. EV can be diagnosed by virus isolation in cell culture and by detection of viral RNA using the polymerase

Organ System	Clinical Syndrome	Common EV Types
Systemic	Febrile illness, acute, without localizing signs (especially in young infants)	Potentially all EVs
	Sepsis (<i>especially in neonates without type-specific maternal antibody</i>)	CB 2-5, Echo 6, 9, 11, 19
Tegmentary (Exanthems & Enanthems)	Exanthem:	
	• Macular	Echo 19 (punctate)
	• Maculo-Papular	CA 9; Echo 16
	• Vesicular	Echo 11; CA 5
	• Petechial	Echo 9; CA 9
	• Rubelliform or Morbilliform	Echo 2, 6, 9, 11, 25
	• Hemangiomatous	Echo 25, 32
	Hand-Foot-Mouth Disease (HFMD)	CA 16 (predominant); EV 71
Stomatitis:	• Vesicular (herpangina)	CB 5, CA viruses
	• Pustular	
Respiratory	Rhinitis (common cold)	CA 21, 24; CB 1-5; Echo 2, 20
	Pharyngitis	Potentially all EVs
	Parotitis	CA; EV 70
	Bronchitis	CB 1, 4
	Pneumonia	CA 9, 16; CB 1-6
	Croup	Echo 11
	Pleurodynia, epidemic (Bornholm disease)	CB 1 & 5
	Pulmonary edema, fulminant, with or without hemorrhage (neurogenic)	EV 71
Neurologic	Meningitis, aseptic	CB 2-5; Echo 4, 6, 9, 11, 16, 30
	Encephalitis, diffuse or localized (e.g., brain stem encephalitis)	EV 71; CA 9; CB 2, 5; Echo 6, 9
	Myelitis (acute flaccid paralysis)	EV 71; Echo 4, 6
	Guillain-Barré syndrome	EV 71; Echo 6, 22
Cardiac	Myocarditis; Pericarditis	CB 5, 2
	Acute cardiac dysfunction with or without myocarditis	EV 71
Alimentary	Gastroenteritis; Pancreatitis; Hepatitis (<i>in neonates</i>)	CA 9, 4, 16; CB 1-5; Echo 6, 9, 11, 19
Ophthalmic	Conjunctivitis, hemorrhagic	CA 24; EV 70
Muscular	Myositis (epidemic myalgia)	CA 2, 9; Echo 18



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chain reaction (PCR). The highest rate of isolation is from specimens from the GI and respiratory tracts, although prolonged shedding from these sites (especially the GI tract) complicates interpretation of EV detection from these sites. PCR is generally more sensitive than viral culture. Chris Robinson, PhD, Dr. Mimi Glodé, et al, have shown that PCR of CSF (and blood) may be especially useful in making rapid clinical decisions about aseptic meningitis (and rule-out SBI) in the ER - significantly reducing antibiotic use and cost. (*Impact of rapid polymerase chain reaction results on management of pediatric patients with enteroviral meningitis.* *Pediatr Infect Dis J* 2002; 21: 283-6) In serious illness, typing of viral isolates or of PCR-amplified nucleic acid may be important. CSF, throat, rectal, and, in neonates and young infants, blood specimens are recommended for PCR and culture. For possible severe EV 71 disease, GI and respiratory specimens are more sensitive than CSF and blood.

EV PCR is performed six days a week at TCH during peak season, with results reported by 5 PM if specimens are received by 6:30 AM (M-F). Typing of EV PCR-positive samples or isolates requires Microbiology approval (303-861-6703).

Treatment: No specific effective therapy is currently available. IVIG may be beneficial in severe infections, particularly in neonates and immunodeficient patients (lacking protective antibodies) and in EV 71 disease, but there is currently no conclusive evidence of efficacy.

Prognosis & Complications: Most EV infections are mild and self-limited. However, significant morbidity or death can occur in neonates and other immunocompromised hosts lacking immunity to the infecting EV type. Complications include encephalitis, hepatitis, and cardiac and/or respiratory dysfunction, which can be direct or indirect (e.g., secondary to brainstem injury caused by EV 71 rhombencephalitis).

Prevention: The multiplicity of types of EVs has hindered the development of a vaccine (other than for polioviruses).

Infection Control: EVs are transmitted by fecal-oral and respiratory routes, as well as by vertical transmission in the peripartum period. Neonatal EV infections are commonly associated with community and nosocomial outbreaks, especially in NICUs. Furthermore, EVs may survive on environmental surfaces long enough to allow transmission from fomites. Fecal-oral spread via hand carriage of staff transmits it to other patients. Intubation and feeding also elevate the risk of transmission. For these reasons, contact precautions are indicated for infected infants and young children who are fecally incontinent. As EV can be shed in the gastrointestinal tract for up to 6-12 weeks, hand hygiene after changing diapers is especially important, and contact isolation should persist for the duration of hospitalization. If there are respiratory tract symptoms, droplet precautions should also be taken for the duration of hospitalization, as EV can be shed in the respiratory tract for up to 3 weeks.

