

Parechoviruses in Neonatal Sepsis and Meningoencephalitis- An Update

Parechoviruses can cause neonatal sepsis and encephalitis in young infants. Recently, an increase in cases has been recognized at Yale. The purpose of this newsletter is to heighten provider awareness of both parechovirus infections in febrile infants and the availability of on-site testing at Yale New Haven Hospital.

In 1956, what we now call parechoviruses were first isolated from the stools of two children with diarrhea, and were designated as enteroviruses (EV), specifically echoviruses types 22 and 23 (1). However, when molecular methods were developed for pan-enterovirus diagnosis in the 1990s, these two echoviruses were not detected. Thus, they were placed in a separate *Parechovirus* (PeV) genus and a separate PeV PCR was required for detection (2,3). Human infections are associated with PeV species A and 18 types have now been identified. Infections occur predominantly in summer and fall but can occur year-round (4).

Subclinical infections and clinical syndromes: Parechoviruses primarily cause inapparent infections in young children and clinical syndromes similar to enteroviruses (5,6). PeV-A1 is the most commonly identified type and is associated with asymptomatic infection, with mild respiratory and gastrointestinal symptoms, or less frequently, with CNS disease. The majority of PeV-A1 infections occur in children less than 1 year old, and almost all children are infected by age 5. Severe disease is rare.

In contrast, PeV-A3 is the most common PeV recovered from CSF and appears to have a 2-3 year cycle. PeV-A3 has been shown to be specifically associated with sepsis and fever in young infants, especially those less than 3 months of age and with neonatal encephalitis with white matter injury (7-10). Indeed PeV-A3 has been reported as the leading cause of CNS infection in children and is more common than any single EV type (11). A striking feature is that neonates with PeV-A3 encephalitis often have normal CSF findings (12). PeV-A3 has also been identified as a cause of neonatal hepatitis-coagulopathy syndrome. It has been postulated that severe PeV-A3 neonatal infections may be due to lower seroprevalence of PeV-A3 antibody in women of child-bearing age and thus the lack of protective transplacental antibody, as well as different cellular tropism (13).

Parechovirus testing: Since July 2013, the Virology Laboratory has offered Parechovirus RT-PCR for neonatal sepsis and meningoencephalitis, as well as a combined Parechovirus and Enterovirus RT-PCR diagnostic panel intended for hospitalized children less than 5 years of age with enterovirus-like illness.

Test offered: The CDC Parechovirus real-time RT-PCR assay (14) is performed once a day, 5-6 days a week, as a single test or as a combined EV/PeV panel. It is also now included in the febrile infant pathway.

Sample options: CSF, Blood (lavender tube), throat or nasopharyngeal swab, and stool.

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