



From the Department of Laboratory Medicine - Yale-New Haven Hospital Medical Center

## Clinical Virology Laboratory Newsletter

Vol. 22 (2)

July 2013

### Parechoviruses in Neonatal Sepsis and Meningoencephalitis

In 1956, what we now call human parechoviruses (HPeV) types 1 and 2 were first isolated from the stools of two children with diarrhea, and were designated as enteroviruses (EV), specifically echoviruses types 22 (E22) and 23 (E23) (1). However, when molecular methods were developed for the diagnosis of enteroviruses in the 1990s, E22 and E23 were not detected using pan-enterovirus PCR primers (2). Thus, E22 and E23 were placed in a separate genus and designated human parechoviruses (3). Since then, the number of HPeV types has increased from 2 to 16, and many more are likely awaiting discovery (<http://www.picornastudygroup.com/types/parechovirus/hpev.htm>).

Since EV PCR does not detect HPeV, the diagnosis of parechoviruses has declined due to the change from culture to PCR for diagnosis of enterovirus-like illnesses (3).

**Subclinical infections and clinical syndromes:** Parechoviruses primarily cause inapparent infections in young children, and clinical syndromes similar to EV (4,5). HPeV Type 1 is the most commonly identified HPeV and is primarily associated with asymptomatic or mild respiratory and gastrointestinal infections, and less frequently with CNS disease. The majority of HPeV1 infections occur in children less than 1 year old, and almost all children are infected by age 5. Severe disease is rare.

HPeV3 is the most common HPeV recovered from CSF and appears to have a biannual cycle. HPeV3 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 (6-9). However, neonates with HPeV3 encephalitis often have normal CSF findings. HPeV3 was also identified as a cause of neonatal hepatitis-coagulopathy syndrome. It has been postulated that severe HPeV3 neonatal infections may be due to lower seroprevalence of HPeV3 antibody in young women due to its recent emergence in the population, as well as different cellular tropism.

**Parechovirus testing:** Beginning in July 2013, the Virology Laboratory will offer a combined HPeV and EV PCR diagnostic panel for hospitalized children less than 5 years of age with enterovirus-like illness, in particular for neonatal sepsis and meningoencephalitis.

**Test offered:** The CDC Parechovirus real-time RT-PCR assay (10) will be performed once a day, 5-6 days a week, and will be available as both a single test and a combined EV/HPeV panel.

**Samples:** 1) Neurologic syndromes: CSF, stool  
2) Neonatal sepsis: **Blood** (lavender tube), CSF, stool, throat.

For questions, contact Marie L. Landry, MD ([marie.landry@yale.edu](mailto:marie.landry@yale.edu)) or David Ferguson ([david.ferguson@ynhh.org](mailto:david.ferguson@ynhh.org)), or the Clinical Virology Laboratory at 203-688-3475.

## References

1. Wigand R, Sabin AB. Properties of ECHO types 22, 23, and 24 viruses. *Arch Ges Virusforsch* **1961**; 11:224-247.
2. Stanway G, Hyypia T. Parechoviruses. *J Virol* **1999**; 73:5249-5254.
3. Landry ML. The molecular diagnosis of parechovirus infection: has the time come? *Clin Infect Dis* 2010;50:362-3.
4. Harvala H, Simmonds P. Human parechoviruses: biology, epidemiology and clinical significance. *J Clin Virol* **2009**; 45:1-9.
5. Harvala H, Wolthers KC, Simmonds P. Parechoviruses in children: understanding a new infection. *Curr Opin Infect Dis.* **2010**; 23:224-30.
6. Boivin G, Abed Y, Boucher FD. Human parechovirus 3 and neonatal infections. *Emerg Infect Dis* **2005**; 11:103-107.
7. Harvala H, et al. Specific association of human parechovirus type 3 with sepsis and fever in young infants, as identified by direct typing of cerebrospinal fluid samples. *J Infect Dis* **2009**; 199:1753-60.
8. Verboon-Maciolek MA, et al. Human parechovirus causes encephalitis with white matter injury in neonates. *Ann Neurol* **2008**; 64:266-273.
9. Wolthers KC, et al. Human parechoviruses as an important viral cause of sepsis like illness and meningitis in young children. *Clin Infect Dis* **2008**; 47:358-63.
10. Nix WA, et al. Detection of all known parechoviruses by real-time PCR. *J Clin Microbiol.* **2008**; 46:2519-24