

repetitive seizures, and continuous normal voltage background in the other 2. (Verboon-Maciolek MA, Groenendaal F, Hahn CD, et al. Human parechovirus causes encephalitis with white matter injury in neonates. **Ann Neurol** Sept 2008;64:266-273). (Respond: Dr de Vries, Department of Neonatology, KE 04.123.1, University Medical Center, Lundlaan 6, 3584 EA Utrecht, The Netherlands. E-mail: [L.s.devries@umcutrecht.nl](mailto:L.s.devries@umcutrecht.nl)).

COMMENT. Human parechoviruses (HPeV) types 1 and 2, formerly known as echoviruses 22 and 23 and belonging to the genus *Enterovirus*, have been reclassified in the new genus *Parechovirus*. HPeV 1 and 2 have not been isolated from neonates with encephalitis, but type 3 and CNS neonatal encephalitis have been reported. HPeV 4 has been found in an infant with fever only, and types 5 and 6 are also identified. The reverse transcription PCR test for HPeV became available in 2006.

Of the 10 neonates with HPeV encephalitis in the above study, only 1 showed CSF pleocytosis, and protein and glucose levels were always normal. Five showed normal neurodevelopment at ages 15 months to 7 years. Repetitive seizures correlated with poor developmental outcome. Neonatal HPeV-related seizures cannot be differentiated clinically from those caused by enterovirus infection; and both viruses should be investigated by PCR tests. The diagnosis of HPeV infection is made by a positive RT-PCR in CSF or blood. HPeV type 3 was identified in 8 of 10 patients tested.

In an editorial, Dr Joseph J Volpe of Boston Children's Hospital (**Ann Neurol** 2008;64:232-236) points out that Verboon-Maciolek and colleagues findings indicate that HPeV3 is a major cause of neonatal encephalitis and seizures, and 3 times more common than enterovirus, accounting for 64% of encephalitis cases admitted to the NICU at Utrecht University Medical Center. Major viral infections of the developing nervous system include rubella, cytomegalovirus, varicella-zoster, and lymphocytic choriomeningitis, acquired intrauterine (transplacental), and herpes simplex, enteroviruses, human parechovirus, and HIV, primarily parturitional or perinatal. Since CSF is normal in 90% cases of HPeV3 encephalitis, diagnosis may be overlooked. PCR analysis for HPeV3, enterovirus, and HSV is important in newborns presenting with unexplained seizures, especially if associated with rash and MRI evidence of white matter lesions.

**CSF findings in herpes simplex, varicella zoster, and enterovirus infections in adults** with viral meningitis are reported from Sheffield Teaching Hospitals, UK. (Ihekwaba UK, et al. **Clin Infect Dis** Sept 2008;47:783-789). Enterovirus was the most common cause of viral meningitis. CSF white cell and protein levels were significantly higher in patients with HSV type 2 than in those with enterovirus meningitis. Rash occurs after meningitis symptoms in varicella zoster infection (median delay 6 days). PCR provides a rapid, specific diagnosis.

## **NEUROPSYCHOLOGICAL OUTCOMES OF NEONATAL HERPES ENCEPHALITIS**

Neuropsychological outcome and the relation to neuroimaging findings are studied in a cohort of 9 children between 2.5 and 13 years of age with neonatal herpes encephalitis, examined at Karolinska University Hospital, Sweden. Diagnosis, established by CSF PCR analysis, was triggered by seizures that occurred in 7 patients. All exhibited EEG abnormalities; and all received acyclovir. CSF showed a high protein content, and CT

performed in 7 infants and MRI in 1 revealed bilateral lesions, chiefly frontal and parietal. The extent of cerebral damage was not correlated with neurodevelopmental outcome. Eight children had cerebral palsy; 5 were mentally retarded, severe in 3; 7 exhibited deficits in attention; 8 had expressive language problems; and 3 attended special education classes. Relapse with reactivation of vesicles and leading to behavioral deterioration occurred in 1 child. (Engman M-L, Adolffson I, Lewensohn-Fuchs I, et al. **Pediatr Neurol** June 2008;38:398-405). (Respond: Dr Engman, Division of Pediatrics, Children's Hospital B57, Karolinska University Hospital, Stockholm, Sweden. E-mail: [mona-lisa.engman@ki.se](mailto:mona-lisa.engman@ki.se)).

COMMENT. Seizures with abnormalities in the EEG should alert to a possible diagnosis of neonatal herpes virus encephalitis. Neuropsychological investigation is recommended early as a measure of outcome and the detection of relapse.

## VIRAL ENCEPHALITIS AND EPILEPSY

The role of viral meningitis in the cause of epilepsy is reviewed by researchers from Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India; and University of Malaya, Kuala Lumpur, Malaysia. Viral meningitis presents with seizures in the acute stage, and increases the risk of late unprovoked seizures and epilepsy. Among sporadic viral encephalitides, herpes simplex virus is most frequently associated with epilepsy, probably because it involves the highly epileptogenic frontotemporal cortex. Among the epidemic viral encephalitides, usually due to flaviviruses, Japanese encephalitis is most common; it is associated with acute symptomatic seizures in 7-46% of children affected. Equine, St Louis, and West Nile viruses, and measles, varicella, mumps, influenza, and entero-viruses may also present with acute symptomatic seizures. The risk of late unprovoked seizures and epilepsy following viral encephalitides is not well determined, and requires prospective studies. The authors propose that the anatomical localization of lesions during the acute viral infection may determine the occurrence and outcome of postencephalitic epilepsy. (Misra UK, Tan CT, Kalita J. Viral encephalitis and epilepsy. **Epilepsia** Aug 2008;49(Suppl 6):13-18). (Respond: Dr Usha Kant Misra, Department of Neurology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow-226014. E-mail: [ukmisra@sgpgi.ac.in](mailto:ukmisra@sgpgi.ac.in)).

COMMENT. This *Epilepsia* supplement is the consensus following a meeting in Feb 2007, arranged at Chandigarh, India by the International League Against Epilepsy, concerning CNS infections as a cause of epilepsy (Singh G et al. **Epilepsia** Aug 2008;49(Suppl 6):1). In addition to viral encephalitis, the association between epilepsy and meningitis, cerebral malaria, *T solium* cysticercosis, and HIV infection were discussed and reviewed. The meeting focused on unremitting long-term seizure activity following CNS infections, and provided suggestions for future research in this neglected area.