COMMENT. In confirmation of previous studies, the main predictors of susceptibility to febrile seizure recurrence are young age (<18 mo) at initial FS, family history of FS in first degree relative, lower temperature (</= 38.9C) and shorter fever duration (<12 hrs) before initial seizure. The lower temperature indicates a low threshold to FS. The present authors also found a maternal preponderance in the families of children with FS recurrence. Daycare attendance and frequent viral infection are additional risks.

Cytokines in acute encephalopathy following prolonged febrile seizures. In a study of 13 children with acute encephalopathy following prolonged febrile seizures compared to 23 without encephalopathy, in Yamaguchi University and other centers in Japan, serum IL-6, IL-10, TNFR1 and CSF IL-6 levels were significantly higher in subjects with encephalopathy compared to controls without encephalopathy. The authors speculate that IL-6 is induced in the CNS to protect damaged brain following prolonged febrile seizure.

PERTUSSIS VACCINATION, EPILEPSY AND *SCN1A* MUTATION

Literature regarding pertussis vaccination and risk of encephalopathy and/or epilepsy is reviewed by researchers from UCL Institute of Neurology, London, UK, and North Illinois University, DeKalb, IL, USA. Current risk estimates of vaccine-related febrile seizure are 1 per 18,496 vaccinations; afebrile seizure 1 per 76,133; and encephalopathy 0-3 per million. The rate of febrile seizures within 2 days of the present acellular vaccine is much lower than that of 1 per 2835 with previous whole-cell vaccine (Cody CL et al. Pediatrics 1981;68:650-660).

As part of a recent study of unexplained encephalopathies in Australia, New Zealand, Canada and Scotland, Berkovic SF et al (Lancet Neurol 2006;5:488-492) identified 14 cases within 72 hours of pertussis vaccination, treated by child neurologists. Of these presumed vaccine-related cases, 11 had an inherited genetic defect of the *SCN1A* gene that corresponded to the phenotype for severe myoclonic epilepsy of infancy (SMEI, Dravet syndrome). The encephalopathy temporally associated with pertussis vaccination may, in some cases, be due to an *SCN1A* mutation and Dravet syndrome. This finding requires replication by further studies. (Shorvon S, Berg A. Pertussis vaccination and epilepsy – an erratic history, new research and the mismatch between science and social policy. **Epilepsia** Feb 2008;49:219-225). (Respond: Dr Simon Shorvon, UCL Institute of Neurology, Box 5, National Hospital for Neurology and Neurosurgery, Queen Square, London, UK).

COMMENT. Fortunately, the risk of neurologic complications of pertussis vaccine has fallen remarkably since the introduction of the acellular vaccine. With whole-cell vaccine, reports of neurologic complications, especially febrile seizures or infantile spasms, were not uncommon in US pediatric neurology practice. In the same time period, encephalopathy attributed to whooping cough was a very rare neurologic diagnosis. In vaccine related encephalopathies, a test for SMEI should be considered in the differential diagnosis.

In Australia and New Zealand, the experience is different from the US. Among 49 unimmunized infants (age 6 weeks) admitted with pertussis to the PICU at Royal Children's Hospital, Melbourne, between 1985-2004, 63% had apnea, 18% pneumonia, and 10% had seizures. Deaths in 7 were due to pneumonia and circulatory failure. (Namachivayam P et al.

Pediatr Crit Care Med 2007;8:207-211). At Starship Children's Hospital, Auckland, NZ, 72 children (<12 months old) were admitted to the PICU with pertussis from 1991-2003. Apnea and cough were presenting symptoms in 83%, 4 died and 6 had neurodevelopmental problems. (Surridge J et al. **Arch Dis Child** 2007;92:970-975). In unimmunized populations, pertussis is a serious disease with complications, principally respiratory.

REVERSIBLE VALPROATE HEPATOTOXICITY AND ASSOCIATED MITOCHONDRIAL DISEASE

A 2-year-old boy with seizures complicated by reversible valproate-induced hepatic failure was subsequently found to have mitochondrial polymerase g gene *(POLG1)* mutations typical of Alpers-Huttenlocher disease, in a study at Newcastle University, UK. Brain MRI showed abnormal white matter signal in occipital and medial temporal lobes bilaterally. After discontinuing sodium valproate and substituting levetiracetam, liver function returned to normal over a 6-month period. Sequencing of *POLG1* is recommended in children with valproate-induced hepatic failure, and prior to commencing sodium valproate in young children (<3 years old) with aggressive focal epilepsy. Serum lactate, ammonia and liver function should be closely monitored in young children treated with valproate. (McFarland R, Hudson G, Taylor RW et al. Reversible valproate hepatotoxicity due to mutations in mitochondrial DNA polymerase g *(POLG1)*. **Arch Dis Child** Feb 2008;93:151-153). (Respond: Dr Robert McFarland, Mitochondrial Research Group, School of Neurology and Psychiatry, 4th Floor, Medical School, Framlington Place, Newcastle University, Newcastle NE2 4HH, UK).

COMMENT. The syndrome of diffuse progressive degeneration of the cerebral gray matter was first described by Alpers in 1931. Ford (1951) differentiated infantile and juvenile types and reported familial cases. Huttenlocher et al (1976) described coincident hepatic cirrhosis. Egger et al (1987) reported 13 cases treated at the Hospital for Sick Children, Great Ormond Street, London, 4 having received sodium valproate. A genetically determined, autosomal recessive, metabolic cause was suggested. Bicknese et al (1992) from Washington University, St Louis, MO, reported 6 patients with Alpers-Huttenlocher syndrome, 4 taking valproic acid (VPA), 2 of whom had a sibling with the same syndrome but no exposure to VPA. Siblings receiving VPA survived only 3 and 5 months after onset of seizures, whereas those not receiving VPA lived for 7 to 16 months. These authors proposed that many of the cases of VPA-associated hepatotoxicity represent undiagnosed hepatocerebral degeneration, Huttenlocher variant of Alpers' syndrome. In 2004, Naviaux et al described POLG mutations associated with Alpers' syndrome and mitochondrial DNA depletion. Patients with the syndrome treated with VPA have developed an irreversible liver failure and neurologic decline. The present case is exceptional, having a more favorable outcome.

A 17-year-old adolescent girl with Juvenile Alpers Disease is reported from the University of Otago, Wellington, NZ and other centers. (Wiltshire E et al. **Arch Neurol** Jan 2008;65:121-124). She presented with clusters of occipital seizures and clumsiness, and showed progressive memory impairment, slurred speech, and hemiparesis. She died of respiratory failure, cerebral degeneration, and liver necrosis. Mutational analysis of *POLG1* showed 2 novel mutations, similar to the abnormality in infantile Alpers disease.