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SEIZURE DISORDERS

HERPESVIRUS-6 INFECTION AND FEBRILE SEIZURES

Human herpesvirus-6 (HHV-6) infection, incidence, course, complications, and its potential for persistence or reactivation, was studied in infants and children under 3 years of age seen in the ER over a three-year period at the University of Rochester School of Medicine, NY. Of 1653 presenting with acute febrile illnesses, 160 (10%) had primary HHV-6 infection, documented by viremia and seroconversion, and of these, 21 (13%) had seizures, many appearing late and prolonged or recurrent. The risk of seizures among children 12-18 months old with HHV-6 infection was 29%. HHV-6 infections accounted for one third of all first-time febrile seizures in children up to 2 years of age. Among 1394 children under 2 years with fever not due to HHV-6, seizures occurred in 9%. The HHV-6 genome persisted in blood mononuclear cells in 66% of 56 children followed for 1 to 2 years after primary infection. Reactivation was suggested by subsequent increases in antibody titers and PCR in 16% and 6%, respectively. Presence of HHV-6 genome in 29% of 41 healthy neonates' mononuclear cells indicates intrauterine or perinatal transmission of the virus. Among children with HHV-6 illness, roseola was diagnosed in 17%. (Hall CB, Epstein LG et al. Human herpesvirus-6 infection in children. A prospective study of complications and reactivation. N Engl J Med Aug 18, 1994;331:432-8).

> COMMENT. Human herpesvirus-6 infection in relation to febrile seizures is discussed in two previous issues of Ped Neur Briefs (April 1992; June 1993). These reports concerned a total of 23 infants with CNS complications of roseola (exanthem subitum) caused by HHV-6. The seizures were often prolonged, some were focal, and the csf showed a pleocytosis in 5. The present report and findings suggest that HHV-6 infection may account for a much larger percentage of seizures with fever in children than previously recognized. In addition to roseola, HHV-6 infection presented as otitis or fever of undetermined cause. Febrile children with HHV-6 had significantly higher temperatures than HHV-negative children, the factor generally proposed to explain

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the frequency of seizures with roseola. The study corroborates the suggestion that seizures with roseola, HHV-6, and fever are not always simple in type. They are frequently prolonged, recurrent, and complex, and sometimes a manifestation of encephalitis or encephalopathy. (Progress in Pediatric Neurology II, Millichap JG, Ed, PNB Publ, 1994, pp 410, 415). These findings further weaken the hypothesis of the so-called *simple febrile seizure* as a distinct disease entity.

For abstracts from the 16th annual conference on febrile convulsions held in Tokyo, Dec 18, 1993, see Fukuyama Y. Brain Dev July/Aug 1994;16:339-346. Papers included neurochemical aspects, EEG studies, and clinical, epidemiological, and treatment reports. The reputed safety and effectiveness of intermittent oral diazepam (0.4 mg/kg, 3 doses) at times of fever for prevention of recurrence of febrile seizures was supported in 23 children treated at Shimane Medical University and Central Hospital, Japan.

GLUTAMATE IN PYRIDOXINE-DEPENDENT EPILEPSY

Cerebrospinal fluid levels of glutamate, g-aminobutyric acid, and pyridoxal-5-phosphate examined in a patient with pyridoxine dependency while on and off vitamin B6 treatment are reported from Universitat Munchen, and Universitats-Nervenklinik, Wurzburg, Germany. Seizures began at age 3 weeks. Despite phenobarbital, status epilepticus occurred at 3 months and was followed by infantile spasms and hypsarrhythmia. The addition of ACTH and vitamin B6 controlled the seizures and the EEG became normal. Seizures recurred on each of several occasions when vitamin B6 was withdrawn. CSF glutamate was elevated 200-fold, whereas GABA and PLP were normal. After vitamin B6 (5 mg/kg BW/day) was reintroduced, seizures stopped and the EEG was normal, but CSF glutamate was still elevated 10 fold. A dose of 10 mg/kg BW/day vitamin B6 lowered the CSF glutamate to normal levels and controlled seizures, without apparent side-effects. At age 45 months, development was normal; the head circumference having dropped from the 25th at birth to the 3rd percentile at 3 months was further reduced during ACTH treatment but rebounded and grew to a 50th percentile after vitamin B6.(Baumeister FAM, Egger J et al. Glutamate in pyridoxine-dependent epilepsy: Neurotoxic glutamate concentration in the cerebrospinal fluid and its normalization by pyridoxine. Pediatrics Sept 1994;94:318-321).

COMMENT. The authors emphasize that control of seizures alone may not suffice in treating pyridoxine dependency. In order to prevent mental retardation, it is important to adjust the dose of vitamin B6 to normalize CSF glutamate levels, but using the minimum effective dosage to avoid neuropathic side effects. Glutamate is an excitatory neurotransmitter and neurotoxin, and elevated brain concentrations in infants with pyridoxine dependency may explain frequent occurrence of psychomotor retardation despite remission of seizures with vitamin B6.

HYPOCALCEMIC AND HYPOMAGNESEMIC SEIZURES

The clinical findings and neurologic outcome of 15 newborn infants with seizures due to hypocalcemia (HC) and hypomagnesemia (HM) admitted to St Louis Children's Hospital are reported from Washington University, St Louis. Patients with perinatal asphyxia, cerebral hemorrhage, or other cerebral lesion were excluded. Seven infants had associated congenital heart