after disease onset). EPC and partial seizures ceased post-surgically in all patients; they recurred within 6 months in 2. (Granata T, Gobbi G, Spreafico R et al. Rasmussen's encephalitis. Early characteristics allow diagnosis. Neurology February (1 of 2) 2003;60:422-425). (Reprints: Dr Tiziana Granata, Division of Neuropsichiatria Infantile, Instituto Nazionale Neurologico C Besta, Via Celoria 11, 20133 Milan, Italy).

COMMENT. A tentative diagnosis of Rasmussen's encephalitis is possible within 4 to 6 months after onset of partial seizures, especially when epilepsia partialis continua occurs at presentation. The focal EEG findings and MRI changes are usually characteristic. Proposed mechanisms are virus-induced inflammation and an immune-mediated process. The use of antiviral and immunosuppressive therapies in the early stages of the disease may be more effective in slowing progression.

**Virological and immunological aspects of seizure disorders** are reviewed by Eeg-Olofsson O, Uppsala University, Sweden (Brain Dev Jan 2003;25:9-13). The etiology of Rasmussen's encephalitis (RE) is thought to be a viral infection coupled with immunodysfunction. HSV-1 DNA has been recovered from the cortex of 3 children with RE, and CMV DNA in brain biopsies in 2 reports. Significantly decreased IgA levels have been reported in 7 patients with RE. Glutamate receptor type 3 (GluR3) antibodies in serum of RE patients, documented in the above study, have been reported previously.

HHV-6 and -7, the causative agents for exanthem subitum, are linked to febrile seizures, but the association is debated. Recurrences of febrile seizures may be associated with reactivation of HHV-6 that has invaded the brain during the acute phase of exanthem subitum.

Defects in human leukocyte antigens (HLA) A1,B8, T4 and T8 lymphocytes, and immunoglobulins in relation to various epilepsies suggest a genetic predisposition to virus persistence that results in neuronal membrane defect and seizures. Virology and immunologic research and trials of antiviral agents may be a promising approach to the cause and treatment of epilepsy in the future.

## RECURRENT SEIZURES AND BEHAVIOR PROBLEMS

The association of seizures and behavior problems in children with new onset seizures was investigated in a prospective study of 224 children (aged 4-14 years) and 159 siblings (4-18 years) at Indiana University and Children's Hospital Medical Center, Cincinnati, OH. Caregiver's ratings of the behavior, based on the Child Behavior Checklist (CBCL) administered by telephone, were collected at baseline, and at 6 months, 12, and 24 months. During the 2-year period of follow-up, 163 (73%) children had at least one seizure recurrence, and 61 (27%) had none. In children with recurrent seizures, CBCL Total and Internalizing Behavior Problem scores on average were higher during seizure recurrence periods than when not experiencing recurrent seizures ($p=0.041$). Siblings had significantly lower Total and Internalizing Problem scores compared to patients either experiencing or not experiencing recurrent seizures. Externalizing Problems scores were not significantly different among children with or without recurring seizures, and siblings. Demographics and antiepileptic medication effects were controlled in these analyses. Both seizures and behavior problems may be caused by the underlying neurological disorder,

the seizures per se may impair behavior, or children may have abnormal psychological responses to seizures. (Austin JK, Dunn DW, Caffrey HM et al. Recurrent seizures and behavior problems in children with first recognized seizures: a prospective study. Epilepsia Dec 2002;43:1564-1573). (Reprints: Dr JK Austin, Indiana University School of Nursing, 1111 Middle Drive, NU492, Indianapolis, IN 46202).

COMMENT. Children with recurrent seizures are at increased risk for behavior problems, even after correcting for possible effects of antiepileptic drug therapy.

Behavioral and emotional disorders are sometimes regarded as a form of epilepsy (see Progress in Pediatric Neurology III, PNB Publishers, 1997;pp70-71), but the concept of a behavioral epilepsy is controversial. In a multicenter Japanese study, a comparison of emotional and behavioral problems of 53 children having epileptiform EEGs and those of children without EEG abnormalities showed no significant differences. The authors concluded that the behavioral problems were coincidental (Okubo Y et al. Epilepsia 1994;35:832-841).

## DEVELOPMENTAL DISORDERS

## EVALUATION OF GLOBAL DEVELOPMENTAL DELAY

The Quality Standards Subcommittee of the AAN and the Practice Committee of the CNS have issued recommendations for the evaluation of the child with nonprogressive global developmental delay (GDD), based on a review of relevant literature and scheme of evidence classification. GDD affects 1% to 3% of children. Routine metabolic screening (blood gas, serum lactate and ammonia, serum amino acids and urine organic acids, T4 and TSH) gave yields of 1% and is not indicated as an initial test, except when universal newborn screening (UNS) was omitted or uncertain. Routine cytogenetic studies and molecular testing for fragile X mutation gave yields of 3.5% to 10% and are indicated, even when dysmorphic and specific syndrome features are absent. Additional genetic studies (including subtelomeric chromosomal rearrangements) may be indicated in children with a family history of GDD. Rett syndrome is considered in girls with unexplained moderate to severe delays. Serum lead levels are mandatory in children with identifiable risk factors of lead exposure or signs of intoxication. Thyroid studies are ordered only if clinically indicated or in the absence of newborn screening; the yield is near 0 in patients included in UNS; 4% if no UNS. EEG is recommended when symptoms suggest epilepsy or a specific epilepsy syndrome. Routine neuroimaging, preferably MRI, is recommended, particularly if the neurological examination is abnormal or the history suggests acquired CNS injury or risk of cerebral malformation. Routine visual and audiometric testing is recommended in all cases, and screening for autism or a language disorder should be considered. A specific etiology can be determined in the majority of children with GDD. In the absence of specific clinical features, a stepwise approach is recommended: MRI, cytogenetic screen/fragile X, metabolic tests, and genetic consultation. (Shevell M, Ashwal S, Donley D et al. Practice parameter: evaluation of the child with global developmental delay. Neurology February (1 of 2) 2003;60:367-380). (Reprints: Dr Stephen Ashwal, Department of Pediatrics, Loma Linda University School of Medicine, 11175 Coleman Pavilion, Loma Linda, CA 92350).