COMMENT. The EEG is particularly important in the recognition of seizures in the newborn, since clinical observation alone may not be diagnostic. An algorithm that extracts rhythmic features from the EEG by spectral analysis may identify paroxysmal patterns indicative of seizure activity, but false detections may be a concern.

In a second publication, the authors evaluated their automatic EEG method of neonatal seizure detection, using recordings from a new set of 54 patients. The average seizure detection rate in the 3 institutions providing recordings was 69%, and the average false detection rate was 2.3/hour. Fluctuations in the false detection rates, ranging from a low of 1 to a high of 4/h, were a reflection of the technical quality and level of supervision of recordings. An experienced electroencephalographer must review "seizure" detections in conjunction with clinical observations, so that false or artifactual patterns may be excluded. (Gotman J, Flanagan D, Rosenblatt B, Bye A, Mizrahi EM. Evaluation of an automatic seizure detection method for the newborn EEG. Electroenceph clin Neurophysiol Sept 1997;103:363-369).

GABAPENTIN MONOTHERAPY FOR REFRACTORY SEIZURES

The results of an 8-day, controlled, multicenter study of gabapentin monotherapy in 82 hospitalized patients with refractory complex partial or secondarily generalized seizures are reported by members of the US Gabapentin Study Group. The study was conducted at 13 centers, 12 in the US and 1 in Canada, between Feb 1994 and Aug 1995. The efficacy and safety of 2 dosages, 300 and 3,600 mg/d, as three equally divided doses every 8 hours, were compared after tapering and discontinuing other antiepileptic medications. Patients exited the double-blind period with the occurrence of 4 seizures (46 patients), prolonged/intensified seizures (4 patients), lack of efficacy (1), or at completion of 8-day treatment (28 patients). Time to exit was significantly longer and rate of completion of the trial period was higher for patients receiving the higher 3,600 mg/d dose of gabapentin. At the higher dosage, 52% completed the study, compared to 16% at the lower dosage. Adverse dose-related events included dizziness (13% of patients), ataxia (12%), and somnolence (11%). No patient exited the study due to adverse effects of gabapentin. (Bergey GK, Morris HH, Rosenfeld W et al. Gabapentin monotherapy: I. An 8-day, double-blind, dose-controlled, multicenter study in hospitalized patients with refractory complex partial or secondarily generalized seizures. Neurology Sept 1997;49:739-745). (Reprints: Dr Elizabeth Garofalo, Parke-Davis Pharmaceutical Research, 2800 Plymouth Rd, Ann Arbor, MI 48105).

COMMENT. This short-term inpatient study in adults demonstrates that gabapentin monotherapy is an effective and safe treatment for refractory complex partial and secondarily generalized seizures. In a further dose-controlled, 26-week, multicenter study of gabapentin in 275 patients, 20% of patients completed the study, but completion rates were higher among patients who had discontinued only one AED (23%) or had been maintained on carbamazepine (27%) in addition to gabapentin. (Beydoun A, Fischer J, Labar DR et al. Neurology Sept 1997;49:746-752).

LAMOTRIGINE OPEN TRIAL IN REFRACTORY EPILEPSY

Lamotrigine, 5 and 15 mg/kg/daily, was administered as add-on therapy in 37 outpatient children and adolescents with refractory epilepsy and mental

delay treated at the Child Neuropsychiatry Unit, Department of Pediatrics, Second University of Naples, Italy. Over a median 7 month trial period, seizures were completely controlled in 22%, and reduced by >50% in 14%. Absence and atonic seizures were controlled more effectively than partial or secondarily generalized seizures. Adverse effects occurred in 16%, but treatment was discontinued only in 1 because of a skin rash. Some improvements in cognition, attention, and speech reported by parents and teachers were unrelated to decrease in seizure frequency. (Coppola G, Pascotto A. Lamotrigine as add-on drug in children and adolescents with refractory epilepsy and mental delay: an open trial. Brain Dev Sept 1997;19:398-402). (Respond: Dr Antonio Pascotto, Clinica di Neuropsichiatria Infantile, Dipartimento di Pediatria, Seconda Universita di Napoli, Via Pansini 5, 80131 Napoli, Italy).

COMMENT. Lamotrigine is an effective add-on therapy in children with refractory absence, atonic, and tonic-clonic seizures. It is relatively safe and free from serious side-effects. In this series, skin rash developed in 3, but only one required drug withdrawal.

Lamotrigine in pregnancy and lactation was investigated in a patient at the Karolinska Institute and Hospital, Stockholm, Sweden. (Tomson T, Ohman I, Vitols S. Epilepsia Sept 1997;38:1039-1041). Plasma levels of lamotrigine (LTG) decreased as pregnancy progressed, suggesting enhanced clearance of LTG. LTG concentrations in the nursing infant (25% of mother's plasma levels) were high due to passage of LTG into breast milk and slow elimination in the newborn.

TERATOGENIC EFFECTS OF ANTIEPILEPTIC DRUGS

Data from 5 prospective European studies totaling 1,221 children exposed to antiepileptic drugs (AED) during pregnancy and 158 children of unexposed control pregnancies were analyzed to quantify the risk of major congenital malformations (MCM) and are reported from University Medical Centers in Rotterdam and Heemstede, The Netherlands; Berlin and Magdeburg, Germany; and Helsinki, Finland. A comparison of a subgroup of 192 children exposed and 158 children unexposed to AED showed an increased risk of MCM (relative risk, RR 2.3 [1.2-4.7]). In those exposed to valproate or carbamazepine monotherapy, the RR was 4.9. Comparing polytherapy exposures in all 1,221 pregnancies, risks of MCM were significantly increased for phenobarbital/ethosuximide combination (RR 9.8), and the combination of PHT, PB, CBZ, and VPA (RR 11). VPA risks were dose related, especially for neural tube defects: offspring exposed to a maternal dose of >1000 mg/day (RR 6.8) were affected more often than <600 mg VPA/day exposures. VPA and CBZ were consistently associated with an increased risk of MCM. (Samren EB, van Duijn CM, Koch S et al. Maternal use of antiepileptic drugs and the risk of major congenital malformations: a joint European prospective study of human teratogenesis associated with maternal epilepsy. Epilepsia Sept 1997;38:981-990). (Reprints: Professor D Lindhout, Dept of Clinical Genetics, Erasmus University Rotterdam, PO Box 1738, NL-3000 DR Rotterdam, The Netherlands).

COMMENT. In a prospective multicenter study with pooled data, valproate and carbamazepine were especially teratogenic. In particular, the offspring of women receiving >1000 mg/day of VPA were at increased risk of having major congenital malformations. The authors suggest that VPA should be avoided during pregnancy when possible. In an editorial comment, Yerby MS cautions regarding conclusions derived from pooled data and multiple pregnancies.