

patients), generalized tonic (90 in 13 patients), and myoclonic (66 in 13 patients). Only 2 neonates had infantile spasms. Clonic seizures with focal EEG seizure activity correlated with focal brain lesions such as infarction or intracerebral hemorrhage and a favorable short-term outcome. Seizures with no or inconsistent relationship to the EEG were correlated with diffuse hypoxic-ischemic encephalopathy and a poor prognosis (>50% with abnormal neurologic exams at discharge, and 20% died). Those with myoclonic seizures had high morbidity (35%) and mortality (29%) compared to those with clonic seizures (71% normal at discharge). The authors question the use of potentially neurotoxic anticonvulsant drugs in neonates with nonepileptic seizures or "behaviorisms" not accompanied by EEG seizure activity. (Mizrahi EM, Kellaway P. Characterization and classification of neonatal seizures. Neurology 1987; 37:1837-1844).

**COMMENT.** I contacted Dr. Gerald Fenichel at Vanderbilt Univ Sch of Med, an authority on neonatal seizures, for his opinion regarding the use of anticonvulsants in the treatment of "subtle" seizures. Unless the motor automatisms or tonic posturings can be correlated with a simultaneous recording of EEG seizure activity, he considers these subtle seizures as non-epileptic and advises against treatment with anticonvulsants. Patients with epileptiform seizures associated with acute hypoxic-ischemic encephalopathy are given IV phenobarbital in a loading dose of 20-30 mg/kg to provide a serum level of 40 ug/ml. If the patient is free from seizures on recovery from the acute illness and at the time of discharge from hospital, anticonvulsants are discontinued. (personal communication). Despite the enthusiastic promotion of newer antiepileptics, there is a growing and greater awareness of the potential toxicity of anticonvulsants in general. Any practical, less hazardous alternative or safe means of withholding medication must be considered seriously, especially in the neonate and young child. See Brent et al (Pediatrics 1987; 80 (Dec):909) re phenobarbital-induced depression and suicidal behavior in epileptic children, another area for concern in the long-term use of anticonvulsant drugs.

#### **PHENACEMIDE IN COMPLEX PARTIAL SEIZURES**

The anticonvulsant phenacemide (phenylacetylurea), discarded for 30 years because of serious toxicity, has been resurrected and used in the treatment of 13 children with refractory complex seizures at Loyola University, Maywood, and Christ Hospital, Oak Lawn, Illinois. Twelve responded, nine were seizure free for 2-12 months, and one developed nausea and vomiting necessitating drug withdrawal. Other side-effects included aggressive behavior in 1, drowsiness (2) ataxia (2), headache (1), and elevated SGPT and GGT in one child aged 3 yrs with tuberous sclerosis. A liquid chromatography assay developed to determine plasma phenacemide concentrations showed a linear relationship between drug peak height and plasma concentration over a range of 0-150 ug/ml. After a single oral dose the peak concentration in a 16 year old patient was at 1 to 2 hours and in a 40 year old volunteer, at 5 hours.

Phenacemide half-life in the adult was 25 hours and was estimated at 25 and 22 hours in two children. A twice-daily dosage regimen seemed appropriate. Therapeutic levels ranged from 16-75 ug/ml (median, 52 ug/ml). (Coker SB, Holmes EW, Egel RT. Phenacemide therapy of complex partial epilepsy in children: Determination of plasma drug concentrations. Neurology 1987; 37:1861-1866).

**COMMENT.** The authors rationalize their re-evaluation of phenacemide as monotherapy, stating that the majority of phenacemide-related deaths from liver failure or aplastic anemia had occurred in adults receiving polytherapy. After 30 years of dormancy, it is surprising that the drug had not been withdrawn from the market, having regard to its well established toxicity. The efficacy of phenacemide in partial complex (temporal-lobe) seizures has been demonstrated repeatedly in earlier studies and reconfirmed in this re-evaluation. Fortunately, none developed liver failure but one patient taking 4 gm daily had symptoms of nausea and vomiting suggestive of liver involvement and sufficient to warrant phenacemide withdrawal. Another showed a behavior or personality disorder, a common and troublesome side effect in previous trials. Is the reactivation of this drug necessary or advisable?

#### POST-ICTAL ACTH AND PROLACTIN PLASMA LEVELS

Significant elevations in ACTH and prolactin plasma levels were found within one hour after generalized tonic-clonic seizures in 10 epileptic patients but not in patients with syncopal attacks investigated at the Service de Neurologie, Hopital General 3, rue Faubourg Raines, Dijon, France. The mean ACTH and prolactin levels were 72.6+/- 3.7pg/ml and 13.9+/-1.9 ng/ml at one hour compared to 17.1+/-2.1 pg/ml and 4.1+/-1.2 ng/ml, respectively, at three to five days after seizures; the differences were significant (p<0.01) and independent of anti-convulsant effects. Levels of FSH, LH, and TSH were unchanged. The post-ictal rise of ACTH and prolactin levels may be used in the differentiation of epileptic seizures and syncope. (Giroud M et al. Les troubles neuro-endocriniens observes en phase post-critique chez les epileptiques. Rev Neurol (Paris) 1987; 143:620-623).

**COMMENT.** In the last 10 years, numerous studies have demonstrated the hormonal effects not only of generalized convulsive seizures but also of complex partial seizures and of interictal epileptiform discharges (Molaie M, Culebras A, Miller M. Epilepsia 1986; 27:724). Plasma prolactin elevations are used to differentiate epileptic from pseudo-seizures (Collins WCJ et al. J Neurol Neurosurg Psychiatry 1983; 46:505). It is postulated that persistent elevations of prolactin may contribute to endocrine dysfunctions in epileptic patients.

In the same issue of Rev Neurol (Paris) (1987; 143:559), Landrieu P of the Hospital de Bicetre reviews the recent progress and perspectives in pediatric neurology in France.