triggered by ethosuximide and methsuximide. The authors found no previous case of PN reported in childhood epilepsy. In 2 of their patients with a typical history of PN, the discontinuance of treatments (ACTH and vigabatrin) resulted in seizure recurrence and a concomitant psychiatric remission. In patient 1, described above, withdrawal of ACTH caused neither seizure recurrence nor change in behavior. Usually, discontinuation of the offending antiepileptic drug is sufficient to reverse the psychiatric symptoms.

This syndrome was particularly common during trials of phenacemide (Phenurone) in the early 1950s, and some drugs appear to have a greater propensity than others to cause personality changes. ACTH is more likely to cause psychiatric side-effects in older children and adults than in infants and young children. As the authors suggest, the association between epilepsy and psychosis is age-dependent.

PRENATAL EVENTS AND CNS MIGRATION DISORDERS

The role of pre-, peri-, and postnatal environmental factors and genetic predisposition in the genesis of neuronal migration disorders (NMD) in 40 patients with epilepsy was determined by standardized questionnaires at the Montreal Neurological Institute and Hospital, Canada. Potentially harmful prenatal events (maternal trauma, medications, roentgenograms, infections) were reported in pregnancy histories of 58% of patients with NMD compared to 15% of 40 epileptic controls without NMD. In contrast, peri- and postnatal factors were present in only 22% of NMD patients compared to 50% of controls. Genetic factors (family history of epilepsy, mental retardation, or CNS malformation) occurred in 13 and 20% of families, respectively. Stillbirths occurred in 3% of NMD sibling pregnancies, but none in controls. Prenatal environmental factors are important in the cause of NMD. (Palmini A, Andermann E, Andermann F. Prenatal events and genetic factors in epileptic patients and neuronal migration disorders. Epilepsia Sept/Oct 1994;35:965-973). (Reprints: Dr E Andermann, Montreal Neurological Institute, 3801 University St, Montreal, Quebec H3A 2B4, Canada).

COMMENT. Maternal physical trauma in the first trimester was the most significant factor associated with NMD. Genetic factors are important in lissencephaly. Dr Harvey B Sarnat comments on advances in neuroblast migratory disorders in Progress in Pediatric Neurology II, PNB Publishers, 1994, pp279-280. Morphological and metabolic abnormalities of the ependyma, and congenital cytomegalovirus were documented as causes, as well as new experimental data on neuroblast migration mediated by radial glial cells.

FOCAL SPECT LESIONS AND INFANTILE SPASMS

Seven of 10 patients with infantile spasms examined by SPECT at Tokushima University School of Medicine, Japan, showed localized cerebral hypoperfusion in the temporal lobes. EEGs near time of SPECT showed corresponding focal abnormalities in 5. The MRI was less revealing, with confirmation of localized lesions in only 3. (Miyazaki M et al. Infantile spasms: localized cerebral lesions on SPECT. Epilepsia Sept/Oct 1994;35:988-992). (Reprints: Dr M Miyazaki, Department of Pediatrics, Tokushima University School of Medicine, Kuramoto-cho, Tokushima 770, Japan).

COMMENT. Infantile spasms may be associated with focal temporal lobe hypoperfusion on SPECT despite normal MRI.

PET studies of infantile spasms have also shown focal abnormalities when MRI was normal. (Chugani HT et al. In: Progress in Pediatric Neurology Vol II, 1994, p35).

ANTIEPILEPTIC DRUGS

VALPROATE-ASSOCIATED HEPATOTOXICITY UPDATE

Eight new fatalities from valproate (VPA)-related hepatotoxicity, 6 reversible cases, and a review of 132 fatal cases Worldwide are reported from various Universities in Germany. In fatal cases, 65% were developmentally delayed, 75% were taking additional AEDs, and 65% were >2 years old. Early symptoms were nausea, vomiting, apathy, coma, exacerbation of seizures, and febrile infections. Two thirds of fatalities occurred within 6 months of introducing VPA. In reversible cases, VPA had been withdrawn promptly. In addition to Alper's disease, a variety of underlying metabolic defects, especially acyl CoA-dehydrogenase deficiency, has been recognized in some cases of VPA-related hepatotoxicity. (Konig St A, Scheffner D et al. Severe hepatotoxicity during valproate therapy: an update and report of eight new fatalities. Epilepsia Sept/Oct 1994;35:1005-1015). (Reprints: Dr S A Konig, Universitats Kinderklinik, Theodor-Kutzer-Ufer, D-68167 Mannheim, Germany).

COMMENT. Metabolic testing is indicated in children <2 years old with developmental abnormalities when considering VPA therapy. Those patients with recognized metabolic disorders should not receive VPA. Further, VPA should be discontinued promptly and alternative AEDs substituted at the earliest sign of liver failure, if seizures are suddenly exacerbated, and particularly with status epilepticus and febrile infections.

IV PHENYTOIN AND SOFT TISSUE REACTION IN A NEONATE

A blue discoloration in the hand following an iv infusion of phenytoin in a term baby with neonatal convulsions is reported from Basildon Hospital, Essex, UK. A dose of 10 mg/kg was inadvertently diluted with sterile water rather than the recommended saline. The phenytoin infusion via a cannula was aborted after 2 ml/10 min when an intense blue discoloration appeared round the iv site at the dorsum of the hand. Capillary return and radial pulse were normal. On removal of the cannula, blood oozed freely, and the discoloration spread to the rest of the hand. Improvement occurred after 20 hrs and a blister appeared at the iv site. The lesion resolved within one week. A second iv phenytoin, diluted in saline, and given via a cannula in the foot was aborted when a similar reaction occurred. No systemic side effects were noted. Two possible factors are postulated for the injury: 1) precipitation of phenytoin with alteration in pH on contact with blood or infusing fluid and direct vascular injury and vasospasm; or 2) infiltration of drug with tissue reaction from alkaline solution. (Sharief N, Goonasekera C. Soft tissue injury associated with intravenous phenytoin in a neonate. Acta Paediatr Nov 1994;83:1218-1219). (Respond: Dr N Sharief, Basildon General Hospital, Nether Mayne, Basildon, Essex SS16 5NL, UK).

COMMENT. The authors refer to similar reports in the literature occurring in adults but none in infants and children. This type of tissue