

COMMENT. Reports of Reye's syndrome declined in the surveillance period between 1982 and 1990, with a greater reduction in the number of classical Reye's syndrome cases than non-classical Reye-like cases after aspirin was withheld in 1986. Cases of classical Reye's syndrome were older and were more likely to have received aspirin. The authors conclude that their findings support a subset of Reye's syndrome but not all cases etiologically associated with aspirin. An inherited metabolic disorder is more likely in the Reye-like, non classical cases.

ANTICONVULSANT DRUGS

GABAPENTIN IN REFRACTORY PARTIAL SEIZURES

The efficacy of gabapentin as an additional medication in 32 children with refractory partial seizures was studied at the Children's Hospital, Boston, MA. A greater than 50% decrease in seizure frequency was obtained in 3-4% and a 25% to 50% decrease occurred in 12%. Approximately half the patients were benefited. Doses ranged from 10 to 50 mg/kg/day, and the mean gabapentin serum concentration correlating with seizure control was 3.7 mcg/ml. Hyperactivity, irritability, and agitation, in 15 (46%) children with mental retardation and attention deficits, were the major side effects. Mild behavior changes not requiring drug withdrawal, including impulsivity, irritability, and hyperactivity, were reported in 11 additional children. Personality was improved in 3 children. (Khurana DS, Mikati MA et al. Efficacy of gabapentin therapy in children with refractory partial seizures. J Pediatr June 1996;128:829-33). (Reprints: Mohamad A Mikati MD, Department of Pediatrics, American University Hospital, c/o American University of Beirut New York Office, 850 Third Ave, 18th Floor, New York, NY 10022).

COMMENT. Gabapentin may be an effective adjunctive medication in children with refractory partial seizures. Behavioral side effects were reversible when the drug was discontinued and were most prominent in the mentally retarded.

MATERNAL AED TREATMENT AND NEONATAL BEHAVIOR

The relationship between antiepileptic drug (AED) treatment during pregnancy, neurobehavior of the neonate, and the neurological outcome in later life of 40 children exposed in utero to a single AED (phenobarbital, phenytoin, valproic acid) was studied at Children's Hospital, Virchow Klinikum of the Humboldt University Berlin; Institute of Toxicology and Embryopharmacology, Free University Berlin; and Department of Neuropediatrics, Children's Hospital, University of Heidelberg, Germany. Tonic seizures during pregnancy occurred in 5 (27%) of the phenobarbital-treated women, in 5 (38%) treated with phenytoin, and in 3 (33%) of valproic acid-treated women. AED exposed neonates had greater neurobehavioral disorders than the controls. Apathy was most pronounced in phenobarbital-exposed neonates, whereas hyperexcitability was more severe after maternal valproic acid (VPA) exposure. Phenytoin-exposed neonates, having the least neurobehavioral side effects, had low serum concentrations, whereas the concentrations of VPA in cord blood were relatively high. VPA concentrations at birth correlated with the degree of neonatal hyperexcitability and neurological dysfunction found at 6 year follow-up. (Koch S et al. Antiepileptic drug treatment in pregnancy: drug side effects in the neonate and

neurological outcome. Acta Paediatr June 1996;84:739-46). (Respond: Dr S Koch, Rehabitationszentrum fur Kinder, Dorfstr 16, 14476 Kartow, Germany).

COMMENT. The authors suggest that the neonatal VPA-induced malformations and neurobehavioral and late neurological side effects may be related to unexpectedly high levels of the drug and its active metabolites during pregnancy, at birth, and in the neonatal period. Mothers taking VPA during pregnancy should have drug levels closely monitored, especially at the time and shortly after conception but also throughout pregnancy.

AED/ORAL CONTRACEPTIVE INTERACTIONS

A national survey to determine obstetricians' and neurologists' awareness of oral contraceptive (OC) and antiepileptic drug (AED) interactions and the risk of birth defects in infants of AED-treated women with epilepsy was conducted by mailed questionnaire at the Departments of Neurology and Psychiatry, Johns Hopkins University, Baltimore, MD. Responses were received from 160 (16%) neurologists and 147 (15%) obstetricians in 47 states. Most neurologists (80%) knew that phenytoin, carbamazepine, and phenobarbital interfered with OCs, but only 38% knew that valproic acid does not interfere with OCs. Most obstetricians knew that phenytoin interfered with OCs (77%), but fewer were aware of interactions with other AEDs and only 29% knew that valproic acid was non-reactive. Both specialties were generally ignorant of the effects on OCs of ethosuximide, gabapentin, and felbamate. OC failure and accidental pregnancies in patients taking AEDs were reported by 27% of neurologists and 21% of obstetricians. Fewer than half of neurologists (41%) and obstetricians (41%) had their patients adjust OC doses when taking AEDs. Neurologists (44%) often underestimated the risk for AED-induced birth defects (actual risk 4-6%), whereas the risk estimate for most obstetricians varied from 1 to 10%. Some respondents guessed the risk was 50%. Only 3% of neurologists and 5% of obstetricians counselled women taking AEDs to avoid pregnancy. (Krauss GL et al. Antiepileptic medication and oral contraceptive interactions: a national survey of neurologists and obstetricians. Neurology June 1996;46:1534-1539). (Reprints: Dr Gregory L Krauss, Johns Hopkins Hospital, Meyer 2-147, 600 N Wolfe Street, Baltimore, MD 21287).

COMMENT. The authors conclude that many women in the US suffering from epilepsy are at risk for unplanned pregnancies because their physicians are not sufficiently aware of the interactions of antiepileptic drugs and oral contraceptives. They admit that the survey may have overestimated the lack of physician awareness of AED/OC interactions because of the small number of respondents and a possible response bias. Enzyme-inducing AEDs, including carbamazepine, phenytoin, phenobarbital, primidone, and ethosuximide, decrease the effectiveness of OCs by increasing metabolism of synthetic estrogens and lowering synthetic sex hormone levels. Valproic acid, gabapentin, and vigabatrin do not induce hepatic metabolism and are unlikely to interfere with OCs. Valproic acid has not been associated with accidental pregnancies when administered as monotherapy. Irregular or breakthrough menstrual bleeding was used as a sign to increase OC doses in women taking enzyme-inducing AEDs.