

prevalence of malformations among infants of mothers taking AEDs other than valproate was only 2.9% ($p < 0.001$). The relative risk of having an infant born with a major malformation for valproate-treated women is 7.3 ($p < 0.001$).

Lamotrigine and risk of malformations. No increase in risk of major birth defects occurred in infants of mothers exposed prenatally to lamotrigine, in reports to the International Lamotrigine Pregnancy Register (ILPR) (Cunnington M, Tennis P, and the ILPR Scientific Advisory Committee. **Neurology** March (2 of 2) 2005;64:955-960). The risk of 2.9% with lamotrigine monotherapy was similar to that in the general population and in women exposed to other AED monotherapy (3.3-4.5%). With lamotrigine polytherapy including valproate, the risk increased to 12.5%; with polytherapy excluding valproate, the risk was 2.7%.

COGNITIVE DEFICITS IN CHILDREN EXPOSED TO VALPROATE IN UTERO

The long-term effects on cognitive functioning of school-aged children exposed to antiepileptic drugs (AEDs) in utero were investigated at Alder Hay Hospital and Walton Centre for Neurology and Neurosurgery, Liverpool, UK. Neuropsychological tests (WISC-III) were performed on 249 children, ages 6-16, of women with epilepsy recruited from epilepsy and obstetric clinics in the region. Children with prenatal exposure to sodium valproate (VPA) showed a significantly lower verbal IQ when compared to other AEDs or no drug exposure; their IQ was more likely to be < 69 , and memory was more often impaired. Patients taking VPA and other AEDs showed no significant differences between maternal IQ and socioeconomic status. In addition to VPA exposure, low maternal IQ and tonic-clonic seizures during pregnancy were risk factors for impaired verbal IQ in the child. Two thirds of children exposed to VPA had a verbal IQ below average and one fifth had a learning disability with a verbal IQ < 69 . Five or more tonic-clonic seizures during pregnancy were associated with impaired verbal IQ. (Vinten J, Adab N, Kini U et al. Neuropsychological effects of exposure to anticonvulsant medication in utero. **Neurology** March (2 of 2) 2005;64:949-954). (Reprints: Prof Gus A Baker, Dept of Clinical Neuropsychology, University Department of Neurosciences, Walton Centre for Neurology and Neurosurgery, Lower Lane, Liverpool, L9 7LJ, UK).

COMMENT. In this retrospective study controlled for maternal IQ, prenatal exposure to VPA and maternal seizures increased the risk of impairment of verbal intelligence and memory functioning in the child.

FOLIC ACID-INDUCED FALL IN PHENYTOIN LEVELS AND SEIZURE RECURRENCE

Recurrence of seizures is reported in an adult after addition of folic acid for treatment of a macrocytic anemia. He had previously been seizure free for 3 years while receiving phenytoin 300 mg/day. After folate, the phenytoin serum level was 4.5 mcg/mL; prior to the addition of 5 mg oral folate, the phenytoin levels were consistently between 12 and 18

mcg/mL. Despite treatment with fosphenytoin (500 and 1000 mg), seizures recurred and the level of serum phenytoin was unchanged (4.8 mcg/mL). After reduction of folic acid to 1 mg/day, all seizure activity was controlled by the maintenance 300 mg dose of phenytoin, and serum levels increased to 17.6 and 11.3 mcg/mL. (Steinweg DL, Bentley ML. Seizures following reduction in phenytoin level after orally administered folic acid. **Neurology** (June 1 of 2) 2005;64:1982). (Reprints: Dr Donald L Steinweg, Carilion Roanoke Memorial Hospital, PO Box 13367, Roanoke, VA 24033).

COMMENT. This case report underscores the risks of adding folic acid to the drug regimen of patients with epilepsy treated with phenytoin. Folic acid appears to be a cofactor in the metabolism of phenytoin. The initial dose of folic acid should be small, and the dose of phenytoin should be increased to maintain therapeutic levels.

Phenytoin pharmacokinetics before and after folic acid administration were reported from University of Iowa (Berg MJ et al. **Epilepsia** 1992;33:712-720; see **Ped Neur Briefs** Sept 1992). All subjects showed decreased serum folic acid following initiation of phenytoin treatment. Folate and phenytoin are interdependent. In an earlier report (Baylis EM et al. Influence of folic acid on blood-phenytoin levels. **Lancet** 1971;297:62-64), phenytoin levels fell significantly during folic acid therapy, with recurrence of seizures in one case.

ATTENTION DEFICIT DISORDERS

IMMEDIATE EFFECTS OF METHYLPHENIDATE ON COGNITION

The immediate effects of methylphenidate on cognitive attention in 15 children (13 males, 2 females; mean age 9y 5m) with attention deficit hyperactivity disorder (ADHD) were assessed at Guy's Hospital, Great Ormond Street Children's Hospital, and Institute of Child Health, University College, London. All subjects were of average intelligence, but they demonstrated significant impairments in cognitive attention, especially sustained attention, at base-line, in comparison with a control group. Significant improvements in attention were measured in the ADHD children compared to untreated controls, when retested on the same day and after receiving methylphenidate in a single 10 mg dose. (Hood J, Baird G, Rankin PM, Isaacs E. Immediate effects of methylphenidate on cognitive attention skills of children with attention-deficit-hyperactivity disorder. **Dev Med Child Neurol** June 2005;47:408-414). (Respond: Jane Hood, Newcomen Centre, Guy's Hospital, St Thomas Street, London SE1 9RT, UK).

COMMENT. Is the cognitive improvement following a single dose of methylphenidate (MPH) predictive of a beneficial long-term response? The clinical judgment of severity of ADHD and improvement in Conners Rating Scales after a single dose of MPH (10 mg) were predictive of cross-situational improvement after 4 weeks of MPH treatment (Buitelaar JK et al. **J Am Acad Child Adolesc Psychiatry** 1995;34:1025-1032; **Ped Neur Briefs** Aug 1995). High IQ, young age, and low rates of comorbid anxiety were additional predictors of a long-term response.

The acute effects of MPH in 3 dosages (0.3, 0.6, and 0.9 mg/kg) on the performance of 17 ADHD children included increased cognitive flexibility and improved persistence (Douglas VI et al. **J Am Acad Child Adolesc Psychiatry** 1995;34:877-885; **Ped Neur**