

# PEDIATRIC NEUROLOGY BRIEFS

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J. GORDON MILLICHAP, M.D., F.R.C.P., EDITOR

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## TOXIC-METABOLIC DISORDERS

### PERINATAL IV ALUMINUM AND DEVELOPMENTAL DELAY

The effect of perinatal exposure to intravenous aluminum on the neurologic development of 227 premature infants (<34 weeks gestation, <1850g weight) from the neonatal intensive care unit of Rosie Maternity Hospital, Cambridge, UK was studied at the Dunn Nutrition Unit, Cambridge, and the Institute of Child Health, London. The 90 infants who received standard IV feeding solutions, containing 25 mcg Al/dl, had a lower Bayley Mental Development Index at 18 months than the 92 infants who received aluminum-depleted solutions (2.2 mcg Al/dl). Aluminum exposure (45 mcg/kg/day) caused a mean loss on the Bayley Index of 1 point per day. Infants receiving standard IV solutions for 10 or more days had a 10 point deficit in their Mental Development Index and were twice as likely to have an index below 85. (Bishop NJ, Morley R, Day JP, Lucas A. Aluminum neurotoxicity in preterm infants receiving intravenous feeding solutions. *N Engl J Med* May 29, 1997;336:1557-1561). (Reprints: Dr Nicolas J Bishop, Genetics Unit, Shriners' Hospital for Crippled Children, 1529 Cedar Ave, Montreal, QC H3G 1A6, Canada).

COMMENT. Aluminum exposure from standard intravenous solutions in preterm infants may cause neurotoxicity and developmental delay at 18 months. The majority of cases of aluminum poisoning occur as dialysis encephalopathy in adult patients on hemodialysis and peritoneal dialysis. Tap water, especially when treated with aluminum sulfate to remove organic contaminants, contains high concentrations of aluminum and is a frequent cause of dementia following repeated dialyses. Memory loss, malaise, and speech disturbance are followed by myoclonus, somnolence, and dementia. The EEG shows bursts of delta activity and high voltage, symmetric spikes. (Millichap JG. *Environmental Poisons in Our Food*. Chicago, PNB Publ, 1993).

### DIABETES MELLITUS AND DRUG REFRACTORY EPILEPSY

Three teenagers with well-controlled epilepsy who developed drug refractory partial seizures correlated with nonketotic hyperglycemia and insulin-dependent diabetes mellitus are reported from the Children's Hospital

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of Eastern Ontario, University of Ottawa, and Children's Hospital, Dalhousie University, Halifax, Nova Scotia, Canada. Seizures were partial in pattern and two patients had associated focal structural cerebral lesions. Blood sugar determinations confirming the diagnosis of diabetes were indicated by the onset of polyuria and polydipsia. Seizures were controlled following treatment with insulin and correction of hyperglycemia. All three patients were receiving phenytoin. (Whiting S, Camfield P, Artab D, Salisbury S. Insulin-dependent diabetes mellitus presenting in children as frequent, medically unresponsive, partial seizures. J Child Neurol April 1997;12:178-180). (Respond: Dr Sharon Whiting, Children's Hospital of Eastern Ontario, 401 Smyth Road, Ottawa, Canada K1H 8L1).

COMMENT: Children with epilepsy, especially those with epilepsia partialis continua refractory to antiepileptic drugs, should be checked for hyperglycemia and possible diabetes mellitus. The diabetes may be precipitated or exacerbated by administration of phenytoin and other antiepileptic drugs.

A hyperglycemic response to phenytoin was first reported from the Division of Neurology, Children's Memorial Hospital, Chicago, at the 1964 meeting of the American Epilepsy Society. (Belton NR, Etheridge JE Jr, Millichap JG. Effects of convulsions and anticonvulsants on blood sugar. Epilepsia 1965;6:243-249). An inhibition of insulin secretion by phenytoin demonstrated in vitro (Kizer JS et al. 1970) was subsequently confirmed in human volunteers (Malherbe C et al. 1972).

## ANTIEPILEPTIC DRUGS

### **BARBITURATE AEDS, EEG AND COGNITIVE PERFORMANCE**

Neuropsychological performance and quantitative EEGs were studied in 11 epileptic children, aged 7 to 14 years, both during treatment and without phenobarbital and mephobarbital, and in comparison to 13 matched controls, at Tulane University Medical School, New Orleans, LA. Barbiturates at therapeutic levels (10-40 mcg/ml) had no effect on the EEG in frequency bands 0.6 to 32 Hz. Compared to controls, the WISC-R Verbal, Performance, and Full Scale Scores, Bender-Gestalt, and Achenbach Behavior Rating Scale showed no significant change during barbiturate treatment; only the Stroop color/word test showed an adverse difference. Compared to scores off-drug in 8 subjects analyzed, adverse on-drug effects were found in the WISC-R Verbal, Stroop, and Achenbach aggression scales. Performance of the Bender-Gestalt improved during treatment with barbiturates. Irritability, oppositional attitude, and overactivity were reported in 6 of 11 subjects, but the parents of 4 elected to continue treatment. Mephobarbital caused less behavioral problems than phenobarbital. (Willis J, Nelson A, Black FW, Borges A, An A, Rice J. Barbiturate anticonvulsants: a neuropsychological and quantitative electroencephalographic study. J Child Neurol April 1997;12:169-171). (Respond: Dr John Willis, Tulane University Medical School, 1430 Tulane Ave, New Orleans, LA 70112).

COMMENT. Contrary to a previous report of adverse effects of phenobarbital in younger children treated for febrile seizures, barbiturates appear to cause negligible cognitive impairments, only mild behavioral changes, and no effects on the EEG in older school age children treated for epilepsy.