BRAIN NEOPLASMS

ASPARTAME AND BRAIN TUMOR RISK

The potential link of aspartame to rising brain tumor rates was analyzed using 1975 to 1992 data from the US National Cancer Institute in a study at the Departments of Psychiatry and Biostistics, Washington University Medical School, St Louis, MO. The incidence curve of primary brain tumors for the years 1975 to 1992 is biphasic, phase I from 1975-1984 and phase II from 1985-1992. In phase I the increased incidence was small and unsustained, whereas in phase II a sharp increase in incidence was accompanied by greater malignancy. Aspartame was first approved in the US in 1981 and wider approval was extended in 1983. The authors propose that aspartame usage may be linked to the onset in 1985 of a sustained increase in rate of malignant tumors in the elderly population, or to the steady climb in incidence of various tumors in younger age groups beginning in 1987. The criteria invoked in judging the carcinogenic potential of environmental agents appeared to be met by aspartame: 1) aspartame has in vitro mutagenic potential related to its nitrosation to nitrosourea; 2) aspartame-fed rats have a high incidence of malignant brain tumors; and 3) an increased incidence of brain tumors in humans following the introduction of aspartame in the diet. (Olney JW, Farber NB, Spitznagel E, Robins LN. Increasing brain tumor rates: is there a link to aspartame? J Neuropathol Exp Neurol Nov 1996;55:1115-1123). (Respond: John W Olney MD, Department of Psychiatry, Washington University School of Medicine, 4940 Childrens Place, St Louis, MO 63110).

COMMENT. This detailed analysis of data pertaining to the potential carcinogenic effects of the artificial sweetener aspartame, conducted by scientists at an independent prestigious university and published after peer review in a recognized medical journal, warrants further assessment of the safety of this widely used dietary additive. Aspartame has been linked to precipitation of migraine headaches, and exacerbation of epileptiform discharges in the EEG of children with seizures. (Progress in Pediatric Neurology I and II, PNB Publ, 1991, 1994). Despite the controversy over the validity of these studies, aspartame is becoming a "food for thought" rather than ingestion, until its safety is reviewed by an unbiased panel of experts.

SEIZURE DISORDERS

CORTICAL HYPOMETABOLISM IN WEST SYNDROME

Serial PET scans and MRIs were performed in 18 infants with West syndrome (WS) to determine the relation between cortical hypometabolism and delayed myelination in a study at Nagoya University School of Medicine, Japan. All 8 patients with symptomatic WS showed hypometabolism at onset, with persistence in 5 at 10 months, whereas only 4 of 10 patients with cryptogenic WS showed hypometabolism at onset and none at age 10 months. Localization of EEG abnormalities at 10 months correlated with the region of hypometabolism in only 2. MRI showed delayed myelination in 2 at onset of epilepsy and in 12 at 10 months. Delayed myelination at 10 months was correlated with hypometabolism. (Natsume J, Watanabe K, Maeda N et al. Cortical hypometabolism and delayed myelination in West syndrome. Epilepsia Dec 1996;37:1180-1184). (Reprints: Dr J Natsume, Department of Pediatrics, Nagoya University School of Medicine, 65 Tsurumai, Showa-ku, Nagoya 466, Japan).

COMMENT. MRIs repeated at age 10 months may disclose delayed myelination in infants with WS. The delayed myelination is not always explained by ACTH therapy and may reflect the organic brain lesion causing the seizures.

FRAGILE X MUTATIONS AND EPILEPSY

A posiible link between predisposition for epilepsy and mutations in the fragile X mental retardation-1 gene (FMR) was investigated in the Neuropediatric Department, Behandlungszentrum Vogtareuth; and Laboratory of Genetic Diagnostics, Munchen, Germany. EEGs performed on 14 patients with an amplification in the FMR-1 gene showed focal sharp waves and partial seizures in sleep in 8 boys, aged 4-8 years. Of 16 children with rolandic epilepsy (BECT) studied for FMR-1 gene mutations, 1 boy was positive. (Kluger G, Bohm I, Laub MC, Waldenmaier C. Epilepsy and fragile X gene mutations. Pediatr Neurol Nov 1996;15:358-360). (Respond: Dr Kluger,Neuropediatric Department, Behandlungszentrum Vogtareuth, Krankenhausstrabe 20, D-83569 Vogtareuth, Germany).

COMMENT. A higher incidence of seizures or EEG abnormalities may be expected in boys with fragile X-1 gene mutations.

ANTIEPILEPTIC DRUGS

PHENYTOIN AND CARBAMAZEPINE TERATOGENICITY

In a prospective, controlled, and blinded study of 36 mother-child pairs exposed to carbamazepine (CBZ) monotherapy, 34 pairs exposed to phenytoin (DPH) monotherapy, and 9 nonmedicated epileptic women and their children, the patterns of malformations in the children exposed to potential teratogenic factors were compared with matched mother-child pairs exposed to nonteratogens, at the Hospital for Sick Children, Toronto, Canada. There was no correlation between the daily dose of DPH or CBZ and number of malformations. Microcephaly occurred in 6% of children exposed to DPH and 8.8% of those exposed to CBZ, but not in medicated nonepileptic or nonmedicated epileptic subgroups. Malformations in 8.8% of DPH and 5.7% of CBZ exposed children were not significantly different from controls. Minor anomalies in children exposed to either AED were more frequent than in controls, with a relative risk of 2.1. Hypertelorism was more frequent among DPH-exposed offspring; 25% incidence vs 11% in controls. High forehead, frontal bossing, malar hypoplasia, epicanthus and micrognathia occurred in association with untreated epilepsy, as well as DPH and CBZ treatment. (Nulman I, Scolnik D, Chitayat D, Farkas LD, Koren G. Findings in children exposed in utero to phenytoin and carbamazepine monotherapy: independent effects of epilepsy and medications. Am J Med Genet Jan 1997;68:18-24). (Respond: Gideon Koren MD, The Hospital for Sick Children, 555 University Avenue, Toronto, Ontario, M5G 1X8, Canada).

COMMENT. AEDs and epilepsy have teratogenic effects that are independent and result in minor anomalies in infants exposed in utero. Previous studies have shown that valproate and carbamazepine are associated predominantly with spina bifida and hypospadias, whereas barbiturates and phenytoin may induce congenital heart malformations and facial clefts. None of the AEDs is free of possible adverse effects on the fetus. Experience with