BUMETANIDE-ENHANCED PHENOBARBITAL IN NEONATAL SEIZURE MODEL

Anticonvulsant efficacy of phenobarbital, bumetanide, and a combination of these drugs was studied in an in vitro hippocampal rat pup (4-7 days) preparation, with recurrent seizures induced by exposure to low-Mg solution, at the Department of Neurology, Massachusetts General Hospital, Boston. The combination of phenobarbital and bumetanide abolished these experimental seizures in 70% of hippocampi and reduced their frequency and duration in the remaining 30%. The GABA-mediated outward flow of Cl in immature neurons is excitatory, contributing to a poor response to GABAergic anticonvulsants such as phenobarbital and benzodiazepines. The diuretic bumetanide blocks the Na K Cl transporter system and prevents the outward flow of Cl ions. Alteration of Cl ion transport by bumetanide facilitates the anticonvulsant action of phenobarbital in immature animal brain, providing a potential effective therapy for neonatal seizures. (Dzhala VI, Brumback AC, Staley KJ. Bumetanide enhances phenobarbital efficacy in a neonatal seizure model. **Ann Neurol** February 2008;63:222-235). (Respond: Dr Kevin J Staley, MD, Department of Neurology, Massachusetts General Hospital, 55 Fruit Street, VBK 910, Boston, MA 02114. E-mail: kstaley@partners.org).

COMMENT. The authors propose a clinical trial of bumetanide in combination with phenobarbital in the treatment of neonates with seizures. Previous studies cited have demonstrated a low risk of side effects with bumetanide in sick infants (Sullivan JE et al. 1996). The above laboratory study and others by my colleague, Dr Sookyong Koh, recipient of the Dreiffus-Penry Epilepsy Award at the AAN meeting, April 15, have advanced our understanding of seizure mechanisms and control of epilepsy-associated behavioral changes in the young.

INFECTIOUS DISORDERS

VARICELLA ZOSTER VIRUS VASCULOPATHIES

The clinical, CSF, imaging, and virological features of varicella zoster virus (VZV) vasculopathies in 30 patients (7 children) are reviewed by researchers at various centers in the US and internationally. The data obtained on the 7 children, ages 1-7 and 18, show rash in 5, CSF pleocytosis in 6, focal lesions on MRI/CT in 7, focal vascular abnormalities by angiography or MRA in 3 of 4 tested, small vessel involvement in 2 and mixed in 5, CSF VZV DNA in 2, and IgG in 5, and reduced serum/CSF ratio of VZV IgG in 5, confirmation of intrathecal synthesis. Average time from rash to neurologic symptoms and signs and virologic analysis was 4.1 months. In children it varied from 1-2 days to 3 months. Detection of anti-VZV IgG antibody in CSF is a more sensitive indicator of VZV vasculopathy than VZV DNA ($p<0.001$). Of 15 patients (13 adults and 2 children) treated with IV acyclovir alone for 10-28 days, 66% improved or stabilized compared to 75% of 12 patients (9 adults and 3 children) who received both IV acyclovir and steroids. Of 2 children not treated, 1 stabilized and the other improved slowly. (Nagel MA, Cohrs RJ, Mahalingam R et al. The

varicella zoster virus vasculopathies. Clinical, CSF, imaging, and virologic features. **Neurology** March 11, 2008;70:853-860). (Reprints: Dr DH Gilden, Department of Neurology, Mail Stop B182, University of Colorado Health Sciences Center, 4200 E 9th Ave, Denver, CO 80262).

COMMENT. VZV is a possible cause of stroke in children and adults, even without a history of rash. Prior rash was absent in 29% of children and in 40% of the total group. Symptoms of vasculopathy can be delayed up to 3 months after the rash in children, 4 months in adults. CSF pleocytosis was present in the majority (86%) of children, but absent in 33% of the total group.

Acute infection, viral or bacterial, is a risk factor for cerebral infarction and stroke in all age groups. The reported prevalence of infection in the week preceding ischemic stroke ranges from 10% to 35%. Influenza vaccination has been correlated with a lower risk of stroke. (Emsley HCA, Hopkins SJ. **Lancet Neurology** April 2008;7:341-353).

Herpes zoster live-attenuated vaccine in elderly subjects was effective and increased VZV-T cell-mediated immunity within 6 weeks after vaccination. Boosting immunity by vaccination should protect older adults against herpes zoster and postherpetic neuralgia, at least 4 years or longer. (Levin MJ et al. **J Infect Dis** March 15, 2008;197:825-835).

BRAIN MALFORMATIONS

CLASSIFICATION OF CORTICAL BRAIN MALFORMATIONS

Clinical, radiological, and genetic classifications of 113 cases of malformations of cortical development (MCD) were evaluated at the Erasmus Medical Center-Sophia Children's Hospital, Rotterdam, the Netherlands. Diagnosis was confirmed retrospectively in 48 patients during a 10-year period, and prospectively in 65 during only 4 years. Increased alertness or improved brain imaging might have accounted for the more recent higher prevalence of diagnosis of MCD. Disorders of proliferation (eg. congenital microcephalies) occurred in 11, disorders of migration (lissencephaly/heterotopia) in 51, disorders of cortical organization (eg schizencephaly) in 49, and MCD secondary to inborn errors of metabolism in 2. An etiologic diagnosis was established in 45 (40%) cases. In 21 patients (19%) molecular and/or genetic confirmation was established (eg. Miller-Dieker syndrome, inborn error of metabolism). Genetic defect was unknown in 17 (15%). A gestational insult had occurred in 7 (6%). In 34 of the remaining 68 patients, a genetic disorder was suspected based on multiple anomalies, family history, or consanguinity. More definitive diagnosis of MCD would lead to improved patient care and genetic counseling. (de Wit MCY, Lequin MH, de Coo IFM et al. Cortical brain malformations. Effect of clinical, neuroradiological, and modern genetic classification. **Arch Neurol** Mar 2008;65:358-366). (Respond: Grazia MS Mancini MD PhD, Department of Clinical Genetics, Erasmus Medical Center, PO Box 1738, 3000 DR Rotterdam, the Netherlands. E-mail: mancini@erasmusmc.nl).

COMMENT. See Sarnat HB. In **Progress in Pediatric Neurology III,** Chicago, PNB, 1997;365-9; and Norman MG et al. **Congenital Malformations of the Brain.** New York, Oxford University Press, 1995;452 pages, for excellent reviews of MCD advances.