

rate of congenital heart defects in exposed infants was 2.9% compared to 1.6% in matched controls and 0.7% in the general control group. No cases of neural tube defect were recorded, an omission thought to reflect a sample size limitation. (Diav-Citrin O, Shechtman S, Arnon J, Ornoy A. Is carbamazepine teratogenic? A prospective controlled study of 210 pregnancies. *Neurology* July (2 of 2) 2001;57:321-324). (Reprints: Dr Asher Ornoy, Department of Anatomy and Cell Biology, Hebrew University and Hadassah Medical School, PO Box 12272, Jerusalem, 91120, Israel).

COMMENT. In this Israeli study, one of the largest series reported, first trimester carbamazepine (CBZ) exposure was associated with a twofold increase in the rate of major congenital anomalies and a reduced infant birth weight compared to controls. Neural tube defect, the most commonly reported teratogenic effect of CBZ, was surprisingly absent. (See *Progress in Pediatric Neurology I and II*, PNB Publishers, 1991(pp112-113) and 1994 (pp109-112), for previous reports of AED teratogenicity, including spina bifida and CBZ). The 10,11-epoxide intermediate metabolite of CBZ has been implicated as the teratogenic agent. Oxcarbazepine (Trileptal®), the recently introduced congener of CBZ, has no epoxide metabolite, but undergoes reduction to form 10-monohydroxy derivative (MHD). Trileptal is reported to have no serious side effects and hopefully, this will include no teratogenicity.

## INTRACRANIAL HYPERTENSION

### IDIOPATHIC INTRACRANIAL HYPERTENSION

The diagnosis and treatment of 32 patients diagnosed with idiopathic intracranial hypertension were analysed in a retrospective chart review at the Hospital for Sick Children, Toronto, ON, Canada, and Great Ormond Street Hospital for Children, Institute of Child Health, London, UK. Ages ranged from 2 to 17.5 years. Twenty three were female. The most common presenting symptom was headache (91%), followed by nausea and vomiting (56%), double vision (38%), and visual loss or blurring (25%). Signs at presentation included papilledema (97%), VIth cranial nerve palsy (31% unilateral, 9% bilateral), retinal hemorrhages (13%), constricted visual fields (12%), and decreased visual acuity (29%). Associated disorders in 59% included obesity in 48%, recent or recurrent otitis media (28%), upper respiratory tract infection (16%), sinusitis (13%), Addison's disease and thyroiditis in 1 patient, and sudden withdrawal of cyproterone acetate for precocious puberty in 1. CT or MRI excluded hydrocephalus or space-occupying lesion, and none had sinus venous thrombosis. All but one had a CSF pressure of >20 cm (a normal opening pressure does not negate the diagnosis, since pressure is known to rise intermittently or infrequently). None developed tonsillar herniation. Treatments intended to alleviate symptoms and prevent visual loss included acetazolamide as first line treatment (44%), corticosteroids (short course) used for deteriorating visual loss or persistent headache (34%), lumboperitoneal shunt (25%), optic nerve fenestration (16%), and repeat lumbar puncture (25%). Combination treatments were used in 40%. Four (13%) received no treatment. Four recovered after the first lumbar puncture and never required further therapy. None of the therapies has been proven effective by randomized controlled trial. The terms "benign" and "pseudotumor" should be discarded in favor of "idiopathic intracranial hypertension." (Salman MS, Kirkham FJ, MacGregor DL. Idiopathic "benign" intracranial hypertension: case series and review. *J Child Neuro* July 2001;16:465-470). (Respond: Dr Michael S Salman, Division of Neurology, The Hospital for Sick Children, 555 University Avenue, Toronto, ON M5G 1X5

Canada).

COMMENT. Idiopathic intracranial hypertension is not "benign" and is associated with significant morbidity and short- or long-term symptoms, often resistant to therapy. None of the proposed therapies is of proven efficacy, and this extensive case series and review emphasizes the need for prospective studies.

## NEUROMUSCULAR DISORDERS

### **PRESYNAPTIC CONGENITAL MYASTHENIC SYNDROME**

Three patients (ages 7, 9, and 14 years) with a new form of presynaptic congenital myasthenic syndrome (CMS) are reported from the University of California, Davis; University of Minnesota; and the University of Chicago. This CMS was characterized by decreased quantal release with normal amplitude miniature end-plate potentials (MEPP), normal size of nerve terminals, and normal number of synaptic vesicles. Symptoms had presented with scoliosis at age 5 years in patient 1, delay in walking and easy fatigability at 17 months in patient 2, and as an infant with hypotonia and motor developmental delay in patient 3. Clinical findings included muscle weakness and fatigability, respiratory crisis, nystagmus (1 case), bulbar deficit, scoliosis - severe in one patient, and mild ataxia. No patient had ophthalmoplegia or mental delay. A similar disorder was reported in a close relative of patient 2, but patients 1 and 3 had no family history of neurologic disease. Electrodiagnostic evidence of abnormal neuromuscular transmission was obtained in all patients. Intracellular microelectrode studies showed a dramatic reduction of the endplate potentials (EPP) quantal content, indicative of presynaptic failure. Screening of reported pathogenic mutations in the CACNA1A and a mutational analysis of AChR subunit genes were negative. Treatment with prednisone and pyridostigmine was ineffective, while a combination of pyridostigmine and 3,4-diaminopyridine reduced the frequency of respiratory crises and resulted in improved muscle strength and exercise endurance in one patient. The deficiency of quantal release of neurotransmitter underlying this form of presynaptic CMS may be explained by an abnormal calcium metabolism or impaired endocytosis and recycling of synaptic vesicles. (Maselli RA, Kong DZ, Bowe CM et al. Presynaptic congenital myasthenic syndrome due to quantal release deficiency. *Neurology* July (2 of 2) 2001;57:279-289). (Reprints: Dr Ricardo A Maselli, UC Davis, 1515 Newton Ct, Rm 510, Davis, CA 95616).

COMMENT. Presynaptic congenital myasthenic syndrome (CMS) results from a deficiency in release of neurotransmitter from the nerve terminal. Familial infantile myasthenia (FIM) and a CMS associated with paucity of synaptic vesicles (PSV) have been fully described, and some additional isolated cases of presumed CMS have been reported. The molecular genetic defect for CMS has not been elucidated. In the 3 cases reported here due to quantal release deficiency, involvement of CACNA1A mutations is considered most likely and deserves further evaluation.

For further review of various types of congenital myasthenic syndromes, see Engel AG et al. 1993; and *Progress in Pediatric Neurology III*, 1997;pp346-7.

### **RECOVERY FOLLOWING NEONATAL BRACHIAL PLEXUS PALSY**

The value of detailed strength testing monthly, up to 6 months of age, in predicting complete recovery was determined in a prospective study of 80 infants with brachial plexus injury followed at the Brachial Plexus Palsy Center, St Louis