However, side-effects with VA and CBZ were significantly different. Weight gain was particularly troublesome with VA, while somnolence, dizziness, and ataxia required modification of dosage of CBZ. Severe rash noted in 10% of patients taking CBZ in previous adult studies necessitated drug withdrawal in only 3% of children in the present report. Carbamazepine-induced skin rash was reported in 10% of 335 children treated at Toyama Medical University, Japan, and additional reports are cited in Progress in Pediatric Neurology II, PNB Publ, 1994, pp107-109.

VIGABATRIN MONOTHERAPY FOR INFANTILE SPASMS

The successful management of 21 children with infantile spasms and hypsarrhythmia using vigabatrin monotherapy is reported from the Alder Hey Children's Hospital, Liverpool, UK. Age at onset of spasms was 3 to 16 months. A symptomatic cause was identified in 17(81%). Spasms were completely controlled in 17(81%) with an initial dose of vigabatrin 25-50 mg/kg/day, increasing to a maximum of 80-120 mg/kg/d in 3-5 days. At a mean 2 year follow-up, 14(67%) remained seizure-free, and vigabatrin was withdrawn in 4 without relapse. Only one patient failed to respond; this child had meningitis at 4 months and spasms were refractory to all AEDs, including ACTH. Transient drowsiness in 2 patients was the only side-effect noted. (Appleton RE. A simple, effective and well-tolerated treatment regime for West syndrome. Dev Med Child Neurol Feb 1995;37:185-187). (Respond: Dr Richard E Appleton, Royal Liverpool Children's NHS Trust, Alder Hey Children's Hospital, Eaton Rd, Liverpool L12 2AP, UK).

COMMENT. Vigabatrin has replaced ACTH and prednisone as the first-line treatment for West syndrome in the Liverpool Children's Hospital. Dr Verity and colleagues in the UK have been very successful in their organization of a multicenter, comparative trial of sodium valproate and carbamazepine. A similar controlled trial of vigabatrin and ACTH based in Liverpool might be necessary to convince other centers to initiate a change in treatment of infantile spasms.

Of interest, only 4 children (10%) were seizure free following vigabatrin monotherapy for intractable epilepsy in a previous report from the Royal Liverpool Children's Hospital. Complex partial seizures responded partially but myoclonic seizures were not benefited.(Gibbs et al. 1992; see Progress in Pediatric Neurology II, 1994, pp 104-5).

An open, add-on trial of vigabatrin in 20 children with Lennox-Gastaut syndrome, reported from Wien, Austria, showed 85% with a 50-100% reduction in seizure frequency, even after valproate dosage was reduced. Dyskinesia in 1 child was the only side-effect. (Feucht M, Brantner-Inthaler S. Epilepsia 1994;35:993). Serious mood disorders, depression and/or aggression, were the main reason for withdrawing vigabatrin in 9 (12%) of 73 adults with refractory epilepsy treated at the Meer & Bosch Epilepsy Centre, Heemstede, The Netherlands. (Aldenkamp AP et al. Epilepsia 1994;35:999). Vigabatrin results in a significant increase in brain GABA concentration by inhibiting GABA transaminase.

THEOPHYLLINE-INDUCED INFANTILE SPASMS

Infantile spasms and hypsarrhythmia developed in a 6-month-old infant with asthma after 3 days treatment with theophylline at the Royal

Belfast Hospital for Sick Children, Northern Ireland. Theophylline blood level was elevated to 108 mcmol/l (30 mcmol above therapeutic level). Spasms stopped and EEG became normal when nitrazepam was started and theophylline was discontinued. Nitrazepam was withdrawn at 10 months, the sleep EEG was normal at 14 months, and seizures had not recurred at 3 year follow-up. (Shields MD et al. Infantile spasms associated with theophylline toxicity. Acta Paediatr Feb 1995;84:215-217). (Respond: Dr MD Shields, Department of Child Health, Royal Belfast Hospital for Sick Children, 180 Falls Rd, Belfast BT12 6BE, Northern Ireland).

COMMENT. A direct causal relationship was considered probable because of the close temporal association of spasms and a toxic level of theophylline and the complete remission when the drug was discontinued. A dose of 6-8 mg/kg/day theophylline is usually recommended for infants <7 months of age with asthma. The toxic dose in this patient was 16 mg/kg/day.

Infantile spasms in 5 children (4 symptomatic) persisted to 5 to 14 years of age in a report from the Steele Memorial Children's Research Center, University of Arizona, Tucson (Talwar D, Griesemer DA et al. Epilepsia Feb 1995;36:151-155).

MECHANISMS OF ABSENCE SEIZURES

A unifying hypothesis for the pathogenesis of absence seizures, involving the thalamocortical circuitry, is proposed in a neurological progress report from the University of Southern California School of Medicine, Childrens Hospital Los Angeles. Abnormal oscillatory rhythms generated in the circuit involve g-aminobutyric acid (GABA)B-mediated inhibition alternating with glutamate-mediated excitation which triggers a low-threshold calcium current in neurons of the nucleus reticularis thalami. The process is modulated by pathways utilizing various neurotransmitters and projected onto the thalamus and cortex, generating bilaterally synchronous spike wave discharges and absence seizures. Ethosuximide and trimethadione block absence seizures by reducing the low-threshold calcium current via a direct action at the T-type calcium channel. Other anti-absence seizure medications have indirect effects on this calcium current within the thalamus. (Snead OC III. Basic mechanisms of generalized absence seizures. Ann Neurol Feb 1995;37:146-157). (Respond: Dr Snead, Box 82, 4650 Sunset boulevard, Los Angeles, CA 90027).

COMMENT. A knowledge of the mechanisms of absence seizures should facilitate the development of more specific antiepileptic medications and the avoidance of drugs (eg. phenytoin and carbamazepine) that exacerbate absence attacks. For an excellent review of mechanisms of antiepileptic drug action see Talwar D, 1990, and commentary, Progress in Pediatric Neurology I, 1991, pp94-5.

MECHANISM OF OPSOCLONUS-MYOCLONUS SYNDROME

Cerebrospinal fluid measurements of the serotonin metabolite 5-hydroxyindoleacetic acid (5-HIAA) and the dopamine metabolite homovanillic acid (HVA) in samples from 27 children with opsoclonus-myoclonus syndrome and 47 controls are reported from the National Pediatric Myoclonus Center, Children's Research Institute, Washington, DC, and other centers. The mean age at onset was 1.5 years, and patients were symptomatic for 3 years before