encephalopathy in 1, and Lennox-Gastaut syndrome in 2 cases. Metabolic acidosis developed in 8 patients after 8-26 days (median, 14 days) of TPM treatment. Median serum bicarbonate was 17 mM, minimal base excess -7.9 mM, and pH between 7.22 and 7.40 (median, 7.35). Four children had clinical signs of hyperventilation and required oral sodium bicarbonate; TPM effectiveness was not affected. Monitoring of acid-base metabolism is recommended in young children during therapy with TPM. (Philippi H, Boor R, Reitter B. Topiramate and metabolic acidosis in infants and toddlers. Epilepsia July 2002;43:744-747). (Reprints: Dr med H Philippi, Department of Pediatrics, Johannes Gutenberg-University, Mainz, Germany).

COMMENT. Metabolic acidosis, a consequence of carbonic anhydrase inhibition, is a frequent side effect of topiramate in infants and toddlers during treatment for refractory seizures. Since the mechanism of anticonvulsant action of carbonic anhydrase inhibitors is unrelated to the metabolic acidosis (Millichap JG, Woodbury DM, Goodman LS. Mechanism of the anticonvulsant action of acetazolamide, a carbonic anhydrase inhibitor. J Pharmac Exp Therap 1955;115:251), the addition of sodium bicarbonate to TPM to correct hyperventilation would not be expected to lead to a recurrence of seizures.

ATTENTION DEFICIT DISORDERS

NONSTIMULANT THERAPY FOR ADHD

The results of a multicenter, open-label, dose-titration study of GW320659, a novel norepinephrine and dopamine reuptake inhibitor, are reported from GlaxoSmithKline, Research Triangle Park, NC. Forty six subjects with ADHD, mean age 9.1 years, received the maximal acceptable dose (mean 14.2 mg/day) continued for a 4-week treatment period. During the initial dose-titration period, a clinical response was judged by a Clinical Global Impression of Improvement score of 1 or 2, and a 5 or more point improvement on at least one Conners Rating Scale T score. At the end of treatment, 76% of subjects showed improvements; 7 of 12 subscales of the Child Health Questionnaire Parent Form 28 showed significant improvements compared with baseline ($p<.05$). Adverse events reported in 92% of subjects included headaches in 31%, abdominal discomfort (25%), excessive crying (20%), anorexia (18%), insomnia (14%), and nausea and vomiting (12%). Five subjects (10%) required reduction in dose during the titration phase because of adverse events: these included crying and emotional lability in 2, mood elevation (1), increased blood pressure (1), and sleep disorder and nocturia (1). No serious side effects occurred that necessitated drug withdrawal. The authors concluded that GW320659 may have "clinically relevant efficacy" in pediatric ADHD and was "well tolerated" in this short-term study. (DeVeaugh-Geiss J, Conners CK, Sarkis EH et al. GW320659 for the treatment of attention-deficit/hyperactivity disorder in children. J Am Acad Child Adolesc Psychiatry August 2002;41:914-920). (Reprints: Dr Asgharnejad, GlaxoSmithKline, Five Moore Drive, PO Box 13398, Research Triangle Park, NC 27709).

COMMENT. Stimulant medications such as methylphenidate and amphetamines are the first line of treatment in most children with ADHD. Alternative treatments such as clonidine and guanfacine have indications for patients with comorbid ODD, insomnia, and tics, and bupropion is sometimes recommended in ADHD patients, especially those who exhibit depressive symptoms. GW320-6590, like bupropion, inhibits norepinephrine and dopamine reuptake. Both stimulants and bupropion may exacerbate tics and increase susceptibility to seizures, side effects not reported in the trial of GW320-6590.