

# PEDIATRIC NEUROLOGY BRIEFS

A MONTHLY JOURNAL REVIEW

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Vol 9, No. 12

December 1995

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## ANTIPILEPTIC DRUGS

### ANTIPILEPTIC DRUG MONITORING

The appropriateness of antiepileptic drug (AED) level monitoring was assessed in a tertiary care center performing more than 10,000 AED level determinations per year and reported from the Brigham and Women's Hospital, Boston, MA. In a total of 330 inpatients with AED levels measured a total of 855 times, only 27% of levels had appropriate indications, and only half of these were sampled correctly as trough levels, resulting in an overall appropriate test rate of 14%. Indications were baseline, control levels after starting treatment or after steady state was achieved with a change of dose (13%), after a seizure relapse (8%), suspected drug toxicity (4%), presumed patient noncompliance (1%), and possible drug interaction (1%). The rate of determination was the same for all drugs (phenytoin, carbamazepine, phenobarbital, valproic acid). Of the 73% of levels considered inappropriate, three quarters had been obtained after starting or changing the drug regimen, frequently on a daily basis, and before achieving a steady state; 23 (3.7%) were above the therapeutic range and potentially toxic. The avoidance of inappropriate testing would have resulted in a saving of >\$300,000. (Schoenenberger RA et al. Appropriateness of antiepileptic drug level monitoring. JAMA November 22/29 1995;274:1622-1626). (Reprints: David W Bates MD, Division of General Medicine and Primary Care, Brigham and Women's Hospital, 75 Francis St, Boston, MA 02115).

COMMENT. Appropriate indications for AED levels include: 1) seizure recurrence, 2) drug toxicity, 3) patient noncompliance. Blood should be drawn at time of steady state (6 days for phenytoin, 3 days for carbamazepine and valproic acid, and 20 days for phenobarbital), as a baseline, after change of dose, after addition of second drug, or after change in liver or gastrointestinal function. Except after seizure relapse or with suspected toxicity, trough levels should be obtained. More frequent AED level determinations may be indicated during pregnancy and labor, after surgery, and in infants and children.

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The authors of this study conclude that appropriate indications and timing of AED level determinations were not followed in 75% of patients in their tertiary care hospital. More careful adherence to appropriate monitoring indications would have resulted in cost reductions without significant risk of ineffective therapy or toxicity.

## AGE FACTORS AND ANTIPILEPTIC DRUG WITHDRAWAL

Age dependent factors concerning the withdrawal of antiepileptic drugs (AED) and seizure relapse rates, after a seizure-free period longer than 3 years, were evaluated in 304 patients with childhood epilepsies treated at the Toyama Medical and Pharmaceutical University, Toyama City, Japan. The incidence of AED withdrawal differed significantly between epileptic syndromes, being higher in idiopathic than in symptomatic epilepsies. Age at withdrawal peaked at preadolescence and early school age. Relapses occurred in 14%, the rate differing between epileptic groups and occurring at a unique age in each epileptic syndrome. Relapse rates were 33% and 20% in symptomatic *generalized* and *partial* epilepsies, respectively, and 5 to 8% in benign infantile convulsions, and idiopathic partial epilepsies. Idiopathic generalized epilepsy syndromes had higher relapse rates: 25% in juvenile absence, 100% in juvenile myoclonic, and 27% in grand mal on awakening epilepsy. Relapses were more frequent in epilepsies of infantile or adolescent onset than in those of school age onset. Age of relapse peaked at ages 7 to 11, mainly benign childhood epilepsy with centrotemporal spikes, and 17 to 19 years, mainly symptomatic partial, juvenile myoclonic, and grand mal.

EEG paroxysmal discharges did not necessarily predict a relapse, but changes in background activity with age showed correlations with rate of seizure recurrence. In patients without relapse, the background showed an increased maturation in mean frequency, with decrease in slow waves and increased alpha activity, during AED control before drug withdrawal. (Murakami M et al. Withdrawal of antiepileptic drug treatment in childhood epilepsy: factors related to age. *J Neurol Neurosurg Psychiatry* 1995;59:477-481). (Respond: Dr Miyako Murakami, Department of Pediatrics, Toyama Medical and Pharmaceutical University, 2630 Sugitani, Toyama City 930-01, Japan).

COMMENT. Age dependent factors are important in time of withdrawal of AED and in prognosis after attempted AED withdrawal. Epileptic syndromes have an age dependent onset and course, related to CNS maturation, and varying relapse rates. Most frequent relapse rates occurred in patients undergoing drug withdrawal in preadolescence, eg benign childhood epilepsy with centrotemporal spikes, and early adulthood, eg symptomatic partial epilepsies. The characteristic course of each epileptic syndrome should be considered when attempting AED withdrawal. Background activity in the EEG is also an important factor, the persistence of slow waves and decreased alpha activity indicating an increased risk of relapse.

## SAFETY OF INTRAVENOUS VALPROATE

A multicenter, open-label study of the safety of intravenous sodium valproate in 318 hospitalized patients with epilepsy is reported from the NYU Hospital for Joint Diseases; MINCEP Epilepsy Care and Minnesota Epilepsy Group, MN; University of Texas, Houston; Medical College of Virginia, Richmond; Bowman-Gray School of Medicine, Winston-Salem, NC; and