

## FOLIC ACID TREATMENT OF ANTICONVULSANT-INDUCED HYPERHOMOCYSTEINEMIA

The prevalence of hyperhomocysteinemia (HHcy) in 123 childhood epilepsy patients treated with antiepileptic drugs (AED) and the effect of folic acid supplements (1 mg/day) on plasma Hcy levels were determined in a study at three regional hospitals and pediatric centers in Austria. HHcy ( $>10.4$   $\mu\text{mol/L}$ ) was present in 19 (15.5%) patients. Those with HHcy were older ( $13.7 \pm 4$  vs  $11.0 \pm 3.9$  years) and had lower folate and cobalamin concentrations. HHcy and low folate correlated with polytherapy and long duration AED therapy. A significant increase of folate and decrease of Hcy levels were observed in 10 patients with HHcy who received folic acid supplements, in a 3-month double-blind randomized, placebo-controlled trial, whereas levels were unchanged in 9 with HHcy who received placebo. Total Hcy levels were not affected by polymorphisms in the methylene tetrahydrofolate reductase gene. (Huemer M, Ausserer B, Graninger G et al. Hyperhomocysteinemia in children treated with antiepileptic drugs is normalized by folic acid supplementation. *Epilepsia* October 2005;46:1677-1683). (Reprints: Dr M Huemer, Landeskrankenhaus Feldkirch, Department of Pediatrics, Carinagasse 47, 6800 Feldkirch, Austria).

COMMENT. Children taking antiepileptic drugs (AEDs) for prolonged periods should be monitored for folate and homocysteine plasma levels. Hyperhomocysteinemia and folate depletion are more prevalent in patients receiving polytherapy. The long-term effects of folic acid supplements in patients taking AEDs requires further study, particularly in relation to the optimal dose and effects on seizure control, cardiovascular disease, and cognitive function.

**The significance of folic acid for epilepsy patients** is reviewed by Moore JL in *Epilepsy & Behavior* Sept 2005;7:172-181. In the 1960s, folic acid was considered epileptogenic by some neurologists, and supplements were used with caution in epilepsy patients. The benefits and risks of folic acid to the nervous system were reviewed by Reynolds EH in *J Neurol Neurosurg Psychiatry* 2002;72:567-571. Now, the beneficial effects of folic acid in the prevention of certain neurologic disorders, especially neural tube defects, are well known, and supplementation is common practice. Case reports of seizure exacerbations by folic acid have led to the emergence of anticonvulsants with folic acid antagonistic effects, such as lamotrigine.

## OUTCOME OF CRYPTOGENIC EPILEPSY

Medical records of 60 children (53% males) with cryptogenic epilepsy, seen over a 12-year period and treated at Montreal Children's Hospital, McGill University, Canada, were reviewed retrospectively to identify clinical and predictive features of outcome. Mean age of initial seizure was 7.7 years (range 2.3–16.4 years). Febrile seizures had preceded the onset of epilepsy in 11 (18.3%), of which 7 were simple in type and 4 complex. Seizure types at presentation were generalized in 22 (35.7%), only 1 a typical absence; partial with secondary generalization in 20 (33.3%), complex partial in 17 (28.3%), and simple partial (1). Physical examination was normal in 46 (76.7%), 9 (15%) were developmentally delayed at onset, 38

(63.3%) attended regular classes, 11 (18.3%) had ADHD and 12 (20%) had a learning disability at onset. After initiating antiepileptic medication, mean follow-up was 53 months (range 24-128 months). Seizures were completely controlled for at least 24 months in 29 (48.3%), patients were seizure free for >12 months in 44 (73.3%), seizures recurred within 12 months in 16 (26.7%), and were intractable in 4 (6.7%). Outcome was poor in 8 (13.3%) and very poor in 4 (6.7%). Risk factors for a poor outcome were a seizure recurrence within 6-12 months after initiating therapy ( $p=0.006$ ), and developmental delay at onset ( $p=0.023$ ). (Tang-Wai R, Oskoui M, Webster R, Shevell M. Outcomes in pediatric epilepsy: seeing through the fog. *Pediatr Neurol* October 2005;33:244-250). (Respond: Dr Shevell, Room A-514, Montreal Children's Hospital, 2300 Tupper Street, Montreal, Quebec H3H 1P3, Canada).

**COMMENT.** Cryptogenic epilepsy refers to seizures without genetic or known cause but presumed to be symptomatic, possibly a subtle cerebral dysgenesis undetected by MRI. The term idiopathic is reserved for seizures solely genetic in origin. Cryptogenic epilepsy in childhood generally has a favorable outcome, approximately 50% being seizure-free for more than 2 years after starting AEDs. Risk factors for a poor outcome include seizure recurrence within 6-12 months of treatment initiation and developmental delay at seizure onset. As expected, seizure intractability and poor outcome are correlated with the need for addition of a second AED. Except for developmental delay, initial clinical features are not helpful in predicting outcome. Despite the frequency of ADHD and learning disabilities, more than half the patients do not require special classes. Normal neurologic examination and the absence of comorbid disorders at onset of seizures do not always correlate with a favorable outcome, 55% requiring more than one AED. Seizure recurrences and developmental delay indicate a need for aggressive therapy.

## **COGNITIVE DEFICITS RELATED TO FOCAL SPIKE LOCATION IN BENIGN PARTIAL EPILEPSY**

The topographic relation between focal spikes and neuropsychological deficits in children with benign partial epilepsy (BPE) was investigated using magnetoencephalography (MEG), electroencephalography (EEG) and MRI in a study of 27 children at University Children's Hospital, Tuebingen, Germany, and University of Trento, Italy. Location of spikes was determined by dipole source estimation. Of 20 children with sufficient MEG data, 13 showed focal spikes in the perisylvian region, and 7 in the occipital region. Five had bilateral or multiple foci. Left perisylvian spikes correlated with significantly lower language test scores ( $p=0.01$ ), and occipital spikes with lower scores in simultaneous information processing ( $p=0.01$ ), especially in visual transformation tasks. Focal interictal spikes may interfere with complex cognitive functions. (Wolff M, Weiskopf N, Serra E et al. Benign partial epilepsy in childhood: selective cognitive deficits are related to the location of focal spikes determined by combined EEG/MEG. *Epilepsia* October 2005;46:1661-1667). (Reprints: Dr M Wolff, University Children's Hospital, Hoppe-Seyler-Str. 1, D-72076 Tuebingen, Germany).

**COMMENT.** Children with BPE frequently have neuropsychological deficits, and the term "benign" is not always appropriate (Deonna T et al. *Dev Med Child Neurol*