

polymicrogyria and subependymal heterotopia. At age 8 months, she developed infantile spasms and modified hypsarrhythmia on EEG. Seizures were controlled with vigabatrin. At age 2.5 years, she is seizure-free on topiramate and clobazam. Case 2 presented at age 3 months with generalized seizures and two 2.5 cm hyperpigmented nevi in the right parietal-temporal area. Eye exam revealed a right esotropia and coloboma. MRI showed right hemimegalencephaly. EEG recorded right hemisphere slowing and interictal spikes and slow waves. Seizures were controlled with phenobarbital. He was readmitted at age 11 months with infantile spasms and hypsarrhythmia, resistant to vigabatrin and controlled by ACTH. At age 3 years he presented with frequent generalized tonic-clonic and myoclonic seizures and developmental delay. The pigmented nevi had each enlarged to 5 cm in diameter. EEG showed a generalized slow-spike and wave pattern, consistent with Lennox-Gastaut syndrome. The literature on linear nevus sebaceous syndrome is reviewed. (Menascu S, Donner EJ. Linear nevus sebaceous syndrome: case reports and review of the literature. *Pediatr Neurol* March 2008;38:207-210). (Respond: Dr Menascu, Atad St, PO Box 69, Omer 84965, Israel).

COMMENT. The neurocutaneous linear nevus sebaceous syndrome is characterized by a triad of epidermal nevi, seizures, and mental retardation. A review of 60 cases by Solomon et al, in 1975, described the dermatologic lesions as epidermal nevi associated with neurologic, ophthalmic, skeletal, cardiovascular, and urological abnormalities. Children with a suspected linear nevus sebaceous syndrome should have EEG, MRI, and ophthalmology exams. Seizures occur in up to 75% cases, frequently infantile spasms, West syndrome and evolving into Lennox-Gastaut syndrome. The term linear nevus sebaceous syndrome is usually reserved for cases with midline nevi, while "epidermal nevus syndrome" is more inclusive for all varieties of epidermal nevi.

SEIZURE DISORDERS

HERBAL MEDICINE AND EPILEPSY

The potentially harmful effects of herbal remedies and herb-antiepileptic drug interactions in patients with epilepsy are reviewed by researchers at the Center for Integrative Complementary Medicine, and Division of Neurology and Toxicology, Shaare Zedek Medical Center, Jerusalem, Israel. In the US, the Dietary Supplement Health and Education Act of 1994 removed herbal preparations from the jurisdiction of the FDA. Physicians are unaware of the degree of usage of complementary and alternative medicine (CAM) by their patients. Less than 40% of patients using CAM share this information with their conventional physician. Case reports of herb-induced seizures published between 1993 and 2004 include 14 infants treated with ginkgo biloba, pennyroyal (in mint tea), or star anise (used for colic). Japanese star anise contains the neurotoxin anisatin, a potent GABA antagonist. Chinese star anise is a spice and tea, used as a sedative for infants with colic. It contains veanisatins that are epileptogenic. Seven infants with star anise-induced seizures were seen at the Miami Children's Hospital ED over a 2-year period (Ize-Ludlow D, et al. *Pediatrics* 2004;114:653-656). Pennyroyal contains seizure-inducing monoterpene R-(plus)-pulegone. Ginkgotoxin, 4-O-methoxyppyridoxine (MPN) is a vitamin B6 derivative that inhibits GABA synthesis from glutamate. The toxin is contained in either ginkgo seeds or

leaves. Herbal preparations may also be contaminated by heavy metals such as lead or arsenic that can induce seizures.

Ginkgo biloba and other herbs may also cause seizures by interference with the absorption and metabolism of antiepileptic drugs (AED). They inhibit cytochrome P450 enzymes (CYP) involved in AED metabolism and oxidation. Ginkgo induces CYP2C19, reducing serum levels of phenytoin and valproate. Grapefruit juice containing furanocoumarins inhibits the effect of CYP3A4 on AEDs. A large glass of fresh grapefruit juice can significantly increase bioavailability of carbamazepine and diazepam. Some herbal preparations (eg green tea) interfere with AED metabolism by inhibiting or activating P-glycoproteins (Pgps) that alter the absorption and transport of AEDs across the blood-brain barrier. Acetazolamide is a Pgp substrate, and other AEDs may have this property. Herbal formulas contain many herbs and several generic names, adding to the difficulty in predicting the likelihood of seizure induction. (Samuels N, Finkelstein Y, Singer SR, Oberbaum M. Herbal medicine and epilepsy: Proconvulsive effects and interactions with antiepileptic drugs. *Epilepsia* March 2008;49:373-380). (Respond: Dr Noah Samuels, The Center for Integrative Complementary Medicine, Shaare Zedek Medical Center, POB 3235, Jerusalem, Israel 91031. E-mail: refplus@netvision.net.il).

COMMENT. The public demand and interest among physicians regarding the practice of complementary and alternative medicine are expanding. Physicians need to be aware of a potential link between herbal medicine and epilepsy in their patients. Parents of infants and children with refractory or unexplained seizures should be asked about possible use of star anise tea, ginkgo biloba, or pennyroyal, among other alternative preparations. The FDA cautions the public against the consumption of teas containing star anise. Herbal supplements are considered "natural," and their presumed safety and lack of side effects are rarely questioned. The benefits claimed are generally unsupported by scientific trials. Further research is needed to examine the role of herbal medicine in refractory epilepsy management and the interactions between herbal and conventional therapies.

A review of the literature on PubMed found 118 entries for epilepsy and herbal medicines, 11 involving ginkgo biloba, 8 ephedra-induced seizures, 6 Chinese and Japanese star anise cases, 2 for pennyroyal, and 2 for eucalyptus-induced seizures. Infants especially are involved.

THE EEG PHOTOPAROXYSMAL RESPONSE

Types of photosensitivity, prevalence and other characteristics of the photoparoxysmal response (PPR), associated seizures, effect of video games, and drug therapy are reviewed by the director of electroencephalography at the University of Illinois, Chicago. Photosensitivity has been graded according to the spread of epileptiform activity: occipital, parietal-occipital, also involving frontal areas, and generalized spike and wave complexes. The majority (65%) of PPR patients have had spontaneous epileptiform abnormalities, generalized spike and wave or partial, temporal lobe, or central rolandic multifocal sharp waves. The prevalence of PPR has diminished over time; in the 1960s it was 3% of all patients having an EEG in this laboratory, whereas now it is a rare occurrence. Studies after 2000 find a prevalence of 0.8%, 1.7% in children, and 1.8% in patients with clinical seizures. PPR is more common in Caucasians and females. Mean age is 12 years.