epilepsy. (Roach ES, et al. **Stroke** 2008;39: 2644-2691). After perinatal brain injury, children tend to "grow into their defects," and the diagnosis of cerebral palsy is often delayed until 18 to 24 months; learning and behavior impairments are not appreciated until school age. (Ricci D et al. **Stroke** 2008;39(2):403-410).

SEIZURE DISORDERS

GENETIC CLASSIFICATION OF INFANTILE SPASMS

Researchers from University of Washington, Seattle, WA, and Washington University, St Louis, MO propose a genetic and biologic classification of infantile spasms. Infantile spasms are of 2 main groups: those with known or unknown predisposing genotypes. Genes associated with lissencephaly are strongly associated with infantile spasms, as high as 80%, whereas 40% of patients with tuberous sclerosis complex may manifest infantile spasms. Inborn errors of metabolism associated with infantile spasms include the aminoacidopathies phenylketonuria, and nonketotic hyperglycinemia, the organic acidemias methylmalonic acidemia, propionic acidemia, and maple syrup urine disease, and Menkes kinky hair disorder of copper metabolism. Mitochondrial disorders are infrequently associated with infantile spasms.

Five chromosomal syndromes comprise predisposing genotypes for infantile spasms, including Miller-Dieker, Down and Williams syndromes. Infrequent associations occur with Smith-Lemli-Opitz, Sotos syndrome, and neurofibromatosis type 1. Unknown predisposing genotypes are suspected in some patients with a global developmental disorder and nonspecific cranial imaging malformations. Aicardi syndrome is an example of a developmental disorder of unknown genotype with unifying phenotype and prominent association with infantile spasms. It affects only females, suggesting a gene located on the X chromosome.

Infantile spasms associated with hypoxic-ischemic encephalopathy or infection may exhibit imaging patterns such as atrophy, calcifications and white matter intensities, suggesting an overlap with predisposing genotypes. Hypoxia or infection could represent a "second hit" in a population made vulnerable to spasms by an undiscovered predisposing genotype. A prospective study of prevalence of infantile spasms in patients with perinatal hypoxia or meningitis is needed to investigate this hypothesis. Children with patterns of extrinsic injury are prime candidates for further study of possible genetic mutations. (Paciorkowski AR, Thio LL, Dobyns WB. Genetic and biological classification of infantile spasms. **Pediatr Neurology** Dec 2011;45:355-367). (Respond: Dr Paciorkowski, Center for Integrative Brain Research, Seattle Children's Research Institute, 1900 Ninth Ave, MS C95-10, Seattle, WA 98101. E-mail: arpac@u.washington.edu).

COMMENT. The authors propose a primary biologic link between infantile spasms and autism, emphasizing connections between infantile spasms and phenotypes other than intractable epilepsy, including tuberous sclerosis. West's son James, the first patient reported with the syndrome, exhibited symptoms compatible with autism, as described by Langdon-Down (of Down's syndrome) who treated the child in later life. (Pies NJ et al. **Brain Dev** 2003;25:84-101). Patients with infantile spasms show

mutations to several genes, and all forms of infantile spasms may be symptomatic. The symptomatic, cryptogenic, and idiopathic classification system of epilepsy syndromes should be replaced, as recommended by the ILAE. (Berg AT et al. **Epilepsia** 2010;51:676-685). This review is considered a first step toward a genetic and biological classification of infantile spasms.

VIGABATRIN TRIALS AND DOSE RECOMMENDATIONS

Major, well-controlled trials of Vigabatrin for infantile spasms in Europe, Canada, and the Unites States are reviewed, including dose recommendations. Effective dosages ranged from 100 to 150 mg/kg/day, decreasing or eradicating spasms and eliminating the hypsarrhythmic EEG in newly diagnosed patients. Studies demonstrated long-term seizure control with no adverse effect on development and few severe adverse effects. Visual field defects were not evaluated. Time to response was within 2 weeks of initiating treatment. If the infant has not shown clinical improvement in 2 weeks, vigabatrin is discontinued and alternate treatment initiated. Treatment duration up to 6 months controlled seizures while limiting potential risks of adverse events and seizure recurrence.

A randomized, comparative trial of vigabatrin (150 mg/kg/day) and hydrocortisone (15 mg/kg/day) in 22 patients with tuberous sclerosis, found vigabatrin more efficacious and better tolerated than hydrocortisone, with 100% response during this 1- to 3-month crossover trial. Vigabatrin is recommended as first-choice treatment of infantile spasms caused by tuberous sclerosis.

In the UK Infantile Spasm Study comparing vigabatrin (100-150 mg/kg/day) with hormonal treatment (oral prednisolone 40-60 mg/day, or intramuscular tetracosactide 0.5-0.75 mg [40-60 IU], a synthetic analog of ACTH, on alternate days), hormonal treatments were superior to vigabatrin in control of spasms; adverse events were common with both forms of therapy. Hormonal treatment was preferred over vigabatrin. Infants with tuberous sclerosis were excluded from this study. Follow-up studies at age 14 months and 4 years indicated equivalent spasm-freedom and developmental outcomes with vigabatrin and hormone treatment, except for infants with cryptogenic spasms; infants with no identified etiology for spasms had higher developmental scores following hormone therapy.

Except for the UK study, all investigators preferred vigabatrin as first-line therapy over hormonal. The most common adverse events with vigabatrin were sedation and irritation. Delay in time to diagnosis and treatment is associated with less favorable outcomes. (Carmant L. Vigabatrin therapy for infantile spasms: review of major trials in Europe, Canada, and the United States, and recommendations for dosing. **Acta Neurol Scand** Dec 2011;124 (Suppl 192):36-47). (Respond: Dr L Carmant, Division of Neurology, Universite de Montreal, CHU-Sainte-Justine, 3175 Cote Sainte-Catherine, Room 5421, Montreal, QC, Canada H3T 1C5. E-mail: lionel.carmant@umontreal.ca).

COMMENT. Vigabatrin is an irreversible GABA inhibitor, effective as adjunctive therapy in control of refractory complex partial seizures in adults and as monotherapy for infantile spasms. Clinical benefits of vigabatrin must be balanced with associated risk of peripheral visual field defects (pVFDs). (Pellock JM. **Acta Neurol**