tested positive for tetrodotoxin. Excitability measurements of sensory and motor nerves showed that, compared with controls, axons were of higher threshold, compound muscle and sensory action potentials were reduced in amplitude, latency was prolonged, and strength-duration time constant was reduced. Threshold electrotonus of motor axons showed less threshold decline than normal on depolarization and greater threshold increase on hyperpolarization. The changes in excitability were reproduced in a mathematical model by reducing sodium permeabilities by a factor of 2. (Kiernan MC, Isbister GK, Lin CS-Y et al. Acute tetrodotoxin-induced neurotoxicity after ingestion of puffer fish. **Ann Neurol** March 2005;57:339-348). (Respond: Dr Kiernan, Prince of Wales Medical Research Institute, Barker Street, Randwick, Sydney, NSW 2031, Australia).

COMMENT. The neurotoxic effects of puffer-fish poisoning are due to tetrodotoxin blockade of Na^+ channels. In an editorial, Kaji R and Nodera H, Tokushima University, Japan (**Ann Neurol** 2005;57:309) discuss the differentiation of puffer fish poisoning and Guillain-Barre syndrome (GBS) with reference to persistent sodium channels. GBS occurs in a demyelinative form (acute inflammatory demyelinating polyneuropathy [AIDP]) and the axonal form (acute motor axonal neuropathy [AMAN]). In AMAN, anti-GM1 antibodies may bind specifically to motor nerves and interfere with axonal sodium channels. Nerve excitability changes in AMAN are different from those in puffer fish poisoning, sensory fibers are spared, and a neurotoxin is not involved. Inflammatory mediators in AMAN are the likely explanation for reduced excitability of axons through sodium channels.

SEIZURE DISORDERS

MIDAZOLAM IN REFRACTORY NEONATAL SEIZURES

The outcome of 45 neonates with EEG-confirmed seizures (ESZ) was analyzed at the University Hospital of the Canary Islands, La Laguna, Spain. Of 32 neonates treated with phenobarbital/phenytoin, ESZ persisted in 17; of these, 13 had a poor outcome and 4 died. Of 13 nonresponders to phenobarbital/phenytoin who were treated with midazolam early, within 1 hr, ESZ were rapidly controlled in 13, only 4 had a poor outcome and 2 died. Neonates treated with midazolam had significantly better neurodevelopment than those receiving phenobarbital (53.9% vs 11.8%). (Conde JRC, Borges AAH, Martinez ED et al. Midazolam in neonatal seizures with no response to phenobarbital. **Neurology** March (1 of 2) 2005;64:876-879). (Reprints: Dr JR Castro Conde, Neonatology Service, University Hospital of the Canary Islands, Ofra S/N, La Laguna 28230, Spain).

COMMENT. Electrographic seizures in neonates correlate with poor neurodevelopmental outcome. (McBride MC et al. **Neurology** 2000;55:506-513). In the above retrospective, nonrandomized study of neonates with refractory EEG-confirmed seizures, midazolam, a GABA agonist, is proven effective as a third-line treatment in patients who have failed to respond to phenobarbital and phenytoin. Patients who respond to midazolam and those whose electrographic seizures are controlled by conventional first line treatments show improved neurodevelopmental outcome when compared to a group with refractory neonatal seizures. Midazolam is currently employed in the treatment of status

epilepticus in children; it is investigative and nonapproved for use in neonates. Prospective studies may be justified.

In an Editorial, Sankar R and Painter MJ (**Neurology** 2005;64:776-777) applaud the study of midazolam and the promising results. However, they raise concerns about potential neurotoxicity of GABA agonists in the immature brain. AMPA antagonists, such as topiramate, might be a safer class of drug to promote in IV form for trial in neonates.

BENIGN FAMILIAL INFANTILE SEIZURES

The history, classification, clinical and EEG features, genetics, differential diagnosis, and outcome of "benign familial infantile seizures" (BFIS) are reviewed from the Neurology Department, Bambino Gesu Children Hospital, Rome, Italy. First reported by Fukuyama (1963) as partial seizures occurring in the first 2 years, idiopathic, and with a benign outcome, the syndrome was later described as benign partial epilepsy of infancy with complex partial seizures (BPE and CPS) and BPE with secondarily generalized seizures in infancy (Watanabe et al. 1987, 1990, and 1993). The term "benign infantile familial convulsions" was proposed by the present author (Vigevano F et al. 1992), cases showing an autosomal dominant inheritance. Finally, in the ILAE classification (2001) the term "benign familial infantile seizures" was preferred, and two forms were listed, familial and nonfamilial. The inheritance is heterogeneous, with chromosome markers on chromosomes 19, 16 (BIFC and paroxysmal choreoathetosis), and on chromosome 2. Two families were also described with onset at the 2nd month, with mutations in the sodium-channel gene SCN2A, and two with neonatal onset had genetic mutations associated with potassium channels. Some cases have been associated with diarrhea and rotavirus.

Clinical characteristics are as follows: Family history of similar seizures; normal early development; onset 3-10 months; normal neurologic exam; seizures in clusters; partial (occipito-parietal) seizures; normal interictal EEG; benign course; and normal developmental outcome. In the absence of a family history of BFIS, early diagnosis may be difficult and only by exclusion of possible etiological factors or by identification of the genetic marker. Sporadic cases may carry the same genetic marker as familial ones, with less expressivity. (Vigevano F. Benign familial infantile seizures. **Brain Dev** April 2005;27:172-177). (Respond: F Vigevano; E-mail: vigevano@opbg.net).

COMMENT. The syndrome of BFIS has characteristic clinical features and benign outcome but variable genetic mutations associated with a channelopathy. The decision to treat depends on the severity and frequency of seizures and the family history. The author cites untreated familial cases having isolated or brief clusters up to 1 year of age.

PROGNOSIS OF BENIGN MYOCLONIC EPILEPSY OF INFANCY

Neuropsychological, cognitive, and behavioral outcome was studied in a long-term follow-up of 7 patients with benign myoclonic epilepsy in infancy (BMEI) at Universita di Palermo, Italy. Mean age at onset of myoclonic seizures (MS) was 15 months (range, 7-35 months). Febrile convulsions had occurred before the onset of MS in 3 infants. Myoclonic jerks involved mainly the upper limbs, with nodding and upward gaze deviation in some, and flexing of the body and lower limbs. Ictal EEG recordings showed generalized spike-wave