were classified in 2 groups: Group I, 12 patients, abnormal, with mental retardation, developmental delay, cerebral palsy or epilepsy; and Group II, 48 patients, normal at follow-up. Proportion of infants small for gestational age (<10th percentile) was high in both groups (75% vs 58%) but was not associated with brain injury. Very low blood glucose levels (<15 mg/dl) occurred in 50% of Group I vs 14.6% of Group II (p=0.015). Duration of hypoglycemia was longer in Group I (median, 14 h) than in Group II (median, 1.75 h) (p<0.001). Associated factors more frequent in Group I than in Group II included toxemia (33.3% vs 8.3%, p=0.043), fetal distress (58.3% vs 14.5%, p=0.004), Apgar score <5 at 1 min (33.5% and 6.4%, p=0.025), neonatal seizures (53.8% vs 4.3%, p<0.001), and pathological jaundice (41.7% vs 6.4%, p=0.006). Eight of 9 patients in Group I had abnormal MRI at follow-up, showing cortical atrophy and white matter lesions, with occipital and parietal predominance. Apgar scores were partially correlated with the extent of brain lesions. Brain injury in neonates with prolonged hypoglycemia may be exacerbated by associated factors such as hypoxia, seizures, and jaundice. (Montassir H, Maegaki Y, Ogura K, et al. Associated factors in neonatal hypoglycemic brain injury. **Brain Dev** October 2009;31:649-656). (Respond: Dr Hesham Montassir, Tottori University, Yonago, Japan. E-mail: hishammontassir@gmail.com).

COMMENT. Neonatal seizures with hypoglycemia are correlated with duration of hypoglycemia and neurological outcome. Seizures may begin at onset of hypoglycemia but usually appear after 12 h of continuous hypoglycemia. (Pildes RS et al. A prospective controlled study of neonatal hypoglycemia. **Pediatrics** 1974;54:5-14).

Of 27 infants and children with seizures associated with hypoglycemia reported from the Mayo Clinic, only 2 had an onset of seizures in the neonatal period, and in 20 the etiology of hypoglycemia was unknown. Neurologic disease preceded the onset of symptoms in 50% of the 20 patients with cryptogenic hypoglycemia. Evidence for a primary neurological cause for seizures included birth injury, kernicterus, hydrocephalus, and cerebral dysgenesis. Level of blood sugar at time of seizure in patients with primary neurologic disorder was significantly lower than in patients with normal neurologic findings. Occurrence of seizures was not closely correlated with the level of blood sugar. A primary cerebral lesion should be considered as an etiologic factor in some neonatal and childhood hypoglycemic seizures. (Etheridge JE Jr, Millichap JG. Hypoglycemia and seizures in childhood. Etiologic significance of primary cerebral lesions. **Neurology** 1964;14:397-404).

SEIZURE DISORDERS

BRAIN SODIUM CHANNEL AND FEBRILE SEIZURE MECHANISM

Researchers at the University of Melbourne, Australia, measured the effect of temperature on brain sodium channel, $Na_v1.2$, properties, using a computer model of the dentate gyrus granule cell. In animal models thermogenic seizures are hippocampal in origin (Dube C et al. 2000). The voltage dependance of activation became 7.6mV more negative when the temperature was increased from 37C to 41C. The direct effect of heat caused an increase in gating rates of sodium ion channels and a more negative activation with increased neuronal excitability. This dramatic increase in excitability due to increased temperature may be an important factor in the mechanism of a febrile seizure. (Thomas EA, Hawkins RJ,

Richards KL, Xu R, Gazina EV, Petrou S. Heat opens axon initial segment sodium channels. A febrile seizure mechanism? **Ann Neurol** Aug 2009;66:219-226). (Respond: Dr Petrou, Howard Florey Institute, University of Melbourne, Parkville, Victoria 3010 Australia. E-mail: spetrou@unimelb.edu.au).

COMMENT. The mechanism of febrile seizures is dependent on several factors, but especially height of body temperature and an individual's febrile convulsive threshold. In addition to genetic susceptibility and cytokines, the neurotropic properties of certain viruses, age and level of immaturity, and water and electrolyte balance are contributing factors. (Millichap JG. **Brain Dev** 2009; Dube CM et al. **Brain Dev** 2009;31:366-371**).** The above study provides further explanations for the febrile seizure mecanism at a molecular level, and specifically the effect of body temperature on brain sodium channels.

ANTIPYRETICS AND FEBRILE SEIZURE RECURRENCE

The efficacy of antipyretic agents in prevention of febrile seizures was examined in a randomized, placebo-controlled, double-blind trial at various hospitals in Finland. A total of 231 children who experienced their first febrile seizure, Jan 1, 1997-Dec 31, 2003, were observed for 2 years. Febrile episodes were treated first with rectal diclofenac or placebo. After 8 hours, treatment was continued with oral ibuprofen, acetaminophen, or placebo. Of 851 febrile episodes, 89 (10%) were associated with a febrile seizure. Febrile seizures occurred in 54 (23.4%) of the 231 children. Recurrence rates were not significantly different in the antipyretic and placebo groups: 23.4% (46 of 197) in those treated with antipyretic, and 23.5% (8 of 34) in those receiving placebo (P=0.99). Fever was significantly higher during episodes with seizure vs those without seizure (39.7C vs 38.9C, P<0.001), independent of the medication. Antipyretic agents were ineffective in the prevention of febrile seizure recurrence. All the antipyretics failed to lower the body temperature in children with fever that was associated with febrile seizure recurrence, but they lowered the temperature in episodes not leading to a febrile seizure. Children with recurrences had received extra antipyretic agents more frequently than those without recurrences. (Strengell T, Uhari M, Tarkka R, et al. Antipyretic agents for preventing recurrences of febrile seizures. **Arch Pediatr Adolesc Med** Sept 2009;163:799-804). (Respond: Heikki Rantala MD, PhD, Department of Pediatrics, University of Oulu, PO Box 5000, Oulu 90014, Finland. E-mail: heikki.rantala@oulu.fi).

COMMENT. The ineffectiveness of commonly prescribed antipyretics in the prevention of recurrence of febrile seizures, as demonstrated in this controlled study, is in agreement with the majority of previous randomized trials. Antipyretics may be useful only in improving the general wellbeing of the febrile child. In patients with a prior complex febrile seizure, to prevent recurrence, many pediatric neurologists recommend a combination of antipyretic with diazepam, administered orally at first sign of fever.

While antipyretics failed to prevent or control temperature elevation that resulted in seizure recurrence, they were effective in lowering temperature in episodes unassociated with seizure. The principal aim in therapy is the prevention of an elevation of temperature above the threshold level at which a seizure has previously occurred. Commonly employed antipyretics, while facilitating heat dissipation by increased peripheral blood flow and