of Neurology, Level 3 Southwood Bldg, Great Ormond Street Hospital NHS Trust, Great Ormond Street, London WC1N 3JH, UK).

COMMENT. The authors have employed serial magnetic resonance angiography to distinguish a relatively benign and self-limiting vasculopathy from progressive types such as moyamoya. Risk factors that determine progression of arteriopathies include a history of varicella zoster, congenital heart anomalies, immunodeficiences, and hemolytic anemias, especially sickle cell disease. In addition to varicella, enteroviruses and Borrelia are reported as triggers for arterial ischemic stroke (Sebire G et al. **Ann Neurol** 1999;45:679-680; Kirkham F. **Ann Neurol** 2006;59:580-582).

EEG hyperventilation in sickle cell disease is a preventable risk factor for arterial stroke, not mentioned by the above authors. Three reports and four childhood cases of sickle cell disease (SCD) with stroke precipitated by routine hyperventilation during EEG recordings are cited in the literature. The earliest report (Protass LM. **Ann Intern Med** 1973;79:451) concerned an 11-year-old girl with SCD who developed a left hemiparesis immediately following hyperventilation during an EEG. Recovery was incomplete in all cases. Additional cases have involved hyperventilation secondary to obstructive sleep apnea, or ingestion of toxic doses of aspirin. Hyperventilation-induced hypocapnea leads to arterial constriction, decreased cerebral blood flow, and in patients with SCD, intravascular sickling precipitated by hypoxia and cerebral ischemia or infarction. Seizures occurring in 12-14% of patients with SCD are a precursor to stroke in 10-33% and may be associated with vasculopathy, focal hypoperfusion, and silent infarction. (Prengler M et al et al. **Ann Neurol** 58:290-302). The lack of appreciation of potential dangers of hyperventilation in SCD in some reports prompted a cautionary comment and review of the literature (Millichap JG, **Ann Neurol** 2005;58:972; Millichap JG. **Clin EEG and Neuroscience**, in press). The avoidance of hyperventilation in patients with SCD is recommended.

SEIZURE DISORDERS

ETIOLOGY AND OUTCOME OF NEONATAL SEIZURES

The prognostic value of seizure etiology, neurologic examination, EEG, and neuroimaging in the neurodevelopmental outcome of 89 term infants with neonatal seizures was determined at the Children's Hospital and Harvard Medical School, Boston, MA. The seizure etiologies were global cerebral hypoxia-ischemia (HI) in 40%, focal HI in 18%, intracranial hemorrhage (17%), cerebral dysgenesis (5%), transient hypoglycemia or hypocalcemia (3%), meningitis or encephalitis (3%), and pyridoxine dependency (1%). Neurologic outcome at 1 year was favorable in 72%, and poor in 28%. Neurologic examination was abnormal in 54% (mild in 26% and severe in 22%) with motor impairment in 53%, mental impairment in 48%, and seizures after NICU discharge in 21%. Long-term outcome was poor in 28% of survivors; neonatal mortality was 7%. Risk factors for a poor outcome were seizures associated with cerebral dysgenesis or global HI, an abnormal EEG background activity, and multifocal cortical or deep gray matter neuroimaging lesions in the neonate. A favorable outcome at 12-18 month follow-up was predicted by a normal neurologic examination in the neonatal and early infancy period, and a normal/mildly abnormal neonatal EEG. An abnormal neurologic exam in the neonate was an unreliable

predictor of outcome. (Tekgul H, Gauvreau K, Soul J, et al. The current etiologic profile and neurodevelopmental outcome of seizures in term newborn infants. **Pediatrics** April 2006;117:1270-1280). (Respond: Andre J du Plessis MD, Fegan 11, Department of Neurology, Children's Hospital, 300 Longwood Ave, Boston, MA 02115).

COMMENT. Mortality is relatively low but long-term neurodevelopmental outcome is poor in 28% of infants with a history of neonatal seizures. Global cerebral hypoxic-ischemia is the most frequent cause of neonatal seizures and a strong predictor of poor long-term outcome. The effect of neonatal seizures on the developing brain is controversial, some finding them harmful (Wasterlain CG. **Epilepsia** 38:728-734) and some, harmless (Camfield PR. **Epilepsia** 1997;38:735-737). Studies in experimental animals have shown that immature rats less than 20 days old respond to electroshock with hyperkinesias, breast stroke swimming movements, tremors, catatonia, and clonic movements, and a major tonic-clonic seizure with post-ictal depression could not be induced until the animal was older. (Millichap JG. **Proc Soc Exper Biol & Med** 1957;96:125-129). Neonatal seizures in infants (Volpe JJ, 1977) are described as subtle and include the swimming movements resembling those seen in animals. The absence of generalized tonic-clonic seizures in the neonate reflects the lack of cortical organization required to propagate the electrical discharge (Aicardi J, 1986). These findings support those of Camfield and others who discount adverse effects of neonatal seizures per se, attributing the poor prognosis to the cause, especially cerebral hypoxia-ischemia. Subtle and focal post-ictal cerebral ischemia affecting subcortical and limbic regions cannot be ruled out.

Relation of pregnancy and neonatal factors to development of childhood epilepsy. Prenatal factors contributed to the subsequent development of childhood epilepsy in a study in Nova Scotia, Canada (Whitehead E, et al. **Pediatrics** April 2006;117:1298-1306). Risk factors for epilepsy included eclampsia, CNS anomalies, placenta abruptio, infection in pregnancy, and unmarried mother. Other factors associated with increased risk of epilepsy were neonatal seizures, neonatal metabolic disorders, low birth weight, and small for gestational age.

PROLONGED FEBRILE SEIZURES AND TEMPORAL LOBE EPILEPSY

The presence of spontaneous limbic seizures using chronic video monitoring with concurrent hippocampal and cortical EEGs, in adult rats (starting at 3 months of age) that had sustained experimental febrile seizures (FS) on postnatal day 10 was compared to hyperthermic control rats whose FS had been controlled, in a study at University of California, Irvine, CA, and University of Pennsylvania, Philadelphia. EEGs were normal in hyperthermic control rats, and none developed spontaneous seizures. In rats subjected to prolonged early-life FS, spontaneous electroclinical seizures were recorded in 6 of 17 (35.2%). The seizures, sudden freezing and typical limb automatisms, were associated with polyspike/sharp waves with increasing amplitude and slowing on EEG. Interictal epileptiform discharges were recorded in 15 (88.2%) of the experimental seizure rats and in none of the controls. A diminished amplitude of cortical EEG preceding the hippocampal seizure suggests involvement of normal cortical neurons. This represents a model for studying the relation between FS and human temporal lobe epilepsy. (Dube C, Richichi C,