COMMENT. The 3243A>G mutation is the most common cause of the MELAS syndrome. Infants may present with the classic mitochondrial encephalomyopathy, lactic acidosis, and strokelike episodes while others show failure to thrive, hypotonia, seizures, cardiomyopathy, and lactic acidosis, dependent on the amount of mutant gene in different tissues. The clinical phenotype varies widely in symptoms and their severity. Many children with the 3243A>G mutation are asymptomatic, and those with symptoms usually present with sensorineural hearing loss, short stature, migraine, exercise intolerance, and learning difficulties. Encephalomyopathy is uncommon and morbidity relatively low.

VASCULAR DISORDERS

RISK OF EPILEPSY AFTER PERINATAL STROKE

The prevalence and severity of epilepsy after 6 months of age in 64 children with a history of perinatal stroke were studied by a retrospective review of patients at Riley Hospital for Children, Indianapolis, IN. Forty eight (75%) presented in the NICU with seizures and were treated with phenobarbital. Comorbidities included infection in 11 (17%), cardiac abnormalities in 11 (17%), ECMO in 4 (6%), and renal failure in 3 (5%). Seven (11%) had a family history of seizures. Prenatal ultrasound was positive for stroke in 4 (6%) patients. Infarction was confirmed by CT or MRI, and an abnormal initial EEG was recorded in 40 (91%). Follow-up data were available on 61 (95%) patients, and 41 (67%) had developed epilepsy between 6 months and last follow-up (mean 43 mos; range 9-178 mos). Five (8%) had infantile spasms. Seizures resolved in 13 (32% of 41 with epilepsy), and medications had been discontinued. Infarct on prenatal ultrasound (p=.0065) and family history of seizures (p=.0093) were significantly associated with an earlier development of seizures after 6 months of age: median time 3.8 months with, vs 53.9 without, positive ultrasound; and 1.1 months with, vs 53.9 without, positive family history. No variables were correlated with time to resolution of seizures, or with epilepsy occurrence after 6 months of age. (Golomb MR, Garg BP, Carvalho KS, Johnson CS, Williams LS. Perinatal stroke and the risk of developing childhood epilepsy. J Pediatr October 2007;151:409-413). (Reprints: Dr Meredith Golomb, Indiana University School of Medicine, Blg XE, Room 040 (Pediatric Neurology), 575 West Dr, Indianapolis, IN 46202).

COMMENT. Perinatal stroke is frequently followed by the development of epilepsy in childhood. Evidence of infarction on prenatal ultrasonography and a family history of epilepsy are predictive of an earlier onset of seizures, but no risk factors used in this study predicted time of seizure resolution or whether the patients would develop epilepsy.

Frequency of electrographic seizures and PEDs after intracerebral hemorrhage was studied in 102 consecutive adult patients with ICH who underwent continuous electroencephalographic monitoring (cEEG) at Columbia University, NY. (Claassen J et al. Neurology Sept 2007;69:1356-1365). Seizures occurred in one third of patients with ICH and more than one half were purely electrographic seizures. Electrographic seizures were associated with expanding hemorrhages, and PEDs were independently associated with cortical ICH and poor outcome. Continuous EEG monitoring is essential for detection of subtle seizures.
NIH Workshop on Ischemic Perinatal Stroke (IPS) is summarized by Raju TNK, Nelson KB and other participants (Pediatrics Sept 2007;120:609-616). The estimated incidence of IPS is 1 in 2300 to 5000 births. It is more likely to occur in the perinatal period than at any time in childhood. Long-term neurologic morbidity is common. Risk factors are not well defined and are unreliable. An agenda for future research is proposed.

INFECTIONOUS DISORDERS

CNS COMPLICATIONS OF PRIMARY HUMAN HERPESVIRUS-6 INFECTION

Central nervous system manifestations of primary human herpesvirus-6 (HHV-6) are described in 9 children, ages 3 to 24 months, with HHV-6 DNA in the cerebrospinal fluid, in a prospective study at the University of Helsinki, and other centers in Finland. Of 393 young children with neurologic infections evaluated in 1995 and 1996, 32 had serological HHV-6 diagnoses, and of 21 less than 2 years of age, 9 tested positive for HHV-6 on the CSF by polymerase chain reaction. In 6 children, HHV-6 DNA was present in CSF on days 1 to 4 after onset. In 2 cases, PCR was negative on days 1 and 2, but was positive on days 9 and 17. In 6 of 9 children, seroconversion of HHV-6 immunoglobulin G antibody confirmed the acute primary infection. A 4-fold increase or decrease in antibody titers was found in sera of 2 children. No HHV-6 specific antibodies were detected in the CSF. The PCR was negative for HHV-6 in CSF in the remaining 12 of the 21 seropositive patients, when tested at comparable times of patients who were CSF positive. CSF glucose and protein levels were normal, and white cells were absent or normal in 8 and increased to 11 to 12x10⁹/L in 2. Neuroimaging was normal in 5 studied, and EEG was slightly abnormal in 2 children.

Clinically, the HHV-6 infection was highly acute with high fever. Convulsions in 6 of 9 patients were generalized, often prolonged, asymmetric, or recurrent. One child had a previous history of 2 febrile seizures. Four had rash, 4 had diarrhea, and 4 were ataxic. Fever and rash lasted 3 to 6 days, ataxia for 2 weeks. Three were treated with acyclovir for suspected herpes encephalitis. Hospital stay ranged from 4 to 11 days. One relapsed and was rehospitalized for 3 weeks with ataxia. Initial recovery in all patients was favorable, but at 4 to 7 year follow-up, 4 had ataxia and developmental delay, and required special education, 1 manifested symptoms of autism, and 1 developed extreme obesity. The patient with a previous history of febrile seizures continued to have recurrent seizures. Neurologic sequelae were severe in 4 (44%) of the 9 patients. (Mannonen L, Herrgard E, Valmari P et al. Primary human herpesvirus-6 infection in the central nervous system can cause severe disease. Pediatr Neurol Sept 2007;37:186-191). (Respond: Dr Mannonen, Haartman Institute, Department of Virology, University of Helsinki, POB 21, FIN-00014 Helsinki, Finland.) E-mail: laura.mannonen@helsinki.fi

COMMENT. Primary HHV-6 infection may invade the CNS of young children, and can cause serious neurologic sequelae. Complex febrile seizures are the most frequent acute manifestations of primary HHV-6 infection, and ataxia and developmental delay are serious long-term sequelae. CSF-HHV-6 DNA is reported in 14.5% of 138 cases of febrile seizures in a review of 10 published series. (Millichap JG and JJ. Pediatr Neurol 2006;35:165-172).