type was mostly complex partial, and seizure control was satisfactory in 6 (47%). Patients with poor seizure control manifested frontal glucose hypometabolism on PET. Nine patients (64%) had hemiparesis, with contralateral frontal hypometabolism. Bilateral frontal and temporal hypometabolism was coupled with severe developmental impairment. No patient with good seizure control had severe developmental impairment. Developmental impairment was not related to age at onset of first seizure. Autism in 2 patients was associated with bitemporal hypometabolism on PET. Three patients who underwent epilepsy surgery had complete remission of refractory seizures but development was only partially improved. With or without resective surgery, good seizure control is achieved in about 50% of patients with bilateral Sturge-Weber syndrome. (Alkonyi B, Chugani HT, Karia S, Behen ME, Juhasz C. Clinical outcomes in bilateral Sturge-Weber syndrome. **Pediatr Neurol** June 2011;44:443-449). (Respond: Dr Juhasz, Dept of Pediatrics, Wayne State University School of Medicine, 3901 Beaubien Blvd, Detroit, MI 48201. E-mail: juhasz@pet.wayne.edu).

COMMENT. PET studies are important in the evaluation of children with bilateral Sturge-Weber syndrome as follows: 1) prediction of outcome, seizure control, and impairment of development and cognition; 2) risk of autism related to bitemporal hypometabolism; and 3) determination of functional integrity of the nonresected hemisphere before surgery. Early resection of a hemisphere or focus may be beneficial in some bilateral cases with intractable seizures. Persistent seizures may contribute to neurocognitive decline.

METABOLIC AND DEGENERATIVE DISORDERS

CEREBRAL FOLATE DEFICIENCY SYNDROMES

Neurologists and geneticists at the University of Barcelona, Spain and other centers analyzed cerebral folate levels in 584 children with neurologic disorders that required diagnostic lumbar puncture. Deficiency of 5-methyltetrahydrofolate (5-MTHF) was detected in the CSF of 71 (12%) patients. Mild to moderate deficiency (n=63; 19-63 nmol/L) was associated with perinatal asphyxia, CNS infection, and diseases of probable genetic origin (inborn errors of metabolism, white matter disorders, Rett syndrome, or epileptic encephalopathies). Severe 5-MTHF depletion (n=8; range, 0.6-13 n/mol/L) was detected in specific mitochondrial disorders, metabolic defects, or cerebral degenerations (severe MTHF reductase deficiency, Kearns-Sayre syndrome, biotin-responsive striatal necrosis, acute necrotizing encephalitis, and FOLRI transporter gene defect). CSF folate levels correlated with plasma levels in cerebral folate deficiency. Thirty-five of 71 patients (49%) with decreased 5-MTHF had other abnormalities of biogenic amines, homovanillic acid, 5-hydroxyindoleacetic acid, and pterins in CSF. (Perez-Duenas B, Ormazabal A, Toma C, et al. Cerebral folate deficiency syndromes in childhood. Clinical, analytical, and etiologic aspects. **Arch Neurol** May 2011;68(5):614-621). (Respond: Belen Perez-Duenas MD PhD, Dept of Neurology, Hospital Sant Joan de Deu, 08950 Esplugues, Barcelona, Spain. E-mail: bperez@hsjdbcn.org).

COMMENT. Partial cerebral folate deficiency may occur as a secondary abnormality in acquired CNS disorders and in genetic and congenital encephalopathies. Severe deficiencies are caused by inborn errors of folate metabolism or cerebral transport defects across the blood-CSF barrier (FOLR1 mutation). In the above study, children younger than 1 year had epilepsy (infantile spasms and neonatal seizures), perinatal asphxia or CNS infection. Older children were diagnosed with inherited disease, mitochondrial disorders or cerebellar atrophy syndrome. The mechanism of acquired cerebral folate deficiency in neurologic disorders is not definitely determined. Children with seizure disorders are at risk of low serum folate, and antiepileptic drugs may be a contributing factor in some cases. The value of folinic acid supplement in cerebral folate deficiency is under investigation.

NEUROLOGIC FEATURES OF WOLFRAM SYNDROME

Researchers at Nice, Marseille, and Montpellier-Nimes, France, studied the nature and frequency of neurologic manifestations in 59 patients with Wolfram syndrome with genotype-phenotype correlations. Wolfram syndrome is a genetically heterogeneous disease characterized by juvenile onset diabetes mellitus and optic atrophy, with progressive development of diabetes insipidus, sensorineural deafness, renal, and neuropsychiatric disorders. In this series of patients, median age at diagnosis was 10 years (range, 4-43 years). The onset of neurologic symptoms in 31 (53%) patients was at a median age of 15 years. These involved dysfunction of brain stem or cerebellum in 17/31 (55%) and included cerebellar ataxia (45%), frequently associated with dysarthria, dysphagia, or nystagmus. Peripheral neuropathy occurred in 39% cases, and cognitive impairment in 32%. Eight patients presented with epilepsy, mainly generalized. MRI was abnormal in 13 patients, showing cerebral, cerebellar and brainstem atrophy. WFS1 mutations (10/56 novel) were identified in 90% of patients. The age of onset of neurologic symptoms was not correlated with genotype, and homozygosity or compound heterozygosity for missense mutation did not influence their development. The location of the WFS1 mutations may play a role in the development of neurologic manifestations. (Chaussenot A, Bannwarth S, Rouzier C et al. Neurologic features and genotype-phenotype correlation in Wolfram syndrome. **Ann Neurol** March 2011;69:501-508). (Respond: Pr Veronique Paquis-Flucklinger, Nice, France. E-mail: paquis@hermes.unice.fr).

COMMENT. The prevalence of Wolfram syndrome in N America is estimated at 1/100,000, and neurologic manifestations have previously received limited attention, especially in children. The authors emphasize the importance of diagnosis and follow-up of neurologic complications because of fatalities associated with brainstem involvement. Genetic testing is recommended to optimize family counseling.

Neurologic findings in 5 patients with Wolfram syndrome, also known as DIDMOAD syndrome, included dysarthria, seizures, anosmia, nystagmus, ataxia, and changes in the EEG, electroretinogram and evoked potentials. Four patients had abnormal CT scans with atrophy of the brainstem and cerebellum, similar to olivopontocerebellar atrophy (OPCA). Wolfram syndrome includes phenotypic manifestations of OPCA. (Leiva-Santana C et al. **Rev Neurol (Paris)** 1993;149(1):26-29).