functioning, and 49% on Tourette syndrome rating scale. The improvements following therapy were maintained at 1 year follow-up, with 14 (82%) of 17 children benefited. (Perlmutter SJ, Leitman SF, Garvey MA et al. Therapeutic plasma exchange and intravenous immunoglobulin for obsessive-compulsive disorder and tic disorders in childhood. Lancet Oct 2, 1999;354:1153-1158). (Respond: Dr Susan E Swedo, 10 Center Drive-MSC 1255, Bethesda, MD 20892).

COMMENT. Immunotherapy with plasma exchange or immunoglobulin are successful in lessening severity of infection-triggered symptoms of obsessive compulsive disorder and Tourette syndrome. These positive results have only been demonstrated in a proportion of children with tics or OCD associated with PANDAS (post-infectious autoimmune neuropsychiatric disorders associated with streptococcal infection). The effects of immunotherapy in patients with chronic symptoms unrelated to PANDAS remains to be determined.

Singer HS in a commentary (Lancet Oct 1999;354: 1137-1138) notes that immunotherapies are not free of risk, two thirds having side effects. The sustained benefits reported might be explained by spontaneous improvements over time, especially for tics. Furthermore, medications had to be continued in at least half the patients.

An uncontrolled pilot trial in a small group of children with tics associated with ADHD and elevated ASO titers, oral penicillin treatment for 2 to 3 weeks has been associated with a decrease in tics (personal observation). The penicillin administered to all patients in the NIH study may have had a beneficial effect.

Abnormal cortical excitability in OCD and Tourette syndrome. Transcranial magnetic stimulation, previously showing decreased neuronal inhibition in the primary motor area of patients with Tourette syndrome, has demonstrated similar findings in 16 OCD patients in a study at the NIH, Bethesda, MD (Greenberg BD, Ziemann U, Cora-Locatelli G et al. Altered cortical excitability in obsessive-compulsive disorder. Neurology Jan 2000;54:142-147). The decreases in intracortical inhibition and motor threshold were greatest in OCD patients with comorbid tics.

Suprasellar germinoma presenting with Obsessive-Compulsive symptoms. A 13-year-old boy with a suprasellar germinoma involving the basal ganglia presented with psychotic and obsessive-compulsive symptoms in addition to hemiparesis, diabetes insipidus and impaired academic function (Mordecal D, Shaw RJ, Fisher PG et al. J Am Acad Child Adolesc Psychiatry Jan 2000;39:116-119). Other neurobehavioral disorders with basal ganglia involvement include Tourette syndrome and PANDAS.

SEIZURE DISORDERS

VALPROATE-INDUCED ENCEPHALOPATHY

Two adults, aged 32 and 37, with focal epilepsy developed hyperammonemic encephalopathy when treated with a combination of valproate (VPA) and topiramate (TPM) at the University of Marburg, Germany. Previously the patients had tolerated combinations of VPA with phenobarbital or carbamazepine. Recovery followed the withdrawal of either VPA or TPM. (Hamer HM, Knake S, Schomburg U, Rosenow F. Valproate-induced hyperammonemic encephalopathy in the presence of topiramate. Neurology Jan 2000;54:230-232). (Reprints: Dr HM Hamer, Department of Neurology, University of Marburg, Rudolf-Bultmann-Str 8, 35033

Marburg, Germany).

COMMENT. The addition of topiramate may have induced the VPA/TPM encephalopathy by the inhibition of carbonic anhydrase and cerebral glutamine synthetase. If correct, a combination of VPA and acetazolamide should be avoided. The addition of phenobarbital may also increase the risk of VPA/TPM encephalopathy by decreasing ammonia detoxification in the liver.

N-acetyl-glutamate synthetase deficiency explains VPA-Reye illness. A boy developed periods of paroxysmal crying resembling seizures, lethargy, ataxia and tremor at 2 1/2 years. His condition worsened after treatment with VPA. When examined at 4 years because of vomiting and jaundice, VPA was discontinued. Liver biopsy was compatible with Reye syndrome. Enzymatic analysis found a deficiency of N-acetyl-glutamate synthetase (NAGS). Treatment with carbamyl-glutamate and arginine was partially effective, liver function and neurologic signs improved but hyperammonemia persisted. The VPA had exacerbated the NAGS by further inhibiting carbamyl-phosphate synthetase. (Forget PPh, van Oosterhout M, Bakker JA et al. Partial N-acetyl-glutamate synthetase deficiency masquerading as a valproic acid-induced Reye-like syndrome. Acta Paediatr Dec 1999;88;1409-1411).

METABOLIC DISORDERS

NEUROLOGIC PRESENTATION OF MITOCHONDRIAL DISORDERS

Nervous system presentations in 42 children with mitochondrial disorders were analyzed by reviewing charts at the Wolfson Medical Center, Holon, and other centers in Israel. Mean age was 8 years; 2.8 yrs at presentation and 4.8 at diagnosis. Six died with neurologic deterioration, 4 of Leigh disease. Nervous system involvement was the first clinical presentation in 28 (66%) children: mental retardation or developmental delay occurred in 24; hypotonia in 18; autonomic manifestations in 18; seizures (generalized tonic-clonic) in 12; microcephaly in 12; cerebellar ataxia in 8; and choreoathetosis in 6 children. Unusual manifestations were stroke-like episodes in only 4; and headache, external ophthalmoplegia, autism, and hyperexplexia. Twenty five had an acute regression or progressive encephalopathy. Myopathy occurred in only 6.

Autonomic symptoms included gastrointestinal dysmotility and dysphagia in 6, central apnea in 6, cardiac irregularities in 4, neurogenic bladder in 3, and alternating anisocoria in 2.

Optic atrophy (5), retinitis pigmentosa (3), and sensorineural deafness (7) were presenting sensory signs.

CT or MRI in 33 patients showed hypodensities in the basal ganglia, thalamus, or brain stem in 7 patients, leukodystrophy in 2, hemiatrophy in 2, cerebral atrophy in 15 and cerebellar atrophy in 2. (Nissenkorn A, Zeharia A, Lev D et al. Neurologic presentations of mitochondrial disorders. J Child Neurol Jan 2000;15:44-48). (Respond: Dr Tally Lerman-Sagie, Pediatric Neurology Unit and Metabolic-Neurogenetic Clinic, Wolfson Medical Center, Holon, Israel 58100).

COMMENT. The most common neurologic presentations of mitochondrial disorders in children are developmental delay, abnormal muscle tone, and seizures, whereas characteristic symptoms including stroke-like episodes and ophthalmoplegia are rare. Unusual features include autism and hyperexplexia. In children presenting with a variety of complex neurologic symptoms, normal intelligence and normal serum lactic acid levels should not preclude a workup for