Pediatr Nov 1993;123:828-830). (Reprints: B Sarkar PhD, Head, Department of Biochemistry Research, Hospital for Sick Children, Toronto, Ontario M5G 1X8, Canada).

COMMENT. In a 13-week-old boy with Menkes disease treated with copper-histidine by daily intramuscular injections, Cu and ceruloplasmin in serum and Cu in CSF became normal after 6 weeks, epileptic discharges and infantile spasms were reduced, muscle tone was improved, motor activities increased, and developmental regression stopped. A marked improvement in osseous changes at 6 months was also noted. (Kreuder J et al. Clinical and biochemical consequences of copper-histidine therapy in Menkes disease. Eur J Pediatr Oct 1993; 152:828-832). This report from Children's Hospital, Justus Liebig University, Giessen, Germany, is the first to demonstrate normalization of dopamine and dopamine/norepinephrine ratio in CSF after copper-histidine therapy.

The recent reports from three independent laboratories of the isolation of a Menkes' gene candidate have narrowed the search for the defective or missing factor in this sex-linked, recessive neurodegenerative disorder. A copper-transporting ATPase may be the important factor in normal copper metabolism. (Harris ED. Menkes' disease: Perspective and update on a fatal copper disorder. Nutrition Reviews Aug 1993;51:235-245).

FETAL VALPROATE SYNDROME

The high frequency of minor abnormalities and major malformations, the withdrawal manifestations, and hypoglycemia in infants born to mothers who received sodium valproate during pregnancy are reported from the Department of Paediatrics, Aalborg Hospital, Denmark. Of 17 mothers, 11 had valproate monotherapy, and 6 had valproate combined with another anticonvulsant, usually carbamazepine. Minor abnormalities (epicanthic folds, hypertelorism, low set ears, etc) affected 9 (53%) infants, of whom 5 also had major malformations, predominantly congenital heart disease, present in 4. The frequency of abnormalities was related to the valproate dosage in the first trimester. Of 6 infants born to mothers receiving >2.5 g daily, 5 had minor abnormalities, and 3 had major malformations. Withdrawal symptoms in 9 (53%) infants included irritability, jitteriness, seizures, and feeding problems; hypoglycemia occurred in 4. At 2.0 - 3.5 year follow up, 3 showed psychomotor retardation. (Thisted E, Ebbesen F. Malformations, withdrawal manifestations, and hypoglycemia after exposure to valproate in utero. Arch Dis Child Sept 1993;69:288-291). (Respond: Dr Ebbe Thisted, Department of Paediatrics, University Hospital of Hvidovre, Kettegards Alle 30, DK-2650 Denmark).

COMMENT. Fetal valproate syndrome is related to the valproate dosage in the first trimester, while withdrawal symptoms are related to the dose and free fraction plasma concentration in the third trimester. These serious complications of valproate therapy for epilepsy during pregnancy occur during monotherapy as well as polytherapy. If the use of valproate during pregnancy cannot be avoided, despite the relatively high risk of teratogenicity, and especially spina bifida, the dosage and blood levels must be meticulously monitored and maintained as low as possible. (Omtzigt JGC, Lindhout D et al. Neurology 1992;42(suppl 5):119-125).

NEUROMUSCULAR DISEASES

JUVENILE MYASTHENIA GRAVIS: DIAGNOSIS AND OUTCOME

The usefulness of various diagnostic tests, treatment, and outcome in 27 juvenile myasthenics seen over a 25 year period are reported from the Departments of Pediatrics, Neurology, and Anatomy, University of Iowa. The age of onset in 56% was after 10 years of age. One fourth had ocular myasthenia, one fourth presented with ocular signs and progressed to generalized myasthenia, and half had generalized myasthenia from onset. Ptosis, the most common presenting sign (81%), was unilateral in 33%. In order of descending frequency, the other presenting signs were generalized weakness, dysphagia, diplopia, facial weakness, dysarthria, ophthalmoplegia, and nasal speech. One patient's mother had MG. The comparative yield of tests showed positive neostigmine and edrophonium tests in 92%, serology was positive for acetylcholine receptor-binding antibodies in 63%, and repetitive distal nerve stimulation showed decrement in 33%. The yield of serology and nerve stimulation tests increased with generalization of myasthenia and when proximal nerves were also tested. Ocular myasthenics responded to pyridostigmine bromide monotherapy, while generalized myasthenia required additional medical and/or surgical therapy. Patients receiving corticosteroids had thymectomy at a later date. Those with normal thymus had a greater chance of remission without medication than patients with thymic hyperplasia. (Afifi AK, Bell WE. Tests for juvenile myasthenia gravis: comparative diagnostic yield and prediction of outcome. J Child Neurol Oct 1993;8:403-411). (Respond: Dr Afifi, Division of Child Neurology, Department of Pediatrics, University of Iowa Hospitals and Clinics, Iowa City, IA 52242).

COMMENT. Thirty-eight percent of these patients were in complete remission and without drugs when followed for more than 4 years (range, days to 20 years). The outcome was better for ocular than generalized myasthenia, 57% cf 30% in remission without drugs. A lower rate of remission in thymectomized (35%) compared to non-