HEREDO-DEGENERATIVE DISEASES

X-LINKED ATAXIC SYNDROME

An X-linked recessive disease with a fatal course in early childhood is reported in a five-generation Dutch family from the Netherlands. Twelve boys were affected and 13 female carriers were identified, some with hearing impairment. Neurological deterioration coincided with recurrent respiratory infections at 1 year of age or earlier and was characterized by hypotonia, ataxia, weakness, absent deep tendon reflexes, nystagmus, and visual and hearing loss. Autopsy in one patient revealed absence of myelin in posterior columns of the spinal cord, and axonal degeneration in the peripheral nerves. The brain was normal in appearance. No biochemical or immunological defects were detected. (Arts WFM et al. X-linked ataxia, weakness, deafness, and loss of vision in early childhood with a fatal course. Ann Neurol May 1993; 33: 535-539). (Respond: Dr Arts, Dept of Neurology, Westeinde Hospital, PO Box 432, 2501 CK The Hague, The Netherlands).

> COMMENT. Mitochondrial encephalomyelopathy and other known metabolic or degenerative diseases were excluded. The autopsy findings in one patient resembled those of Friedreich's ataxia, but the age of onset and early death were atypical.

ALPERS SYNDROME WITH HEPATIC CIRRHOSIS

Four children, from two families, with fatal degeneration of the cerebral grey matter and terminal hepatic dysfunction are reported from the Royal Belfast Hospital for Sick Children, Northern Ireland. The disease presented with intractable generalized or partial seizures during infancy in 3 and at 5 years of age in one patient. Epilepsia partialis continua was associated with ataxia and progressive neurologic deterioration. The EEG showed high amplitude slow waves with smaller poyspikes. Visual evoked responses were delayed, and CTs showed cerebral atrophy. Post mortem findings in one patient included neuronal loss and gliosis and hepatic cirrhosis. (Wilson DC et al. Progressive neuronal degeneration of childhood (Alpers syndrome) with hepatic cirrhosis. Eur J Pediatr 1993; 152(3): 260-262). (Respond: Dr DC Wilson, Neonatal Unit, Royal Maternity Hospital, Grosvenor Road, Belfast BT126BJ, N Ireland).

> COMMENT. Valproic acid, sometimes implicated in deaths of young infants with this syndrome, was apparently not a factor in these cases. Early diagnosis allows appropriate genetic counselling.

MITOCHONDRIAL MYOPATHY AND CONGENITAL CATARACT

The autosomal recessive syndrome characterized by mitochondrial myopathy of cardiac and skeletal muscle, congenital cataract and lactic

acidosis is described in two forms following a retrospective study of 16 patients at the University of Nijmegen, The Netherlands. Four patients with the fatal form died from hypertrophic obstructive cardiomyopathy in the neonatal period. In those with the relatively benign form, cardiomyopathy developed late, causing death in 7 patients at a median age of 23 years. The prognosis in patients without subvalvular aortic stenosis is dependent on the metabolic function of skeletal muscle. It varies between moderate exercise intolerance and wheelchair existence. In both forms, bilateral cataracts, lactacidemia and mitochondrial myopathy are present from birth. If a propositus has an affected sib, he will probably suffer from the same form, and genetic counselling is important. (van Ekeren GJ et al. A retrospective study of patients with the hereditary syndrome of congenital cataract, mitochondrial myopathy of heart and skeletal muscle and lactic acidosis. Eur J Pediatr 1993; 152(3): 255-259). (Respond: Dr RCA Sengers, Dept of Paediatrics, University of Nijmegen, PO Box 9101, NL-6500 HB Nijmegen, The Netherlands).

> **COMMENT.** Cataracts present at birth are the first manifestation of the syndrome in most patients. Some present with muscular hypotonia, and others with cardiac symptoms. The metabolic cause is unknown. Skeletal muscle biopsy showed abnormal mitochondrial structure or number with matrix vesicles, and the sarcoplasm contained large quantities of lipid or glycogen. Morphometric analysis demonstrated an increased volume density of subsarcolemmal mitochondria, a possible compensatory mechanism for a deficit in energy production. The findings were similar in the fatal and benign forms. Mitochondrial function showed no abnormalities. Qualitative and quatitative defects in mitochondrial DNA in infants with fatal metabolic disorders are discussed by Moraes CT (Int Pediatr 1993; 8: 40).

ATYPICAL LEBER'S OPTIC NEUROPATHY

The diagnosis of Leber's hereditary optic neuropathy (LHON) in 6 female atypical cases seen at Harvard, Emory, and Johns Hopkins Medical Centers required molecular analysis and demonstration of the 11778 mitochondrial DNA mutation for accurate confirmation. Features atypical for LHON included a negative family history, a normal fundus, bitemporal hemianopia, optic disc cupping, and premonitory episodes of transient monocular visual loss. Molecular analysis allows accurate identification of most cases. The 11778 point mutation accounts for 50%. (Weiner NC et al. Atypical Leber's hereditary optic neuropathy with molecular confirmation. Arch Neurol May 1993; 50: 470-473). (Reprints: Nancy J Newman MD, Neuro-ophthalmology Unit, Emory Eye Center, 1327 Clifton Rd NE, Atlanta, GA 30322).