syndromes.

DEMYELINATING AND DEGENERATIVE DISEASES

NATURAL HISTORY OF EARLY ONSET MULTIPLE SCLEROSIS

The clinical course of multiple sclerosis (MS) in 116 patients with onset before age 16 (prevalence 3.6% in total MS clinic attendees) was evaluated by longitudinal study (mean duration 19.76 +/- 0.9 years) at the University of British Columbia MS Clinic. Mean age of onset of MS was 12.73 +/- 0.25 years; 23 (19.8%) had onset at age 10 or younger, and 6 (5.2%) at age 7 or younger. The female to male ratio was 2.87:1. Female preponderance was highest for patients with onset at ages 13 - 14 (pubertal age). Most frequent initial symptoms were sensory disturbances (25.9%), optic neuritis (21.6%), brainstem dysfunction (12.9%), gait disorders (9.4%), and cerebellar incoordination (6.9%). Sensory and brainstem disturbances were more frequent in girls, whereas boys were affected more by motor and gait disturbances. The MS course was primary progressive (PP) in 3 cases (2.6%), and secondary progressive (SP) in 60 (53.1%),with 50% probability of SP by 23 years after onset. For relapsing remitting (RR) or SPMS cases, the mean duration from onset to an Expanded Disability Status Scale (EDSS) 3 was 16.03 +/- 1.17 years, at a mean age of 28.47 +/- 1.14 years. EDSS 6 was reached by 19.39 +/- 1.43 years, at a mean age of 32.32 +/- 1.44 years. Annual relapse rate was 0.54 +/- 0.05 per year. The course of MS was significantly correlated with the number of relapses in the first year after onset. The majority of cases had a RR course, and early age at permanent disability. Disease-modifying therapy should be considered early in the course of early onset MS. (Boiko A, Vorobeychik G, Paty D et al. Early onset multiple sclerosis. A longitudinal study. Neurology October (1 of 2) 2002;59:1006-1010). (Reprints: Dr DW Paty, Room S195, 2211 Wesbrook Mall, UBCH, Vancouver, BC V6T 2B5, Canada).

COMMENT. Patients with early onset MS (EOMS) tend to recover from the initial manifestations and have a relatively long first and second remission. However, EOMS cases include patients with frequent relapses, early age at permanent disability, and occurrence of malignant cases. In those with duration more than 10 years, 65% are disabled. The frequency of relapses in the first 5 years after onset, and the duration of first and second remissions correlate with the risk of permanent disability. Initial brainstem symptoms are predictive of a poor prognosis. Therapy should be considered sooner rather than later in EOMS.

PATTERNS OF REGRESSION IN RETT SYNDROME

Patterns and features of regression in a case series of 53 girls and women with Rett syndrome were studied at the Institute of Child Health and Great Ormond Street Children's Hospital, London, UK. Diagnostic criteria for classical Rett syndrome were met in 46 cases, and 7 had an atypical/variant form. The most common period for regression was 12 - 18 months, reported by parents or in casenotes in 49% of patients. Mean age of regression was 16 months. Skills lost in order of frequency were hand use (85%), non-verbal vocalizations and simple gestures (59%), non-verbal play (51%), motor skills (49%), and words (45%). Pre-regression developmental delays were noted in more than two-thirds of cases (85% in youngest cases when parental reports were most reliable). Age at regression was not an index of neurological severity (epilepsy, breathing abnormalities, mobility, joint contractures, and oral-motor dysfunction). (Charman T, Cass H, Owen L et al. Regression in individuals with Rett syndrome.

Brain Dev Aug 2002;24:281-283). (Respond: Dr Tony Charman, Institute of Child Health, 30 Guildford Street, WC1N 1EH London, UK).

COMMENT. Signs of abnormal or delayed development (hypotonia and delayed motor milestones) are commonly observed in cases of Rett syndrome in the pre-regression period. Earliest and most frequent signs of regression are loss of hand use and communication skills. Early developmental history can aid in detection of risk factors for Rett syndrome, and before the onset of growth delay, gait ataxia, and hand stereopathies.

FAMILIAL INFANTILE BILATERAL STRIATAL NECROSIS

The clinical and radiological evolution of familial infantile bilateral striatal necrosis (IBSN) was evaluated in 11 of 15 affected children born to consanguineous Israeli Bedouin parents and reported from the Schneider Children's Medical Center, Petah Tikva and Sackler School of Medicine, Tel Aviv University, and other centers in Israel. Three were treated with oral biotin 100 mg/day. Inheritance was autosomal recessive. Untreated children showed signs of developmental arrest with onset at age 7 to 15 months, choreoathetosis and dysphagia, and a later onset of pendular nystagmus. MRI showed severe basal ganglia atrophy. Postmortem findings in one patient showed severe atrophy of lenticular nuclei with gliosis and neuronal loss. Biotin therapy resulted in arrest or improvement of disease in 2 patients when administered early, and slowed progression in the proband with treatment over a 15 month period. (Straussberg R, Shorer Z, Weitz R et al. Familial infantile bilateral striatal necrosis. Clinical features and response to biotin treatment. Neurology October (1 of 2) 2002;59:983-989). (Reprints: Dr Rachel Straussberg, Neurogenetic Clinic, Department of Neurology, Schneider Children's Medical Center of Israel, Petah Tikva, Israel 49202).

COMMENT. Infantile bilateral striatal necrosis (IBSN) is a rare clinically heterogeneous syndrome characterized pathologically by symmetric spongy degeneration of the caudate nucleus, putamen, and occasionally the globus pallidus. Clinical manifestations are developmental regression, choreoathetosis, dystonia, dysphagia, and mental retardation. Prognosis is usually poor with spastic quadriparesis and early morbidity. Reported cases have been described in 3 groups: 1) subacute necrotizing encephalomyelopathy (Leigh disease); 2) familial striatal degeneration with slow progression; and 3) abrupt neurologic onset following an acute systemic illness. The Israeli familial cases described above are in group 2, with poor prognosis. Biotin is worthy of trial and early treatment is recommended.

NOVEL ACTIN AND COFILIN AGGREGATIONS IN JUVENILE-ONSET DYSTONIA

The brains of identical twins with juvenile-onset dystonia were examined at Emory University, Atlanta, Georgia. Clinically, the twins had only a mild developmental delay until age 12 years, and they then showed a rapidly progressive generalized dystonia and dementia, with death occurring at ages 21 and 22 years. Clinical findings and course were distinct from primary and secondary dystonias previously described. The twins were born with cleft lip and palate, their limbs were small, and skeletal abnormalities included high foreheads, hypoplastic scapulas, and kyphoscoliosis by age 10 years. Achalasia was diagnosed at age 2, cataracts at age 3, and sensory-neural deafness at age 4. Dystonia developed first in the leg by age 14, and progressed over 5 years from a clumsy gait to an inability to walk. Oculogyric and opisthotonic crises occurred as