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

the dystonia became generalized. Grimacing, dysarthria, tongue protrusion, and dysphagia with pseudobulbar palsy occurred by age 14.

Macroscopically, the brains were unremarkable. Microscopic examination showed diffuse glial fibrillary acidic protein-immunoreactive astrocytes, and iron accumulation in neurons of the globus pallidus and substantia nigra. Additional degenerative findings included; 1) eosinophilic, rod-like cytoplasmic inclusions found in neocortical and thalamic neurons that were actin depolymerizing factor/cofilin-immunoreactive and rarely actin positive; and 2) eosinophilic spherical structures in the striatum that were actin- and actin depolymerizing factor/cofilin-positive. Aggregation of actin is a novel finding in neurodegenerative disease associated with dopa-unresponsive dystonia. (Gearing M, Juncos JL, Procaccio V et al. Aggregation of actin and cofilin in identical twins with juvenile-onset dystonia. Ann Neurol October 2002;52:465-476). (Respond: Dr Marla Gearing, Center for Neurodegenerative Disease, Whitehead Research Building, 615 Michael Street, 5th Floor, Atlanta, GA 30322).

COMMENT. An extensive aggregation of actin and actin regulatory proteins ADF/cofilin in twins with progressive and fatal dystonia is indicative of a dysfunction of regulatory turnover of active filaments in the cytoskeletal system. This is a novel neuropathological finding in a neurodegenerative disease causing dystonia. Other well known examples of a secondary dystonia include Wilson's disease, Hallervorden-Spatz disease, and Huntington's disease. Secondary dystonias may be complicated by parkinsonism, myoclonus, and tremor, and some are without defined pathology, as in drug-induced and occupational, and with known pathology, such as traumatic, metabolic, and vascular. Another example of secondary dystonia is the myoclonus-dystonia syndrome, with onset in childhood.

MYOCLONUS-DYSTONIA SYNDROME AND E-SARCOGLYCAN DEFICIENCY

Clinical and genetic findings in 9 European families with myoclonus-dystonia syndrome (MDS) are reported from Ludwig-Maximilians-Universitat, Munich, Germany. In 24 affected and genetically proven patients, the clinical presentation was homogeneous, with "lightening-like" myoclonus of the neck, trunk, and upper limbs in 23 and cervical dystonia and/or writer's cramp in 13 (54%) cases. The mean age at onset of myoclonus was 5.4 years (range 0.5-20 years), and of dystonia 8.8 years (range 1-38 years). Myoclonus was improved by alcohol ingestion in 21, some having severe or periodic heavy drinking. None showed progression of symptoms after age 20. Five patients had a history of panic attacks, depression, and agoraphobia. Pedigree analyses identified 8 maternal transmissions of SGCE mutations in 5 families, 7 of the mutation carriers being asymptomatic. Six novel and one known heterogeneous mutations in the gene for E-sarcoglycan (SGCE) were identified. The data confirm the role of SGCE mutations and deficiency in the pathogenesis of MDS. (Asmus F, Zimprich A, Tezenas du Montcel S et al. Myoclonus-dystonia syndrome: E-sarcoglycan mutations and phenotype. Ann Neurol October 2002;52:489-492). (Respond: Dr Gasser, Neurologische Klinik Grosshadern, Ludwig-Maximilians-Universitat, Munchen, Marchioninistrasse 15, D-81337 Munchen, Germany).

COMMENT. Myoclonus-dystonia syndrome (MDS) is an autosomal dominant disorder with brief, "lightening" myoclonic jerks and cervical or brachial dystonia, with onset in childhood or early adolescence. The myoclonus is alcohol sensitive, and many develop an alcohol dependence as well as panic attacks and obsessive-compulsive disorder. In contrast to primary generalized dystonias, the