Molecular Neurogenetics, National Neurological Institute Carlo Besta, via Temolo 4, 20126 Milan, Italy).

COMMENT. The clinical syndromes associated with *POLGI* mutations, the gene encoding the subunit of mitochondrial DNA (mtDNA) polymerase (pol-yA), include familial progressive external ophthalmoplegia, autosomal recessive sensory atactic neuropathy with ophthalmoplegia, juvenile sensory and cerebellar atactic syndrome with myoclonus epilepsy, and Alpers' hepatopathic poliodystrophy, first described by Alpers in 1931, and later by Ford (1951), Blackwood et al, 1963, and Huttenlocher et al, 1976. Huttenlocher emphasized the coincident hepatic cirrhosis. Alpers' syndrome is characterized by refractory seizures (epilepsia partialis continua), progressive neurologic deterioration, and progressive hepatic failure. The present report shows that *POLGI,* found in 8 of 10 cases examined over 10 years, is a prevalent disease gene in Alpers' syndrome, and tissue-specific, partial mtDNA-depletion is a molecular feature of the disease.

The hepatic complication has sometimes been attributed to valproate toxicity during treatment of refractory seizures, and 2 of the above Italian cases received valproate just prior to acute liver failure. In a report of 13 cases of Alpers' syndrome (termed progressive neuronal degeneration) from Great Ormond Street Hospital, London, UK (Egger J et al. **Clinical Pediatrics** 1987;26:167-173), 4 patients received sodium valproate and 2 of the 4 died. Both had abnormal liver enzymes before treatment, and valproate was not accepted as the primary cause, a genetically determined metabolic explanation being preferred.

DEVELOPMENTAL DISORDERS

IMPROVED GLOBAL AND LOCOMOTOR DEVELOPMENT FOLOWING SURGERY FOR SAGITTAL SYNOSTOSIS

Twenty eight children with sagittal synostosis (SS) were assessed pre- and postoperatively and their psychomotor development was compared with that in 28 normal controls and with 13 children with SS without surgical intervention, in a prospective longitudinal design study at St James's University Hospital, Leeds, UK. Using the Griffiths Mental Developmental Scales, children with SS had significantly lower gross locomotor function scores than normal controls, 35.7% having LD scores, when tested at a mean age of 8 months. Following surgical intervention (at a mean age of 6.9 months), the global development improved ($p=0.001$), locomotor deficit resolved ($p=0.0001$), often suddenly, particularly the delay in head control, and the developmental attainment continued to improve over time (11 children had a second postoperative assessment and 4 had a third). A lesser improvement was demonstrated in eye-hand coordination and performance skills ($p=0.05$). Children with SS not surgically corrected failed to show the improvement in development demonstrated in operated cases. Surgery for SS is more than a cosmetic procedure, but the mechanism for the improved development is not definitely determined. (Bellew M, Chumas P, Mueller T et al. Pre- and postoperative developmental attainment in sagittal synostosis. **Arch Dis Child** April 2005;90:346-350). (Respond: Dr M Bellow, Department of Plastic, Reconstructive, and Hand Surgery, St James's University Hospital, Beckett Street, Leeds LS9 7TF, UK).

COMMENT. The authors list three novel findings: 1) the quantifiable delay in early development of infants with sagittal synostosis (SS) demonstrated in a controlled, prospective, longitudinal study; 2) a preoperative delay in gross locomotor development; and 3) a significant postoperative resolution of locomotor deficits. Previous studies have reported developmental delay only in older patients and without normal controls and prospective follow-up; mental rather than motor development has been considered; and delayed gross locomotor development with improvement after surgery has not previously been demonstrated in young infants. One study is cited that supports the present findings but in young children: 35.5% of 50 children with SS had cerebral palsy, psychomotor retardation, and/or neurological signs, and many of the deficits resolved after surgery, only 14.5% having persistent abnormal signs (Kaiser G. **Childs Nerv Syst** 1988;4:223-230). Raised intracranial pressure was considered an unlikely factor in the mechanism of improved locomotor function following surgery in the Leeds series.

BEHAVIORAL AND SLEEP DISORDERS IN NEUROFIBROMATOSIS

The behavior and sleep patterns of 64 children (mean age 10 years 7 months) with neurofibromatosis type 1 (NF1) were determined by mail and telephone questionnaire in a study at Park Hospital, University of Oxford, UK. Compared to the general population, increased numbers of children with NF1 had scores in the borderline and abnormal range for peer problems ($p<0.001$), hyperactivity ($p<0.001$), emotional symptoms ($p<0.001$), and conduct disorders ($p<0.05$). Parasomnias (sleepwalking and sleep terrors) were more frequent in the NF1 patients ($p<0.05$), and those with frequent sleep disturbance had a higher incidence of conduct, hyperactivity, emotional, and total behavioral disorders ($p<0.05$ or 0.01). (Johnson H, Wiggs L, Stores G, Huson SM. Psychological disturbance and sleep disorders in children with neurofibromatosis type 1. **Dev Med Child Neurol** April 2005;47:237-242). (Respond: Dr Hilary Johnson, Park Hospital for Children, Old Road, Headington, Oxford OX3 7LQ, UK).

COMMENT. NF1 is associated with an increased prevalence of behavioral and sleep problems, including attention deficit hyperactivity disorder.

Cognitive impairments and specific learning disabilities occur in 30-65% of patients with NF1, and the association is reviewed by Ward BA and Gutmann DH (**Pediatr Neurol** April 2005;32:221-228). These authors cite several studies showing a correlation between unidentified bright objects (T2 hyperintensities) in the brain MRI and cognitive dysfunction, but the observation is controversial and not universal. The role of neurofibromin, the NF1 gene product, in learning is discussed in relation to laboratory and genetic studies in Nf1+1- mice. The increased RAS proto-oncogene activity in these mice is responsible for a spatial learning impairment that is related to g-aminobutyric acid-mediated inhibition. Active RAS, as a result of reduced neurofibromin, leads to tumor formation in NF1. Experimental therapies in trial phase, such as farnesyl transferase inhibitors that decrease RAS levels, are intended to decrease tumor size and these may lead to a reversal of the learning disability. For further articles on NF1 and learning disabilities, see **Progress in Pediatric Neurology 111, PNB Publishers,** 1997;pp291-294, 441.