

## CNS DEVELOPMENTAL DISORDERS

### FRAGILE X SYNDROME

Japanese patients with infantile autism were studied cytogenetically for the occurrence of fragile X (fra(x)) syndrome at the Universities of Kurume and Nagasaki. Fra(X) chromosome was detected in 2 (siblings) of 39 boys and in none of 8 girls; a frequency of 2.6% (1/38) in the study population of male autistic children. (Matsuishi T et al. Fragile X syndrome in Japanese patients with infantile autism. *Pediatr Neurol* 1987; 3: 284-7).

**COMMENT.** The fragile X syndrome is the most common familial form of mental retardation known, with an incidence of 1 in 1000 in the general population. The classical physical features in males are a long narrow face, large ears, and large testes. The pediatric neurologist may encounter cases referred because of large head circumference, hyperactive behavior and short attention span (ADD), and hand-flapping movement disorders. Poor eye contact and stereotyped movement have led to confusion with autism, reported in 5-53% of males with fragile X syndrome, and the classical manifestations have matched the DSM III diagnostic criteria for autism in some, as in the above study. For a comprehensive current overview of fragile C syndrome, see Hagerman RJ. *Curr Probl Pediatr* 1987;17:621-674.

### VALPROATE-INDUCED MALFORMATIONS

Two children born with birth defects after intrauterine exposure to valproic acid are reported from the Dept Pediatrics Hospital Sainte-Justine, University of Montreal, Quebec, Canada. The drug was taken by the mothers throughout pregnancy as monotherapy for primary generalized epilepsy. One baby had facial dysmorphism, hypertelorism, anti-mongoloid palpebral fissures, a naevus flammeus on the forehead, portwine palpebral and nasal angiomas, arachnodactyly, triphalangeal thumbs, syndactyly, and a septum pellucidum cyst and dilated veluticles on CT scan. The second baby had facial dysmorphism, laryngeal hypoplasia, tracheomalacia, aberrant innominate artery and hydronephrosis. The authors concluded that valproic acid has probable teratogenic potential in humans but the spectrum of anomalies is broad and a definite fetal valproate syndrome is difficult to delineate. (Huot C et al. *Congenital malformations associated with maternal use of valproic acid. *Can J Neurol Sci* 1987;14:290-293).*

**Comment.** Approximately 50 malformed babies born to epileptic mothers taking valproate monotherapy have been reported. Contrary to the above opinion, Diliberti et al (*Amer J Med Genetics* 1984;19:473-481) have recognized a "fetal valproate syndrome", and the frequency of reports of valproate-induced congenital malformations together with other side-effects (liver failure, pancreatitis, endocrine abnormalities, weight gain) tend to contraindicate its use in pregnancy.

Portwine angioma noted in the first baby in this study of valproic acid toxicity may also be induced by thalidomide and alcohol ingestion during pregnancy (Jones et al. *Lancet* 1974;1:1076. Colver GB, Savin JA. Editorial. *J Roy Soc Med* 1987; 80:603). Dilated ventricles, defined by CT in the first baby, are reported as a reversible cerebral pseudoatrophy for the first time as a side-effect of valproic acid monotherapy in a 17-year-old with epilepsy (McLachlan RS. *Can J Neurol Sci* 1987;14:294).