PYRIDOSTIGMINE-INDUCED MICROCEPHALY

The association of high-dose pyridostigmine (PYD) during pregnancy with microcephaly and CNS injury in an infant is reported from the Children's Hospital Los Angeles, CA. The mother was diagnosed with myasthenia gravis (MG) at 10 years of age, and had undergone thymectomy and plasmapheresis. PYD was the only medication during pregnancy, and the dose was increased steadily because of persistent diplopia and ptosis. The dose of 40 mg/kg day (average of 1500-3000) g/day) continued for the entire pregnancy was four to eight times the usual recommended amount. The infant delivered by cesarean section at 36 weeks because of fetal bradycardia weighed 1880 g ($\langle 2\% \rangle$) and the head circumference (HC) was 33.5 cm (10%). Apgars were 3 and 8. He was hypotonic with poor respiratory efforts and required intubation. A Tensilon test was positive for neonatal MG, and he was treated by exchange transfusion and IV immunoglobulin. He was weaned from the respirator at 3.5 months. At 3 months his HC was 37 cm (<5%), and at 5 months, it was 38 cm (<2%). He had dysmorphic facial features, short neck, broad chest, campylodactyly, bilateral cryptorchidism. and ankle clonus, MRI revealed mild ventriculomegaly. (Niesen CE, Shah NS. Pyridostigmine-induced microcephaly. Neurology May (1 of 2) 2000;54:1873-1874). (Reprints: Dr CE Niesen, Department of Pediatrics, Cedars-Sinai Medical Center, 8700 Beverly Blvd, Room 1165W, Los Angeles, CA 90048).

COMMENT. Pyridostigmine, a cholinesterase inhibitor, has been used safely in pregnant myasthenic patients in doses less than 600 mg/day. This is the first report of high-dose PYD being associated with microcephaly, growth retardation, and evidence of CNS damage in the infant. PYD passes readily into the fetal circulation, with concentrations amounting to 90% of the maternal plasma levels.

TOXIC DISORDERS

METHYLMERCURY-INDUCED FETAL NEUROLOGIC DYSFUNCTION

The effects of seafood contaminants in maternal diet during pregnancy on neonatal neurologic function were examined in 182 singleton term births in the Facroe Islands, and reported from the Institute of Public Health, Odense University, Denmark. Maternal serum, hair, and milk and umbilical cord blood were analysed for contaminants, Each infant's neurologic optimality score (NOS) was determined at 2 weeks of age and adjusted for gestational age. Exposures to methylmercury and polychlorinated phenols and cord blood fatty acid concentrations were increased in proportion to maternal seafood intake. Thyroid function tests were normal. A 10-fold increase of cord-blood mercury concentration was correlated with a decrease in NOS of 2.0 (P= .03). (Steuerwald U, Weihe P, Jorgensen PJ et al. Maternal seafood diet, methylmercury exposure, and neonatal neurologic function. <u>I Pediatr</u> May 2000;136:599-605). (Reprints: Philippe Grandjean MD PhD, Institute of Public Health, Odense University, Winslowparken 17, 5000 Odense C, Denmark).

COMMENT. Increased exposures to methylmercury from maternal seafood intake are associated with a significant decrease in neonatal neurologic optimality scores and an increased risk of neurodevelopmental deficit. The NOS used in this study is based on the Prechtl exam technique and includes functional abilities, reflexes and tone, and behavior. The NOS is the number of items rated optimal out of 60. In the Faeroe Islands, whale meat is the source of methylmercury in the diet. For previous reports of neuropsychological effects of methylmercury and PCP exposures see <u>Progress in Pediatric Neurology III</u>, PNB Publ, 1997;pp278-280.

latrogenic exposure to mercury after hepatitis B vaccination in preterm infants is reported by Stajich GV et al. (<u>1 Pediatr</u> May 2000;136:679-681). Thimerosal, a mercury-derived preservative, has been used in some vaccines since the 1930s. Thimerosal is composed of 49.6% ethylmercury, which behaves like methylmercury. According to a review editorial by Pless R and Risher JF (<u>1</u> <u>Pediatr</u> May 2000;136:571-573), infants may be exposed to cumulative doses of mercury from vaccines in the first 6 months, exceeding the EPA limit of 0.1 mcg/kg/d for chronic daily exposure to methylmercury. The Advisory Committee on Immunization Practices has recommended that hepatitis B vaccine used in infants at birth should not contain thimerosal.

PRE- AND PERI-NATAL DISORDERS

EARLY PREDICTORS OF HIE ADVERSE OUTCOME

A retrospective study of 35 term infants with post-asphyxial hypoxicischemic encephalopathy (HIE) was conducted at the KK Women's and Children's Hospital, Singapore, to determine early predictors of mortality or major motor morbidity at 18 months of age. A severe adverse outcome occurred in 23: thirteen died and ten had major neurological sequelae. Risk factors included a low 5 min Apgar score (<4), the use of adrenaline, low arterial pH (<7.1) and high base deficit (>20 mEq/L). The high base deficit and low Apgar score combined had a positive predictive value of 100%. (Toh VC. Early predictors of adverse outcome in term infants with post-asphyxial hypoxic ischaemic encephalopathy. <u>Acta Paediatr</u> March 2000;89:343-347). (Respond: Dr Veronica C Toh, Department of Neonatology, KK Women's and Children's Hospital, 100 Bukit Timah R4, Singapore).

COMMENT. The combination of a low Apgar score and high base deficit in term infants with post-asphyxial HIE is an early predictor of mortality or major neurologic sequelae.

Serum CPK and outcome of HIE. An elevated serum CPK measured within 4 hours after birth is a sensitive indicator of brain damage in asphyxiated term infants but is of limited prognostic value in assessment of neurological outcome, according to one previous report, whereas another study showed that CPK measured in cord blood correlates with outcome after asphyxia and compares favorably with imaging studies. (Progress in Pediatric Neurology 1, 1991;pp 332).

Cranial ultrasonography and spectroscopy are of value in the prediction of neurodevelopmental outcome of HIE (see <u>Progress in Pediatric Neurology II</u>, 1994; 313-331).

MATERNAL THYROID FUNCTION AND INFANT DEVELOPMENT

The effect of maternal thyroid function in the first half of pregnancy on the neurologic development of 20 infants in the first two years of life was studied at the University of Amsterdam and Emma Children's Hospital, The Netherlands. At the age of 6 and 12 months, the mean mental developmental index (MDI) score was 16 points lower for 7 infants born to mothers with subclinical hypothyroidism compared to 6 with euthyroid mothers (P=.03 and .02, respectively). At 24 months, a mean 6 point lower MDI score was not statistically significant. One infant out of