Valproate-induced biochemical abnormalities in pregnancy, including increased excretion of a-ketoglutarate, lactate, pyruvate, and other metabolites, were corrected by treatment with multivitamin supplements given from 13 to 28 weeks' gestation. Fetal head growth, normal up to 30 weeks, was later slowed, and bitemporal narrowing was noted at birth. (Baggot PJ, Kalamarides JA, Shoemaker JD. Epilepsia April 1999;40:512-515). Metabolic abnormalities, possibly related to the teratogenic effects of valproate, can be corrected with high-dose vitamin supplementation.

Valproate-induced male infertility is reported in a previously fertile 32-year-old man with epilepsy treated with valproate monotherapy. A low and abnormal sperm count returned to normal when valproate was discontinued and felbamate was substituted. (Yerby MS, McCoy GB. Epilepsia April 1999;40:520-521).

HYPOGLYCEMIC SEIZURES AND COGNITIVE FUNCTION

The effect of hypoglycemic seizures on cognitive function was evaluated in 16 children treated for insulin-dependent diabetes mellitus at the Hospital for Sick Children, Toronto, Canada. Mean age at diagnosis was 4.5 years (range 1-11 yrs), and 9 (53%) had suffered hypoglycemic seizures. Psychological evaluation at diagnosis and after 1, 3, and 7 years found significant deteriorations in verbal IQ, vocabulary and digit span but not visuospatial skills over 7 years, primarily between 3 and 7 years. Full-scale IQ, performance IQ, and achievement test scores were unaffected. These selective declines in cognitive function, targeting working memory, were associated with hypoglycemic seizures. Children having seizures had weaker perceptuomotor, attention, memory, and executive processing skills after 7 years treatment for diabetes. (Rovet JF, Ehrlich RM. The effect of hypoglycemic seizures on cognitive function in children with diabetes: A 7-year prospective study. J Pediatr April 1999;134:503-506). (Reprints: Joanne F Rovet PhD, Department of Psychology, The Hospital for Sick Children, 555 University Ave, Toronto, Ontario, Canada M5G1X8).

COMMENT. This long-term, prospective study demonstrates the risks of neurocognitive sequelae attending insulin control of diabetes mellitus and complicated by hypoglycemic seizures in young children. Intensive therapy and over-control of blood glucose should be avoided unless closely monitored to prevent hypoglycemic seizures.

Several articles on the effects of hypoglycemia on the developing brain are included in the April issue of Journal of Pediatrics.

Duvanel CB et al, Lausanne, Switzerland, investigate the long-term effects of neonatal hypoglycemia on brain growth and psychomotor development in small-for-gestational-age preterm infants (J Pediatr 1999;134:492-498). Recurrent episodes of hypoglycemia are correlated with neurodevelopmental and physical growth deficits until 5 years of age. Without close screening of blood glucose, hypoglycemia in the neonate can be overlooked, since classical signs (apnea, seizures, jitteriness, lethargy, etc) may be absent. Rapid correction of even mild hypoglycemia in the neonate is recommended.

Hume R et al, University of Dundee, Scotland, report "Failure to detect preterm infants at risk of hypoglycemia before discharge." (J Pediatr 1999;134:499-502). Fourteen (18%) of 79 consecutive preterm infants ready for discharge were found to be hypoglycemic (<47 mg/dL) but without classical symptoms. When a newborn is identified as susceptible to hypoglycemia, feeding regimens should be frequent and regular to avoid hypoglycemic episodes.

Cowett RM, Cleveland Clinic, reviewing neonatal hypoglycemia in an editorial (J Pediatr 1999;134:389-391), concludes that the study of neonatal glucose homeostasis is in its infancy. Further investigations should better define euglycemia relative to gestational age and the optimum timing and method of measurement of blood glucose in the neonate.

Becker DJ, Ryan CM, University of Pittsburgh, (Editorial), comment on "Intensive diabetes therapy in childhood: Is it achievable? Is it desirable? Is it safe?" (J Pediatr 1999;134:392-394). These authors advocate careful monitoring of diabetes control in young children, not only in those receiving intensive therapy but also for conventional diabetes control. Mild hypoglycemia (blood glucose level of 60-65 mg/dL) in a young child may induce a transient inattention and cognitive dysfunction ("hypoglycemic absence episode"), interfering with memory and the ability to learn. Further, episodes of mild hypoglycemia may obscure the warning symptoms of subsequent attacks, increasing the risk of severe hypoglycemia. The authors caution that chronic hyperglycemia with inadequate diabetes therapy may also have detrimental effects on brain function in children, and the emphasis on dangers of intensive therapy should not neglect the benefits of close control of blood glucose levels.

NEUROCUTANEOUS SYNDROMES

LATE NEUROLOGIC COMPLICATIONS OF NEUROFIBROMATOSIS I

A hospital-based series of 158 patients with neurofibromatosis I, including 138 adults aged >18 years and 20 children, were evaluated for neurological complications in adulthood at the Services de Neurologie and Neuroradiologie, Hopital Henri Mondor, Paris, France. Neurological manifestations observed in 87 (55%) of patients (both children and adults) included headache (28 patients), hydrocephalus (7), epilepsy (5), lacunar stroke (1), white matter disease (1), intraspinal neurofibroma (3), facial palsy (1), radiculopathy (5), and polyneuropathy (2). Tumors included: optic pathway (20), meningioma (2), cerebral glioma (3), and malignant peripheral nerve sheath tumors (6). Pain related to nerve and spinal tumors occurring in 11 adults, and malignant nerve tumors were found predominantly in adults. Optic pathway tumors, cerebral gliomas, aqueductal stenosis, and spinal compression were childhood-related complications. (Creange A, Zeller J, Rostaing-Rigattieri S, et al. Neurological complications of neurofibromatosis type 1 in adulthood. Brain March 1999;122:473-481). (Respond: Dr A Creange, Service de Neurologie, Hopital Henri Mondor, 94010 Creteil Cedex, Paris, France).

COMMENT. The authors recommend follow-up with serial ophthalmological examination rather than repetitive neuroimaging in adults with neurofibromatosis 1 (NF1). This policy agrees with that of Listernick and colleagues at Children's Memorial Hospital, Chicago, who find that serial MRIs are of limited value in asymptomatic children (J Pediatr 1994;125:63-66).

In adult patients with NF1, disabling and life-threatening neurological complications, except for malignant peripheral nerve sheath tumors, are usually absent, and chronic painful symptoms related to nerve and spinal tumors are the chief neurologic complications. In contrast, children with NF1 are at greatest risk of optic pathway tumors, especially in the first 6 years of life. Tumor growth after 6 years is unusual. Other neurologic complications of NF1 in childhood include infantile spasms, CVA, and learning disabilities. For further references to NF1, see Progress in Pediatric Neurology III, PNB Publ, 1997;pp439-442; Vol II, 1994;362.