COMMENT. Studies of the cognitive effects of AEDs in children are few and largely inadequate. Future studies should be controlled and of sufficient duration to evaluate the effects of AEDs on school performance and social adjustment.

NEUROLOGY OF SIGN LANGUAGE

The neurology of American Sign Language, which originated from French signing about 200 years ago, is reviewed by a pediatric neurologist in the UK. Sign language has its primary site of organization in the dominant hemisphere. Neuroimaging studies have shown the right cerebral hemisphere is also involved in prosodic functions and in the encoding of objects. Studies of congenital and acquired deafness and dysphasia contribute to our knowledge of cerebral localization, especially since the advent of functional MRI and PET. Broca’s area of the dominant hemisphere is specialized for sign production, and the non-dominant hemisphere is involved with visual-spatial functions and processing of signing, but an interplay between both hemispheres is important in the development of sign language. In childhood epileptic aphasia (Landau-Kleffner syndrome) sign language may provide an alternative means of communication, and it does not impair the acquisition of spoken speech. The importance of sign language in the deaf is shown in the book Seeing Voices (Sacks O, 1991). Cochlear implants may increase in use in the future, but sign language remains the mainstay of communication among the deaf. (Gordon N. The neurology of sign language. Brain Dev 2004;26:146-150). (Respond: Dr Neil Gordon, Huntlywood, 3 Styal Road, Wilmslow SK9 4AE, UK).

COMMENT. Sign language comprising gestures executed in space and dependent on visual spatial orientation might be thought to involve chiefly the non-dominant right cerebral hemisphere. Both hemispheres contribute to sign language but the dominant hemisphere is the primary site of organization.

TOXIC AND VASCULAR DISORDERS

ACUTE MARIJUANA USE AND CEREBELLAR INFARCTION

Three adolescent cases of ischemic stroke involving the posterior fossa circulation and cerebellum occurred within days after the illicit use of marijuana and presented over a span of 5 years at St Louis University School of Medicine, MO. Headache, fluctuating consciousness or lethargy, visual disturbance, variable dysphagia/dysarthria, and ataxia were the common presenting manifestations. Cerebellar infarction was confirmed by biopsy (1 case) or necropsy (2 cases). Cerebellar and cerebral edema without brainstem compromise or herniation led to death in the 2 fatal cases. (Geller T, Loftis L, Brink DS. Cerebellar infarction in adolescent males associated with acute marijuana use. Pediatrics April 2004;113:e365-e370). (Reprints: Thomas Geller MD, St Louis University School of Medicine, 1465 S Grand Blvd, St Louis, MO 63104).
COMMENT. Marijuana use may cause systemic hypotension and vasospasm, leading to CNS ischemia and infarction. The cerebellum is considered more susceptible because it lacks collateral circulation. Early diagnosis of marijuana-induced stroke is necessary to permit prompt neurosurgical relief of cerebellar edema and brainstem compression.

ENVIRONMENTAL CAUSES OF CNS MALDEVELOPMENT

Developmental processes and the effects of toxic agents in the environment that alter CNS growth and maturation are reviewed by a researcher in the Department of OB/GYN, University of Rochester Medical Center, Rochester, NY. Processes discussed include: establishment of neuron numbers, migration of neurons, connections, neurotransmitter activity, receptor numbers, myelin deposition, and postnatal neurogenesis. The neuroteratological effects of toxic chemicals (eg lead, methylmercury, alcohol) and new drugs (antiepileptic drugs) have been studied in relation to prenatal and early postnatal life, but little attention is given to toxins in later childhood and adolescence. Valproic acid (VPA) exposure is linked to neural tube defects, developmental delays, and possibly autism. VPA inhibits histone deacetylase, causing a change in chromatin structure and gene transcription. Ectopias can result from exposure to radiation, methylmercury, toluene, and ethanol between the 5th and 6th week postconception (when the cortical plate is formed) or the 5th month postconception (when all cortical neurons have reached final migration). Genetic factors control migration: eg Reelin is critical for normal migration. Lack of normal Reelin protein underlies lissencephaly and cerebellar hypoplasia, and increased Reelin expression is reported in polymicrogyria. Reelin expression is thyroid hormone dependent. Any exposure that changes hormone or transmitter levels (eg psychoactive drugs, pesticides, cocaine, nicotine) can be teratogenic. Myelin deposition is impaired by malnutrition. Pruning, the trimming back of connections, occurs after age 2 years when the number of synapses in the brain reaches a peak. Normally, synapses decrease by 40% to the adult number during adolescence. Little is known about environmental factors and alteration in pruning. Autism, which is associated with above-average head size, may be an example of a deficit in pruning. (Rodier PM. Environmental causes of central nervous system maldevelopment. Pediatrics April 2004;113:1076-1083). (Reprints: Patricia M Rodier PhD, Department of OB/GYN, University of Rochester Medical Center, Rochester, NY 14642).

COMMENT. A new classification of CNS malformations based on patterns of genetic expression integrated with descriptive morphogenesis is proposed by Sarnat HB and Flores-Sarnat L (Eur J Paediatr Neurol 2001;5:57-64; see Ped Neur Briefs 2001;15:57-58). In addition to neurotoxins, infarcts acquired in fetal life or infections may disrupt development and result in heterotopias. In an overview of recent advances, Sarnat HB cites the discovery that mutations in the organizer gene Sonic Hedgehog may be involved in malformations of the embryonic neural tube (In Progress in Pediatric Neurology III, PNB Publishers, 1997;365-369). In the past 5 years several publications have described the teratogenic effects of lead, methylmercury, alcohol, nicotine, thyroid dysfunction and other environmental factors during pregnancy. Antiepileptic drugs (AEDs) pose a continuing threat to the developing fetus. Teratogenic toxicity of traditional AEDs has been investigated, but the increasing use of newer AEDs requires caution and careful evaluation in younger female patients with epilepsy.