processes depend on induction by the protein sonic hedgehog (SHH), which is mutated in some forms of familial HPE (Roessler E et al, 1996, cited by Barkovich, 2002). The finding of normal myelination in MIH supports the theory of a normal floor plate in this subtype of HPE, and separate genetic and environmental factors in etiology.

TOXIC DISORDERS

NEUROLOGIC COMPLICATIONS OF STEM CELL TRANSPLANTS

The incidence and risk factors of severe neurologic events (SNE) were evaluated in 272 consecutive children who received allogeneic or autologous hematopoietic stem cell transplantation (HSCT) for hematologic or nonhematologic diseases at the G Gaslini Children's Research Institute, Genova, Italy. Median age at transplant was 8.5 years (range, 2 months to 19.5 years); and median follow-up was 15 months (range, 2 days to 15.6 years). SNE developed after a median of 90 days (range, 5 days to 8.8 years) after HSCT in 37 children (13.6%). Seizures occurred in 19 (51%), impaired consciousness in 12 (32%), involuntary movements in 3 (8%), and miscellaneous SNE in 10. Symptoms were attributed to cyclosporine A (CSA) toxicity in 21 (54% of all SNE), to irradiation or chemotherapy injury in 7 (17%), CNS infection in 7 (17%), CNS hemorrhages in 3 (7%), and to immune-mediated complications in the remaining 2 (5%). Four children had more than one SNE. Eleven (30%) died because of neurologic complications. Risk factors for SNE included the type of HSCT (allogeneic vs autologous; p=0.002); treatment with total body irradiation (TBI) (p=0.02); development of severe acute graft-vs-host disease (GvHD >grade 2); and treatment with CSA. (Faraci M, Lanino E, Dini G et al. Severe neurologic complications after hematopoietic stem cell transplantation in children. Neurology Dec (2 of 2) 2002;59:1895-1904). (Reprints: Dr Maura Faraci, Department of Hematology?Oncology, Bone Marrow Transplant Unit, G Gaslini Children's Research Institute, Largo G Gaslini, 5, 16147 Genova, Italy).

COMMENT. Severe neurologic complications (SNE), especially seizures and impairment of consciousness, may be expected in 14% of children receiving bone marrow transplants, and a mortality rate of 8.5% is reported. Risk factors for SNE include transplant from allogeneic donors, severe acute graft vs host disease, total body irradiation, and treatment with cyclosporine A (CSA). CSA toxicity is the most common neurologic event, with an incidence of 11% among all allogeneic transplant recipients, and 17% if only unrelated hematopoietic stem cell transplant (HSCT) recipients are considered. CSA toxicity is usually reversible when CSA is discontinued. SNE caused by radio/chemotherapy, CNS infections, brain hemorrhage, or immune-mediated complications of HSCT are rare events.

COGNITIVE EFFECTS AND MECHANISMS OF LEAD TOXICITY

The effects of lead on the cognitive development of children, behavioral effects, reasons for the child's exquisite sensitivity, and the long-term prognosis of lead toxicity are reviewed at the Center for Trace Element Studies and Environmental Neurotoxicology, Staten Island, NY. The direct neurotoxic effects of lead include apoptosis, and damage to
neurotransmitter storage, mitochondria, cerebrovascular endothelial cells, astroglia and oligodendroglia. The ability of lead to substitute for calcium is a common factor in the mechanism of lead toxicity. Lead suppresses Ca-dependent release of acetylcholine, dopamine and amino acid neurotransmitters. Indirect neurotoxic effects include iron deficiency anemia, disruption of the blood-brain-barrier (BBB), disruption of thyroid hormone transport to the brain, substitution for zinc in zinc-mediated processes, and altered regulation of gene transcription.

A greater proportion of ingested lead is absorbed from the gastrointestinal tract of children than of adults, and the BBB permits more circulating lead to reach the brain of children less than 5 years of age. In contrast to IQ tests, more specific neuropsychological tests (eg attention, visuomotor integration, reaction time etc) are more sensitive to the effects of brain damage resulting from low levels of lead toxicity, and may be expected to uncover subtle cognitive signs of toxicity. Cognitive deficits due to lead are found to persist in to adulthood. Factors influencing the vulnerability of children to lead include socioeconomic status, dietary factors, genetic factors, and lead concentrations. Even with blood lead levels lower than 5 mcg/dl, there is an inverse relation between lead level and arithmetic and reading scores (Lanphear et al, 2000). The present threshold at which blood lead levels are considered to be unacceptable (10 mcg/dl) is too high. Once in the brain, lead cannot be removed by chemical chelating agents (Rogan et al, 2001), and the deleterious effects of lead on the developing brain cannot be prevented. The only prevention of adverse toxicity is prevention of lead ever entering the body. (Lidsky TI, Schneider JS. Lead neurotoxicity in children: basic mechanisms and clinical correlates. Brain January 2003;126:5-19). (Respond: Theodore I Lidsky, Center for Trace Element Studies and Environmental Neurotoxicology, NYS Institute for Basic Research in Developmental Disabilities, Staten Island, NY 10314).

COMMENT. There are accumulating research data showing that toxic effects of lead on learning and behavior occur at levels of lead much lower than the currently accepted threshold of 10 mcg/dl adopted in 1991. It may be argued that there is no ‘safe’ level of lead.

ATTENTION, LEARNING AND COMORBID DISORDERS

NEUROMOTOR INCOORDINATION PREDICTIVE OF ADHD

Quantitative and qualitative motor performance on the Maastricht Motor test was evaluated in 401 children ages 5 to 6 years (232 males, 169 females) who were tested 18 months later for attention deficit hyperactivity disorder (ADHD) and ODD/CD, in a study at the University Hospital of Maastricht, Department of Neurology, the Netherlands. Thirty-five children were diagnosed with ADHD and 26 also had ODD/CD. Two of four qualitative motor domains (dynamic balance and diadochokinesia and manual dexterity) and the total qualitative score for motor performance at 5 to 6 years of age were predictive for the diagnosis of ADHD 1 year later, but not for ODD/CD. Both gross and fine motor performance impairments were predictive, but only qualitative test performances showed significant correlations with later diagnosis of ADHD. (Kroes M, Kessels AGH, Kalff AC et al. Quality of movement as predictor of ADHD: results from a prospective population...