COMMENT. Interleukin 1 receptor antagonist may be a useful marker for predicting susceptibility to febrile convulsions. In an editorial, Lewis DB of Stanford University comments that interleukin 1 was one of the first cytokines discovered and is an endogenous pyrogen (Arch Pediatr Adolesc Med June 2002;156:529-530). Febrile seizures may be added to the list of diseases associated with IL-1Ra polymorphisms. The frequency of IL1RN allele 2 is decreased in Taiwanese children with febrile convulsions compared with controls. However, the frequency of allele 2 in the case controls was lower than that reported in US and European studies. The finding should be confirmed in other populations.

Febrile convulsions and SIDS showed no shared susceptibility in a study of siblings of children with a history of febrile convulsions compared to siblings of children who never had a febrile convulsion. The rate of SIDS was 1.64/1000 person years in the two cohorts. There was no increased risk of SIDS in siblings of children hospitalized with a febrile convulsion. (Vestergaard M et al. Arch Dis Child 2002;86:125-127). A possible etiological relation between SIDS and febrile convulsions was suggested by Sunderland R, Emery J. (Lancet 1981;2:176-178). Hyperthermia is reported to be common in SIDS (Stanton AN. Lancet 2:1199-1201).

ATTENTION DEFICIT DISORDERS

ATOMOXETINE OPEN-LABEL TRIAL IN ADHD

Atomoxetine (originally named tomoxetine), a new therapy for attention deficit hyperactivity disorder (ADHD) marketed by Eli Lilly, was compared to methylphenidate in a prospective, randomized, open-label study for 10 weeks duration, at the University of Nebraska Medical Center, Massachusetts General Hospital, Mount Sinai Medical Center, Carolinas Medical Center, and Lilly Research Laboratories. Boys aged 7 to 15 years and girls aged 7 to 9 who met DSM-IV criteria for ADHD were admitted to the study. Of 228 patients randomized, 184 received atomoxetine and 44 methylphenidate. Atomoxetine was titrated to a maximum of 1 or 2 mg/kg per day, in 2 divided doses AM and late afternoon. Methylphenidate was initiated at 5 mg one to three times daily, not to exceed 60 mg daily. Both drugs resulted in marked improvement in inattentive and hyperactive-impulsive symptoms, with no significant differences in effectiveness and toxicity. ADHD-IV Rating Scale total scores were as follows: atomoxetine baseline 39.4 [8.5], endpoint 20 [13.9]; and methylphenidate baseline 37.6 [9.7], endpoint 19.8 [16.6]. Adverse events requiring drug withdrawal occurred in 10 of 184 (5.4%) patients receiving amoxetine and 5/44 (11.4%) for methylphenidate (p=.175). Results of amoxetine treatment for ADHD are comparable to those of methylphenidate. (Kratochvil CJ, Heiligenstein JH, Dittmann R et al. Atomoxetine and methylphenidate treatment in children with ADHD: a prospective, randomized, open-label trial. J Am Acad Child Adolesc Psychiatry July 2002;41:776-784). (Reprints: Dr David Michelson, Lilly Corporate Center, DC 6026, Indianapolis, IN 46285).

COMMENT. Atomoxetine is an inhibitor of presynaptic norepinephrine transporter with minimal affinity for other noradrenergic receptors. Efficacy in children with ADHD has previously been demonstrated in 3 double-blind, placebo-controlled trials. The present study shows comparable efficacy to that of methylphenidate.

Atomoxetine is metabolized through the cytochrome P450 2D6 isoenzyme (CYP 2D6) pathway, with 2 phenotypes, one being rapid or extensive metabolizers

(90% of the US population) and the other, slow or poor metabolizers (10% of population). CYP 2D6 genotype was determined at study entry to determine which patients should receive smaller doses and those who may require higher amounts. The final dose in poor metabolizers was one third that used in extensive metabolizers (0.5 mg/kg/d versus 1.5 mg/kg/d). Although the safety and tolerability of these doses appeared to be similar in the 2 groups, further studies will be needed to define safety in the poor metabolizers. Should determination of the genotype for slow metabolizers be necessary before starting treatment, this would seriously detract from the use of atomoxetine in practice.

CHROMOSOMAL ABNORMALITIES IN ADHD

The prevalence of fragile X syndrome, velocardiofacial syndrome (VCFS), and other cytogenetic abnormalities among 100 children (64 boys) with combined type ADHD and normal intelligence was assessed at the NIMH and Georgetown University Medical Center. One girl with ADHD had a sex chromosome aneuploidy (47,XXX); 1 boy had a premutation-sized allele for fragile X and none showed the full mutation. Testing for 22q11.2 microdeletion characteristic of VCFS was negative for all subjects screened. The results were not different from those expected by chance. Prevalences exceeding 5.5% for chromosomal abnormalities, 3.7% for VCFS, and 3.6% for fragile X full mutations were excluded. In children with ADHD and normal intelligence with no clinical signs and absent family history of chromosome anomalies, testing for cytogenetic abnormalities is not warranted. (Bastain TM, Lewczyk CM, Sharp WS et al. Cytogenetic abnormalities in attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry July 2002;41:806-810). (Reprints: Dr F Xavier Castellanos, NYU Child Study Center, 577 First Ave, New York, NY 10016).

COMMENT. In the absence of clinical indications, including developmental delay, physical signs, or positive family history, testing for chromosomal abnormalities, VCFS, or fragile X is not indicated in children with ADHD of normal intelligence.

Cigarette smoking in adolescents with ADHD. Cigarette smoking was associated with family and peer smoking and with clinically significant ADHD inattention symptoms in a confidential self-report survey of 1066 tenth-grade students in five public high schools conducted at the Lombardi Cancer Center, Washington, DC. ADHD inattentive type is a significant risk factor for cigarette smoking in adolescents. (Tercyak KP et al. J Am Acad Child Adolesc Psychiatry July 2002;41:799-805).

Altered cortical activity in ADHD during attentional load task is demonstrated by quantitative electroencephalography performed with eyes open and during Continuous Performance Task. Increased slow activity over frontal areas and decreased fast cortical activity were observed, indicating a different arousal pattern and possible delay in cortical maturation. (El-Sayed E, et al. J Am Acad Child Adolesc Psychiatry July 2002;41:811-819).

LEARNING DISABILITIES

PATTERN OF LEARNING DISABILITIES IN ELBW CHILDREN

The prevalence and pattern of specific learning disabilities (LD) in neurologically normal children with extremely low birth weight (ELBW) (<800 g)