ATTENTION DEFICIT DISORDERS

PRETERM BIRTH AND ADHD IN SCHOOL CHILDREN

Researchers at Karolinska Institutet, Sachs Children's Hospital, Stockholm, and Uppsala and Stockholm Universities, Sweden, analyzed the effect of moderate and extreme preterm birth on the risk for ADHD in school age children who have survived from NICUs, and allowing for genetic, perinatal, and socioeconomic confounders. Children in a Swedish national register born between 1987 and 2000 were followed up for ADHD medication in 2006 at age 6 to 19 years. Genetic confounding was estimated in a subpopulation of offspring of mothers who had given birth to preterm (<34 weeks) as well as term infants. In a total of 7,506 children in the study population with a record of ADHD medication, corresponding to 1.05% of the boys and 0.29% of girls, the most commonly prescribed drug was methylphenidate (87.8%), followed by atomoxetine (9.2%) and amphetamine (3%).

The odds ratios for ADHD medication were 2.1 for 23 to 28 weeks gestation, 1.6 for 29 to 32 weeks, 1.4 for 33 to 34 weeks, 1.3 for 35 to 36 weeks, and 1.1 for 37 to 38 weeks. The odds ratios for within-mother-between-pregnancy analysis were similar, excluding a genetic confounder effect. The effect of moderate (week 33 to 36) preterm birth on ADHD medication was higher in mothers with a low education ($p<0.01$). Low Apgar score had a marginal effect on the risk of ADHD medication and did not modify the effect of preterm birth. (Lindstrom K, Lindblad F, Hjern A. Preterm birth and attention-deficit/hyperactivity disorder in schoolchildren. **Pediatrics** May 2011;127(5):858-865). (Respond: Anders Hjern MD PhD, Centre for Health Equity Studies, Karolinska Institutet/Stockholm University, 106 91 Stockholm, Sweden. E-mail: anders.hjern@chess.su.se).

COMMENT. An association of preterm birth with ADHD is related to degree of immaturity and exists with moderate in addition to extreme preterm birth. The main effect is not explained by genetic, perinatal, or socioeconomic confounding, but social adversity, as expressed by low maternal education, may modify the risk of ADHD in moderately preterm births.

Low Apgar scores and increased risk of ADHD is reported in a nationwide population-based cohort study of singletons born in Denmark from 1988 to 2001 (Jiong L et al. **J Pediatr** May 2011;158:775-779). Compared with children with Apgar scores of 9 or 10 at 5 minutes, the risk of ADHD was 75% higher in children with scores of 1 to 4 and 63% higher for those with Apgar scores of 5 to 6 ($p<0.001$). In this Danish study, Apgar scores are inversely associated with risk of ADHD. Low Apgar and ADHD may have a common cause or low Apgar may reflect one causal factor for ADHD.

Genetic factor in etiology of ADHD is reviewed in a report from Radboud University Nijmegen Medical Centre, the Netherlands, and Massachusetts General Hospital, Boston. (Poelmans G et al. **Am J Psychiatry** 2011;168:365-377). A bioinformatics pathway analysis revealed 45 of 85 ADHD candidate genes that fit into a neurodevelopmental network involved in neurite outgrowth. The authors propose that since stimulants are

known to regulate neurite outgrowth and network proteins, this study may be useful in the development of pharmacological therapy for ADHD.

CONTROLLED STUDY OF ATOMOXETINE IN ADHD

Researchers at the Department of Psychiatry, University of Nebraska Medical Center, Omaha, and other centers in the US conducted an 8-week, double-blind, placebo-controlled study of atomoxetine for treatment of ADHD in 101 children 5- and 6-years of age and older. The dose was titrated to a maximum of 1.8 mg/kg per day (mean final dose 1.4 mg/kg). Parent and teacher ADHD-IV Rating Scale scores were significantly decreased with atomoxetine (P=.009 and .02, respectively). Clinical Global Impression-Improvement Scale-criteria indicating much or very much improved were met by 40% of children treated with atomoxetine compared with 22% of children on placebo (Not significant, p=0.1). Side-effects significantly more common with atomoxetine than placebo were decreased appetite, gastrointestinal upset, and sedation. Laboratory tests including electrocardiograms and mean blood pressure and weight showed no clinically significant changes. Despite benefits, 62% of children in the atomoxetine group remained significantly impaired at the end of the study. Some children demonstrated a robust response to atomoxetine whereas in others, the response was more attenuated. (Kratochvil CJ, Vaughan BS, Stoner JA, et al. A double-blind, placebo-controlled study of atomoxetine in young children with ADHD. **Pediatrics** April 2011;127:e862-e868). (Respond: Christopher J Kratochvil MD, Nebraska Medical Center, Omaha, NE 68198. E-mail: ckratoch@unmc.edu).

COMMENT. Atomoxetine in children under 6 years of age is off-label. In this study, the efficacy and tolerability of atomoxetine for 5- and 6-year-old children is similar to that seen in older children. Even with the maximum FDA approved dose (1.4 mg/kg per day), combined with psychoeducational intervention, only 40% of atomoxetine-treated subjects were "much" or "very much" improved at study end. The authors acknowledge that comorbid ODD may have influenced the ADHD ratings in the young age group, and further longer treatment studies should be performed.

DEMYELINATING DISORDERS

RISK FACTORS FOR MULTIPLE SCLEROSIS IN CHILDREN

Risk factors for multiple sclerosis in 302 children presenting with CNS demyelination to health-care facilities in Canada included HLA-DRB1*15 alleles, previous infection with Epstein-Barr virus, and low serum 25-hydroxyvitamin D. MRI brain lesions, and CSF oligoclonal bands are probable precursors of multiple sclerosis (MS). Children with a normal MRI are likely to have a monophasic illness. At follow-up, 63 (21%) were diagnosed with MS after a median of 127 days. (Banwell B, Bar-Or A, Arnold DA, et al. Clinical, environmental, and genetic determinants of multiple sclerosis in children with acute demyelination. **Lancet Neurol** May 2011;10:436-445). (Response: Dr Banwell, Hospital for Sick Children, Toronto. E-mail: brenda.banwell@sickkids.ca).