N Engl J Med Nov 1, 2011;10:1056-1064. (Lead author: Dr WO Cooper, Division of General Pediatrics, Vanderbilt University, Nashville, TN).

COMMENT. Confounders in the above study unaccounted for include the unapproved use of stimulants and the uncertainty of diagnosis of ADHD in children younger than 6 years. Although some studies have failed to demonstrate an increased risk of stimulant-associated serious cardiovascular events, one study provides convincing evidence and reason for concern. In a case-control study of mortality data among children and adolescents ages 7 through 19 years, 10 (1.8%) of 564 cases of sudden unexplained death occurred in subjects taking stimulants, whereas only 2 (0.4%) of 564 who died in motor vehicle accidents had taken stimulants. (Gould MS et al. **Am J Psychiatry** 2009;166(9):992-1001).

The need for cardiovascular risk screening before starting stimulant medication in children with ADHD is controversial. The American Heart Association initially advised routine pretreatment ECG (with later modification) whereas the American Academy of Pediatrics considers routine ECG to be unnecessary. Cardiac history and examination are recommended, and ECG and cardiac consultation only if clinically indicated. (Perrin JM et al. **Pediatrics** 2008;12;451-453). Pretreatment ECG and/or cardiac consultation indications are suggested as follows: heart murmur, high blood pressure, palpitations, or syncope, and personal or family history of early heart disease. Involvement in competitive sports might also be added as an indication for pretreatment ECG in adolescents. The cardiologist may clear the child for stimulant medication, but the treating physician makes the final decision to treat or not to treat in each individual case.

EFFECT OF METHYLPHENIDATE ON PUBERTY IN ANIMALS

Researchers at the National Institutes of Health, Bethesda, MD, studying the genetic and behavioral effects of methylphenidate (MPH) in juvenile male rhesus monkeys, observed after 14 mo of treatment a delay in puberty with impaired testicular descent and reduced testicular volume. Testicular volume was significantly reduced ($P<0.05$) at months 15 to 19 and month 27 after high oral doses 12.5 mg/kg twice a day. Significantly lower serum testosterone levels were detected in both the low 2.5 mg/kg dose ($P=0.0017$) and high 12.5 mg/kg dose ($P=0.0011$) animals through month 33 of treatment. Serum inhibin B levels increased in low-dose animals ($P=0.0328$) but differences between groups disappeared by the end of the study. The findings indicate that MPH administration, beginning before puberty, and with clinically relevant blood levels of the drug, impaired pubertal testicular development until -5 years of age. MPH started before puberty either delayed initiation of the onset of puberty or reduced the rate of testicular and pubertal development.

Deficits in testicular volume and testicular secretion resolved over the 40-month observation period, which suggests that the effect of MPH on puberty is not permanent. (Mattison DR, Plant TM, Lin HM, et al. Pubertal delay in male nonhuman primates (Macaca mulatta) treated with methylphenidate. **Proc Natl Acad Sci** USA Sep 27, 2011;108(39):16301-6. Epub 2011 Sep 19)(Lab Reports. ADHD drug may affect puberty. **JAMA** Nov 2, 2011;306(17):1853).

COMMENT. Findings of this type in laboratory animals are disturbing and require confirmation. Pending further studies, the clinician should be aware of a possible effect of stimulants on pubertal development, and management of ADHD patients with MPH and other stimulants should be monitored carefully, especially in younger children.

SEIZURE DISORDERS

COMPLETE REMISSION IN CHILDHOOD-ONSET EPILEPSY

Researchers at Children's Memorial Hospital, Chicago, IL, and Yale School of Medicine, New Haven, CT determined the probability of attaining complete remission of nonsyndromic epilepsy in a community-based cohort of 347 children with onset of epilepsy between ages of 1 month and 16 years (average, 5.5 years). None met criteria for well-defined electroclinical syndromes. The average length of follow-up was 14.4 years (maximum 17.9 years), and families were contacted frequently (3-4 times per year). Complete remission was defined as 5 years seizure-free and medication-free. Of 294 (85%) children followed prospectively for >10 years, 170 (58%) achieved complete remission, and 10 (6%) of these relapsed. Another 46 had a 5-year seizure-free, but not drug-free remission. Relapses occurred 0.4 to 7.5 years after attaining complete remission; and the probability of relapse at 1, 5, and 8 years after remission was 1%, 5%, and 8%. The probability of achieving complete remission by 5, 8, 10, and 15 years after diagnosis of epilepsy was 3%, 31%, 46%, and 60%. The average duration of follow-up after attaining complete remission was 6.4 years (range, 0.2 to 11.3). Relapses were marginally associated with underlying cause (0.06). MRIs were obtained in 262 (89%) of participants and were abnormal in 55 (21%), of whom 18 (33%) achieved complete remission. Groups with complete remission for >10 years were distinguished by seizure outcome at 2 years ($p<0.0001$) and by underlying cause ($p<0.0001$). Good early seizure outcomes and epilepsy of unknown cause had a higher likelihood of complete remission whereas status epilepticus and older age at onset were associated with a poorer outcome. (Berg AT, Testa FM, Levy SR. Complete remission in nonsyndromic childhood-onset epilepsy. **Ann Neurol** (October 2011;70(10):566-573). (Respond: Anne T Berg PhD, Children's Memorial Hospital, Northwestern University, Chicago, IL 60614. E-mail: atberg@childrensmemorial.org).

COMMENT. We rarely speak of cure of epilepsy, an outcome desired by both patient and physician. This well-defined study provides evidence of complete remission or cure of seizures in more than 50% of young people with focal or generalized nonsyndromic epilepsy. A medication-free outcome may be predicted by early seizure control and an epilepsy of unknown cause. Negative imaging and metabolic studies performed early have a role in the identification of epilepsies amenable to complete remission and cure.