Both in utero tobacco exposure and serum lead levels appear to be associated with ADHD.

Data from the National Health and Nutrition Examination Survey (NHANES) cohort was used to examine associations between prenatal tobacco exposure, current lead exposure, and ADHD in a nationally representative group of children. Between 2001 and 2004, nearly 4000 children aged 8–15 years participated in the NHANES study, including 222 (9%) who met DSM-IV criteria for ADHD or reported using ADHD medications. Maternal smoking during pregnancy was self- or caregiver-reported and serum lead levels, divided into tertiles, were used to determine current lead exposure. Odds ratios* (ORs) for ADHD were 2.4 for children whose mothers smoked during pregnancy, compared with those who did not, and 2.3 for the highest vs lowest lead levels. The combination of prenatal tobacco exposure and current high lead level was associated with an 8-fold increase in ADHD diagnosis. Children with both risk factors comprised <8% of the population, but accounted for nearly 25% of ADHD cases.

Froehlich T, Lanphear B, Auinger P, Hornung R, et al: Association of tobacco and lead exposures with attention-deficit/hyperactivity disorder. Pediatrics 2009;124:e1054–e1063. From the University of Cincinnati College of Medicine, Ohio; and other institutions. Funded by an Academic Pediatrics Association Young Investigator Grant; and other sources. The authors disclosed they have no commercial relationships that might pose conflicts of interest.

*Reference Guide Item.

Aripiprazole Improved Mania

Current guidelines for pediatric bipolar mania recommend either a mood stabilizer or atypical antipsychotic as first-line treatment. The study presented below is one upon which the 2008 approval of aripiprazole (Abilify) for bipolar disorder in patients aged 10–17 years was based.

Methods: Participants in the manufacturer-sponsored multicenter controlled trial were 296 patients aged 10–17 years (mean, 13 years; 78% were aged >11 years) experiencing a bipolar I manic or mixed episode. All had a Young Mania Rating Scale (YMRS) score of ≥20. After a washout, patients were randomized to 4 weeks of double-blind placebo or aripiprazole at 10 or 30 mg/day.

Continued
**Results:** Both aripiprazole dosages produced significantly greater declines than placebo in YMRS score (p<0.0001). After 4 weeks of treatment YMRS scores decreased from a baseline mean of 30 to 16 with the lower aripiprazole dose, 13 with the higher dose, and 23 with placebo. Overall severity of bipolar illness also decreased significantly with both aripiprazole doses. Response criteria (≥50% YMRS reduction) were met by 45% of patients treated with 10 mg/day aripiprazole, 64% of those treated with 30 mg/day aripiprazole, and 26% of the placebo group. Remission (YMRS score ≤12 and Clinical Global Impression-Severity* score of 1 or 2) rates were 25%, 48%, and 5%, respectively.

Serious adverse events included seizure, aggression, oppositional defiant symptoms, suicidal ideation, and respiratory arrest; none were judged related to medication. One patient had an accidental aripiprazole overdose. Reasons for stopping 10 mg aripiprazole included fatigue and sedation in 2 patients each, and akathisia, aggression, and suicidal ideation in 1 patient each. In the 30 mg group, 3 patients withdrew because of extrapyramidal symptoms, 2 for clinical worsening of bipolar disorder, and 1 each for vomiting, dystonia, and somnolence. Heart rate, blood pressure, and ECG parameters were not significantly altered. The most frequently reported adverse effects were extrapyramidal symptoms and somnolence and they appeared to be dose related. No clinically meaningful metabolic effects occurred, but the study duration was short.

**Discussion:** This study provides additional support for the use of atypical antipsychotics and particularly aripiprazole in pediatric bipolar disorder, but comparative efficacy among the agents will need to be evaluated in head-to-head trials.

**Study Rating—17 (100%):** This study met all criteria for a randomized controlled trial.

Findling R, Nyilas M, Forbes R, McQuade R, et al: Acute treatment of pediatric bipolar I disorder, manic or mixed episode, with aripiprazole: a randomized, double-blind, placebo-controlled study. *Journal of Clinical Psychiatry* 2009; 70 (October):1441–1451. From Case Western Reserve University, Cleveland, Ohio; and other institutions. **Funded by Otsuka Pharmaceutical Co. Two study authors disclosed commercial relationships that might pose conflicts of interest; all other authors are employed by Otsuka, manufacturer of Abilify.**

*Reference Guide Item.

**Can Repeat Sexual Offenses be Predicted?**

According to a review in *Behavioral Sciences and the Law,* "measures that have demonstrated some use in predicting general violence among adolescents do not appear profitable for predicting sexual recidivism, even in adolescents with a history of sex offenses."

Risk assessment in young patients is complicated by developmental changes and maturation occurring during adolescence. Several risk assessment measures specific to sexual recidivism such as the Juvenile Sex Offender Assessment Protocol–II and the Estimate of Risk of Adolescent Sex Offender Recidivism have been developed, but none have been validated and the predictive value is limited. Peer associations, family dynamics, and community involvement should be factored into the assessment as these can have protective or aggravating effects. In addition, the patient’s attitude about the offense and the presence of substance use and other mental health and developmental issues must also be considered. As these factors can change, risk prediction can only be valid for only a short period of time (about 6 months).

Although predicting which adolescents are likely to repeat sexual offenses is problematic, a recent as yet unpublished study (in press) concluded that recidivism rates in juvenile sex offenders appear to be low. Other studies have shown treatment can reduce the risks.

PANDAS: New Information

The evidence to support pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS) comprises a case series and a case-control study.1 The results of a new case-control study reported in Neurology do not support the association.2

Methods: Records were retrieved from a computerized U.K. medical database for patients aged 2–25 years between 1995 and 2007 who were treated at 1 of 330 medical practices. Case patients (n=255) were those who had received a diagnosis of obsessive compulsive disorder (OCD) or Tourette's syndrome (TS)/tics, and each was matched with up to 20 control subjects without a neuropsychiatric disorder. Occurrence of clinically diagnosed streptococcal infection in the 2 years before the neuropsychiatric diagnosis was compared.

Results: Of the 225 case patients, 33 (15%) had a strep infection in the 2 years prior to diagnosis. The infection rate in the control group was also 15%, indicating no association between OCD or TS/tics and infection. The association was confirmed in 1 subgroup analysis. OCD was significantly associated with possible streptococcal infection not treated with antibiotics in the prior 2 years (odds ratio,* 2.59; p=0.02). However, given the number of analyses conducted this may have been due to a type I statistical error.

Discussion: These results contradict those of the previous case-control study conducted in the U.S. The present population was substantially larger, thus increasing the statistical power of the comparison, and the study included a longer "exposure" period for infection. All information, including diagnosis of TS, OCD, and tics, was gathered from general practitioner records, and patients who had been referred for specialist diagnosis would not have been identified. However, the rate of infection in the control group was similar to that of the previous study.


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Clinical Global Impression Severity (CGI-S) Scale: A 7-point rating of the severity of illness. A score of 1 corresponds to a rating of normal; 2=borderline mentally ill; 3=mildly ill; 4=moderately ill; 5=markedly ill; 6=severely ill; 7=extremely ill.

Odds Ratio: A comparison of the probability of an event in two groups. An odds ratio of 1 implies that the event is equally likely in both groups. An odds ratio greater than 1 indicates that the event is more likely to occur in that group than in the comparison group.
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