JOURNAL WATCH
PEDIATRICS & ADOLESCENT MEDICINE

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Bee stings in children: a 20-year follow-up study ►

The natural history of bee sting allergy has important therapeutic and prognostic implications. Investigators in Baltimore followed 512 patients who had been diagnosed with insect sting allergy 10 to 20 years earlier (median age at diagnosis, 8 years). A total of 402 had systemic reactions; 163 of these patients received venom immunotherapy, and 239 did not. The remaining 110 children had large local reactions and did not receive therapy.

During follow-up, the following events occurred:

- In the local-reaction cohort, 44 patients were stung again, and 3 had systemic reactions, although none were severe (e.g., marked respiratory distress or hypotension).
- In the systemic-reaction cohort, 250 patients had initially experienced mild systemic reactions (involvement confined to the skin). Among those who *did not* receive immunotherapy, 13% who were stung again had systemic reactions (none severe). In contrast, among patients who *did* receive immunotherapy, none who were stung again had systemic reactions.
- In the systemic-reaction cohort, 152 patients had initially experienced moderate-to-severe systemic reactions; these patients had the highest risk for future systemic reactions. Among those who *did not* receive immunotherapy, 32% who were stung again had systemic reactions. In contrast, among those who *did* receive immunotherapy, only 5% who were stung again had systemic reactions.

Comment ► These data provide guidance on whom to refer for venom immunotherapy. Therapy is not necessary for children with large local reactions or mild systemic reactions but *is* warranted for children with moderate-to-severe systemic reactions.

Howard Bauchner, MD
Published in *Journal Watch Pediatrics and Adolescent Medicine*
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▲ **Golden DBK** *et al.* Outcomes of allergy to insect stings in children, with and without venom immunotherapy. *N Engl J Med* 2004;**351**:668–74.

▲ **Gruchalla RS.** Immunotherapy in allergy to insect stings in children. *N Engl J Med* 2004;**351**:707–9.

Statin therapy is effective and safe for children with hypercholesterolemia ►

Statins are commonly used to treat adults with hypercholesterolemia, but the safety and efficacy of these drugs for children are not well studied. Investigators placed 214 children (mean age, 13 years) with familial hypercholesterolemia (LDL-C ⩾155 mg/dL and demonstration of the LDL-receptor-gene mutation) on a regimen of dietary fat restriction and physical activity. The children were then randomized to receive placebo or pravastatin (10 or 20 mg/day) for 2 years.

At study end, declines in total and LDL cholesterol levels were significantly greater among pravastatin recipients than among placebo recipients. Echosonographic examination of carotid intima-media thickness showed that treated children had a trend toward regressed thickness, whereas children receiving placebo had a trend toward progressed thickness. Children in both groups had similar safety profiles: There were no differences in intellectual, pubertal, or physical development at the end of the study. Results of endocrine hormone studies and liver function studies were also similar in treated and untreated children.

Comment ► Results of this elegant, well-controlled study show that statins are effective and well tolerated in children with genetic hypercholesterolemia. The findings also show that a low-fat diet, exercise, and statin therapy can benefit the carotid vascular wall during childhood. If, as the poet says, ''the child is father to the man,'' this news suggests an improved health outlook in adulthood for these patients.

F. Bruder Stapleton, MD
Published in *Journal Watch Pediatrics and Adolescent Medicine*
August 30, 2004

▲ **Wiegman A** *et al.* Efficacy and safety of statin therapy in children with familial hypercholesterolemia: A randomized controlled trial. *JAMA* 2004;**292**:331–7.

Pertussis: still with us, but easier to treat ►

Cases of pertussis, and occasional outbreaks, continue to occur despite widespread vaccination. Erythromycin estolate (EE) has been considered the gold standard for both therapy and prophylaxis. It is widely assumed that azithromycin (AZ) would work as well, but comparative studies have been lacking. These authors report a large, drug-company-sponsored, randomized, controlled trial of EE (40 mg/kg/day given in 3 divided doses for 10 days) versus AZ (10 mg/kg on day 1, and 5 mg/kg on days 2 through 5) for the treatment of clinical pertussis in 477 patients aged 6 months to 16 years.

Efficacy, as determined by eradication of *Bordetella pertussis* in culture-positive patients, was 100% in those who returned for follow-up culture (53 in each group). Side effects were measured in all patients who received at least one dose of medication, including those who did not have proven pertussis. Gastrointestinal adverse effects were more common in those treated with EE (41.2% vs. 18.8%). Adherence to the regimen was 90% in the AZ group but only 55% in the EE group.

Comment ► These results clearly demonstrate that AZ is as effective as and better tolerated than EE for the treatment of pertussis. Though the study does not address the efficacy of AZ as prophylaxis for contacts, its use seems reasonable for this indication as well. Another important finding is that pertussis syndrome occurred in patients who were, on average, 6 years old and who had received an average of four prior vaccinations. This reminds us that pertussis should be considered in patients with paroxysmal cough and post-tussive emesis, even if they have been immunized.

Peggy Sue Weintrub, MD
Published in *Journal Watch Pediatrics and Adolescent Medicine*
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▲ **Langley JM** *et al.* Azithromycin is as effective as and better tolerated than erythromycin estolate for the treatment of pertussis. *Pediatrics* 2004; **114**:e96-101.

Fluoxetine plus CBT effective for major depressive disorder in adolescents ►

Major depressive disorder (MDD) is a significant threat to adolescents and a therapeutic challenge. This national, randomized study evaluated four treatments (medication management with fluoxetine [10 to 40 mg/day], fluoxetine plus cognitive-behavioral therapy [CBT], CBT alone, and placebo) in a volunteer sample of 439 adolescents with moderate-to-severe MDD (average depressive episode, 72 weeks). CBT consisted of 15 treatment sessions, including family sessions. Adolescents at high risk for suicide were excluded from the study.

Fluoxetine plus CBT significantly improved depression ratings compared with other therapies: 71% of the fluoxetine-plus-CBT group had a measurable improvement by the 12-week endpoint, compared with 61% of the fluoxetine-alone group, 43% of the CBT-alone group, and 35% of the placebo group. Suicidal ideation declined in all treatment groups; fluoxetine plus CBT was superior to the other therapies in reducing such ideation. Seven patients attempted suicide; the number of attempts did not differ by treatment group.

Comment ► In this study, MDD was treated successfully within 12 weeks with fluoxetine (the only SSRI approved for children and adolescents), with the best outcome occurring when drug treatment was coupled with CBT. Children treated for MDD must be carefully monitored. It is sobering to note that 29% of these adolescents did not respond to the ''best'' therapy. Treating MDD in adolescents is serious business, and the availability of experienced mental health professionals for this important group is woefully deficient.

F. Bruder Stapleton, MD
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▲ **March J** *et al.* Fluoxetine, cognitive-behavioral therapy, and their combination for adolescents with depression: Treatment for Adolescents With Depression Study (TADS) randomized controlled trial. *JAMA* 2004;**292**:807–20.

▲ **Glass RM**. Treatment of adolescents with major depression: Contributions of a major trial. *JAMA* 2004;**292**:861–3.

Febrile seizures after MMR do not increase risk for epilepsy ►

The safety of the MMR vaccine has been a subject of great public concern. In a population-based study of all children born in Denmark from 1991 through 1998, researchers evaluated the risk for and outcomes of febrile seizures in children vaccinated at 15 months of age. The vaccine was identical to the vaccine used in the U.S. at that time.

In this cohort of 537,171 children, 439,251 were vaccinated, and 17,986 had at least one febrile seizure. The overall risk ratio for febrile seizure during the 2 weeks following vaccination was 2.75 (2.45 in the first week and 3.17 in the second). After the first 2 weeks, vaccinated children had a risk similar to that of unvaccinated children. Among children who had postvaccination febrile seizures, no subgroups based on perinatal or socioeconomic factors were found to have significantly higher RRs.

The cumulative incidence of postvaccination febrile seizures in all vaccinated children was 2.46 per 1000; it was highest in children with a prior febrile seizure (30.97 seizures per 1000) and in children whose siblings had a history of febrile seizure (6.6 seizures per 1000). During 105 months of follow-up, children who had had a febrile seizure in the 2 weeks after vaccination had a 19% greater risk for further seizures but no increased risk for epilepsy.

Comment ► Parents can be reassured that although the rate of febrile seizures rose moderately in the first 2 weeks after MMR vaccination, there was no increased risk for epilepsy.

F. Bruder Stapleton, MD
Published in *Journal Watch Pediatrics and Adolescent Medicine* August 30, 2004

▲ **Vestergaard M** *et al.* MMR vaccination and febrile seizures: Evaluation of susceptible subgroups and long-term prognosis. *JAMA* 2004;**292**:351–7.