# Tips from Other Journals



Tips from Other Journals are written by the medical editors of *American Family Physician.*

The trade names of drugs listed in Tips from Other Journals are based on what is currently available and not necessarily the brand of drug that was used in the study being discussed.

## Maternal Influenza Vaccine Reduces Hospitalization in Infants

**Background:** Inactivated influenza vaccine is recommended for all pregnant women and children, except for infants younger than six months for whom the vaccine is poorly immunogenic. Maternal vaccination during pregnancy could possibly protect infants through the cross-placental transport of immunoglobulin G antibodies to the fetus, and through the transfer of immunoglobulin A to infants via breast milk. Benowitz and colleagues conducted a matched case-control study of infants to assess the effectiveness of influenza vaccine given to pregnant women in decreasing hospitalizations for influenza among their infants.

**The Study:** Infants younger than 12 months who were hospitalized for influenza that was confirmed by direct fluorescent antibody testing were eligible. Case infants were matched to control infants (i.e., infants hospitalized for reasons other than influenza). Mothers were considered to be vaccinated against influenza if they had written documentation of receiving the vaccine during pregnancy. Women vaccinated within 14 days of delivery were excluded. A matched odds ratio was calculated for mothers of case infants, compared with mothers of matched control infants.

**Results:** A total of 113 case infants were matched to 192 control infants. Among infants younger than six months, two of 91 case infants (2.2 percent) had mothers who were vaccinated during pregnancy, compared with 31 of 156 control infants (19.9 percent). Overall, vaccination during pregnancy was 90.7 percent effective in preventing influenza hospitalization among infants younger than six months ($P = .001$). This increased to 91.5 percent effectiveness ($P = .001$) after adjusting for potential confounders. No statistical benefit was seen among infants six to 12 months of age regarding hospitalization rates, although the study was not adequately powered to detect differences in this age range.

**Conclusion:** Inactivated influenza vaccine given to pregnant women is highly effective in preventing hospitalization from influenza among their infants who are younger than six months. This strategy can protect young infants at risk of influenza for whom no vaccine is currently available.

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**Source:** Benowitz I, et al. Influenza vaccine given to pregnant women reduces hospitalization due to influenza in their infants. *Clin Infect Dis.* December 15, 2010;51(12):1355-1361.

## Do Antibiotics Improve the Treatment of Acute Otitis Media?

**Background:** Acute otitis media is the most common childhood infection for which antibiotics are prescribed in the United States. In children, treating otitis media, which includes both acute otitis media and otitis media with effusion, costs an estimated $2 billion annually. A 2001 evidence report from the Agency for Healthcare Research and Quality focused on the management of uncomplicated acute otitis media in children, and concluded that treatment with ampicillin or amoxicillin reduced clinical failure rates when compared with observation. However, the microbiology of acute otitis media has shifted following widespread use of the 7-valent pneumococcal conjugate vaccine (PCV7) in children. Shekelle and colleagues systematically reviewed evidence on the accuracy of diagnosis, the effect of PCV7, and the effectiveness of different treatments for acute otitis media.

**The Study:** The authors conducted a meta-analysis of six key questions that addressed the following topics: accuracy in the diagnosis of uncomplicated acute otitis media; effect of PCV7 immunization on acute otitis media microbial epidemiology; effectiveness of treatment options for uncomplicated acute otitis media; effectiveness of treatment options for recurrent otitis

media; treatment outcomes for specific subpopulations; and the adverse effects of available treatment options. Articles included in the evidence report were found by a literature search of PubMed, Cochrane Central Register of Controlled Trials, Cochrane Databases of Systematic Reviews, Web of Science, and the Science Citation Index using specific search terms and strategies. Systematic reviews, randomized controlled trials, controlled clinical trials, and observational studies (only when more rigorous studies were insufficient to answer the study question) were included. Two pediatricians who had been trained to critically analyze scientific literature independently reviewed each study for inclusion in the evidence report based on whether it reported original data (or was a systematic review) and if it answered one of the report questions.

**Results:** Each study defined clinical success by one of the following findings: absence of symptoms, improvement in acute symptoms, absence of otorrhea, resolution of otoscopic findings, or cumulative clinical resolution. The random effects pooled rate difference for clinical success was calculated for each comparison by looking at clinical outcomes by day 14 or day 16. All but one study were of moderate quality; therefore, further high-quality research will likely change the confidence in the estimated difference and the calculated estimated difference itself.

*Ampicillin or amoxicillin versus placebo.* Seven studies reported a pooled difference for clinical success by day 14 of 12 percent (number needed to treat [NNT] = 9).

*Ampicillin or amoxicillin versus ceftriaxone (Rocephin; single dose).* Four studies estimated the pooled difference in clinical success by day 14 to be 0 percent; no advantage or equivalence of antibiotics could be established.

*Amoxicillin/clavulanate (Augmentin; seven to 10 days) versus ceftriaxone (single dose).* Five studies determined that the pooled difference for clinical success by day 16 was 3 percent in the amoxicillin/clavulanate group; neither antibiotic has a notable advantage.

*Amoxicillin/clavulanate (seven to 10 days) versus azithromycin (Zithromax; five days or less).* Nine studies reported a pooled difference for clinical success by day 14 of –0.3 percent. Neither antibiotic has been established to be superior, and equivalence could not be determined.

*Azithromycin (less than five days) versus cefaclor (seven to 10 days).* Three studies estimated the pooled difference for clinical success by day 14 to be –0.7 percent. The two antibiotic treatments were equally effective and, because the quality of evidence was high, further high-quality studies are unlikely to change the results.

*Antibiotics versus wait-and-see and prescription-to-hold.* Four studies compared various antibiotics with delayed treatment approaches. Two studies of amoxicillin compared with wait-and-see and prescription-to-hold found a clinical success rate difference of 15 and 16 percent, respectively, demonstrating that immediate treatment has a higher rate of clinical success than the delayed treatment approach. However, the other two studies were inconclusive because otalgia and fever were improved by the trials' end points, regardless of antibiotic use. In all four studies, compliance in the prescribed antibiotic groups was high; additionally, up to 38 percent of patients in the delayed treatment groups ultimately received antibiotics.

*Short- versus long-duration treatment.* One study comparing a five-day and a 10-day course of antibiotics concluded that the treatment lengths were equally effective. However, longer antibiotic use was associated with less risk of signs and symptoms, relapse, or reinfection during days 8 to 19 (NNT = 17).

**Conclusion:** The authors conclude that treatment of otitis media with ampicillin or amoxicillin demonstrates greater clinical success rates than placebo. The results are mixed about whether immediate treatment improves clinical success rates compared with delayed treatment strategies. In this review, short- and long-duration courses of antibiotics were essentially equally effective. No difference in clinical success was reported for ampicillin or amoxicillin versus single-dose ceftriaxone, amoxicillin/clavulanate versus single-dose ceftriaxone, or amoxicillin/clavulanate versus short-duration azithromycin. Additionally, treatment with azithromycin was found to be equivalent to treatment with cefaclor. Future high-quality research will likely change the estimated difference or confidence in the estimated difference for the studied comparisons.

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**Source:** Shekelle PG, et al. Management of acute otitis media: update. Evidence Report/Technology Assessment No. 198. Rockville, Md.: Agency for Healthcare Research and Quality. November 2010. AHRQ Publication No. 11-E004.

## Is Echinacea an Effective Treatment for the Common Cold?

**Background:** Echinacea is believed to enhance immune response by macrophage activation and cytokine expression; however, its effectiveness at treating the common cold remains debatable. Although early industry-sponsored trials reported statistically significant benefits, subsequent randomized trials, reviews, and meta-analyses have yielded conflicting results. Barrett and colleagues conducted a randomized controlled trial to determine the benefits of echinacea as a treatment for the common cold. ▶

**The Study:** A total of 719 patients with cold symptoms were randomized to one of four study groups: no treatment, placebo (blinded), echinacea (blinded), or echinacea (unblinded). The type of echinacea used was a root-based, alkamide-rich preparation containing the equivalent of 675 mg of *Echinacea purpurea* root and 600 mg of *Echinacea angustifolia* root, each standardized to 2.1 mg of alkamides, which is believed to be more effective than the nonroot portions of echinacea.

Eligible patients had developed at least one cold symptom (i.e., nasal discharge, nasal obstruction, sneezing, or sore throat) within 36 hours of enrollment. Patients receiving other upper respiratory treatments (e.g., antibiotics, vitamin supplements, nonprescription cold treatments) were excluded, as were patients with a history of allergic rhinitis or asthma. The primary outcome was global severity, with duration and symptom severity assessed twice daily. Secondary outcomes included self-report on psychosocial questionnaires and biomarkers of immune response and inflammation.

**Results:** Both echinacea groups had lower mean severity scores than the control groups, although this did not reach statistical significance. Mean illness duration was also shorter in the echinacea groups (6.34 versus 6.76 days for the blinded and unblinded groups, respectively) than in the control groups (6.87 versus 7.03 days for placebo and no-pill groups, respectively). However, this was not statistically significant. A subgroup analysis of patients enrolled within 24 hours of their first symptoms showed similar, albeit nonsignificant, trends for lower severity and illness duration in the echinacea groups. Immune response markers (i.e., nasal neutrophil counts and interleukin-8 levels in nasal wash) also increased faster in the echinacea groups, but this was not statistically significant. Adherence rates and the incidence of adverse effects were similar across all groups.

**Conclusion:** Although there were trends toward decreased illness severity, decreased duration, and enhanced immune response among patients treated with echinacea, they did not reach statistical significance. The effect was not large, amounting to about half a day's reduction in illness duration and a 10 percent reduction in overall illness severity. The authors conclude that it is likely that echinacea has only a small beneficial effect in persons with the common cold.

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**Source:** Barrett B, et al. Echinacea for treating the common cold: a randomized trial. *Ann Intern Med.* December 21, 2010;153(12):769-777. ■