What is the best treatment for pertussis?

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EVIDENCE-BASED ANSWER

A short-term course of erythromycin, azithromycin, or clarithromycin is as effective as a long-term (2-week) erythromycin therapy in eradicating *Bordetella pertussis* from the nasopharynx (strength of recommendation [SOR]: **A**; based on one meta-analysis of randomized controlled trials [RCTs]). Evidence is insufficient to determine the benefit of antibiotic prophylaxis for pertussis contacts. However, due to high mortality and morbidity, prophylaxis is recommended for families who have an infant less than 6 months old (SOR: **C**; based on expert opinion).

CLINICAL COMMENTARY

Fewer doses and lower cost make compliance more likely

I found this Clinical Inquiry on the treatment and prophylaxis of *Bordetella pertussis* invaluable as it addresses ease of dosing and cost, 2 things important in my pediatric community health practice with its inherent financial and social constraints. The alternatives suggested are easy to use and are as equally effective as the first-line therapy of erythromycin estolate, the long-term treatment recommended by the CDC and the AAP. These alternatives, clarithromycin and azithromycin, require either twice a day or a once a day dosing for 7 days or 3 days respectively, can be accommodated in busy households, thus promoting better compliance.

The cost of medication also relates to compliance. The cost difference between the first-line therapy and the alternative therapy is significant, and may be as much as $89. In an underinsured population, this out-of-pocket cost for the alternatives would prove prohibitive, resulting in decreased compliance. Where cost is not a great issue and concerns of compliance important, choosing the short-term treatment may be a preferable option. For the financially strapped, the 1-week regimen of erythromycin estolate would be preferable. The importance of counseling cannot be overstated in all dosing regimens, especially in those with a more difficult dosing schedule and in cases of prophylaxis in a household with an infant less than 6 months old.

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Evidence summary

A 2005 Cochrane review of 11 RCTs and 1 quasi-randomized trial, with a total of 1720 adults and children, investigated several antibiotics for treatment and prophylaxis of pertussis. The outcome measures used to assess the efficacy of antibiotic treatment or prophylaxis vary between the trials and most of them did not report the immunization status of the participants. The Cochrane review included 1 meta-analysis of 3 studies with 252 participants, comparing azithromycin for 3 days, erythromycin estolate for 7 days, and

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TABLE

Antibiotics for treatment and prophylaxis of pertussis in children and adults

FIRST-LINE THERAPY	DOSAGE FOR CHILDREN	DOSAGE FOR ADULTS	COST*
Erythromycin	40–50 mg/kg orally or intravenously in 4 divided doses for 14 days[5,7]	1–2 g orally or intravenously in 4 divided doses for 14 days[5,7]	56 tabs (500 mg), $16 (generic)
ALTERNATIVE THERAPY IF PATIENT DOESN'T TOLERATE ERYTHROMYCIN			
Clarithromycin	15–20 mg/per kg orally divided every 12 hours for 10–14 days[7] **or** 14-15 mg/kg orally divided every 12 hours for 7 days[1,5]	500 mg orally every 12 hours for 7 days[5]	20 tabs (500 mg), $78 28 tabs (500 mg), $109 (generic)
Azithromycin	10–12 mg/kg orally as single daily dose for 5 to 7 days[5,7] **or** 10 mg/kg orally single daily dose for 3 days[1]	500 mg orally once, then 250 daily on days 2–5[5,7]	5 tabs (500 mg), $75 7 tabs (500 mg), $105 (no generic)
Trimethoprim-sulfamethoxazole	8 mg of TMP, 40 mg/kg SMX per kg orally divided every 12 hours for 14 days[5,7]	160 mg of TMP, 800 mg SMX orally (1 tab DS) every 12 hours for 14 days[5,7]	28 tabs $8 (generic)

All these therapies have gastrointestinal side effects and risk for hypersensitivity reactions.
*Approximate retail price for adult dose. Available at: http://www.drugstore.com. Accessed on June 28, 2005.

clarithromycin for 7 days (short-term treatment) with erythromycin estolate for fourteen days (long-term treatment). The study showed equal efficacy in eradication of *B pertussis* from the nasopharynx of 99.2% to 97.7% (absolute risk reduction [ARR]=1.44%; 95% confidence interval [CI], –1.58 to 4.46). There were fewer side effects with the short-term treatment (32.1% vs 48.9%; ARR=16%; 95% CI, 7.84 to 25.84).[1]

A large, multicenter RCT of 477 children of 6 months to 16 years of age demonstrated that a 5-day treatment with azithromycin eradicated *B pertussis* from the nasopharynx as effectively as a 10-day course of erythromycin estolate.[2] Similarly, trimethoprim/sulfamethoxazole proved as effective as erythromycin in eliminating B pertussis from the nasopharynx.

Although tetracycline and chloramphenicol are effective treatments for pertussis, they are not recommended because of their side effects.[1] Six randomized trials failed to show any statistically significant difference between antibiotics and placebo on frequency and severity of cough or duration of pertussis disease.[1] A randomized, placebo-controlled trial studied 300 household contacts of children with culture-positive pertussis. There was no statistically significant difference in either the frequency of pertussis disease or rate of positive cultures in household contacts between the erythromycin group (2.1%) and the placebo group (5.1%) (ARR=2.95%; 95% CI, –1.21 to 7.11).[1]

Another Cochrane review of 8 trials examined the effectiveness of the symptomatic treatment of cough in children and adults with pertussis. There were many problems with the methodological quality of these trials, including small sample sizes and poor reporting of the methods.

FAST TRACK

Due to high mortality, pertussis prophylaxis is recommended for families with an infant <6 months old

Diphenhydramine, pertussis immunoglobulin, corticosteroids and salbutamol were compared with placebo. There were no statistically significant differences in coughing paroxysms, mean number of whoops per 24 hours or in duration of hospital stay between these interventions and placebo.[3]

Extracorporeal circulatory life support has been used to maintain perfusion for patients with severe disease. The mortality of these patients is very high.[4] No RCTs of the effectiveness of this intervention has been performed.

Recommendations from others

The Centers for Disease Control and Prevention recommends erythromycin for 14 days as a first choice for the treatment and prophylaxis of pertussis. Antibiotics should be started no later than 3 weeks after the onset of cough. Trimethoprim-sulfamethoxazole can be used as an alternative treatment for patients who do not tolerate erythromycin. Prophylaxis is recommended for all household and close contacts if pertussis is highly suspected.[5]

The American Academy of Pediatrics recommends the use of azithromycin and clarithromycin as an alternative treatment for patients who do not tolerate erythromycin.[5]

A national consensus conference on pertussis held in Canada recommended prophylaxis for household contacts of an infant aged <1 year, pregnant women during the third trimester, and for vulnerable individuals who have had face-to-face exposure, or have shared confined air for >1 hour.[6]

FAST TRACK

Good news for the underinsured: relatively inexpensive antibiotics are among the drugs effective against pertussis

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