A Randomized, Placebo-Controlled Trial of Erythromycin Estolate Chemoprophylaxis for Household Contacts of Children With Culture-Positive *Bordetella pertussis* Infection

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ABSTRACT. *Context.* **Household contacts of patients with pertussis are at increased risk of acquiring infection. Chemoprophylaxis has been recommended to decrease transmission, particularly to young infants who are at increased risk of severe disease. Although epidemiologic investigations of outbreaks have suggested a benefit, there have been no prospective studies evaluating the efficacy of chemoprophylaxis in preventing secondary cases of pertussis.**

Objective. **To determine whether erythromycin estolate chemoprophylaxis is effective in household contacts of children with culture-positive pertussis.**

Design. **Randomized, double-blind, placebo-controlled study.**

Setting. **Community based.**

Subjects. **All household contacts of 152 children with culture-positive pertussis who provided consent (n = 362). After withdrawals, there were 135 households with 310 contacts. Exclusions included pregnancy, age <6 months, already receiving an erythromycin-containing antibiotic, and erythromycin allergy.**

Interventions. **Erythromycin estolate (40 mg/kg/day in 3 divided doses; maximum dose 1 g) or placebo for 10 days. Nasopharyngeal cultures, pertussis antibodies, and clinical symptoms were assessed before and after treatment.**

Primary Outcome. **Measure efficacy of erythromycin estolate chemoprophylaxis calculated by the proportion of households in each group with a member who developed a nasopharyngeal culture positive for *Bordetella pertussis*.**

Results. **There was no difference in the development of respiratory tract symptoms compatible with a case definition of pertussis in the erythromycin- and placebo-treated groups. There were 20 households with secondary culture-positive cases of pertussis; 4 households in the erythromycin-treated group and 15 in the placebo-treated group (efficacy of erythromycin chemoprophylaxis for bacterial eradication 67.5% [95% confidence interval: 7.6–88.7]). However, medication-associated adverse reactions were reported by 34.0% of erythromycin and 15.7% of placebo recipients.**

Conclusions. **Under the conditions of this study, erythromycin estolate prevented culture-positive pertussis in household contacts of patients with pertussis but did not prevent clinical pertussis.** *Pediatrics* **1999;104(4). URL: http://www.pediatrics.org/cgi/content/full/104/4/e42; *pertussis, whooping cough,* Bordetella pertussis, *antimicrobial prophylaxis, erythromycin estolate.***

ABBREVIATIONS. GEE, generalized estimating equations; IgG, immunoglobulin G; IgA, immunoglobulin A.

Pertussis, an acute respiratory infection caused by *Bordetella pertussis*, can affect people of all ages. Although adults and older children usually have mild or moderate symptoms, infants are at highest risk of severe disease and complications including death.[1] Universal immunization has controlled pertussis in North America; however, the protective efficacy of the vaccine is incomplete.[2,3] Outbreaks of pertussis have continued to occur in unimmunized, underimmunized, and highly immunized populations.[4–9] Over the past decade, the reported incidence of pertussis has increased in both Canada and the United States.[10,11] Intrafamilial spread of pertussis by close contact with respiratory secretions is common in both immunized and unimmunized individuals[12,13] and has led to recommendations for the use of erythromycin for the chemoprophylaxis of household contacts of patients with pertussis.[14,15] Although several pertussis outbreak investigations have suggested a benefit,[16–22] there have been no prospective clinical trials demonstrating the efficacy of erythromycin chemoprophylaxis. Gastrointestinal side effects are common with erythromycin and may diminish compliance. Therefore, we performed a prospective, randomized, double-blinded, placebo-controlled trial to determine whether erythromycin estolate chemoprophylaxis in household contacts of children with culture-positive pertussis prevents secondary cases of pertussis.

METHODS

Recruitment, Eligibility, and Ethical Considerations

Household contacts of children participating in a study comparing 7 and 14 days of erythromycin estolate treatment for culture-positive pertussis[23] were eligible for enrollment. Household contacts were recruited after identification of a culture-positive

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index case. Household members (defined as individuals living in the same home as the index case) were excluded from enrollment if they were: pregnant; <6 months of age; already receiving an erythromycin containing antibiotic; or had a history of culture-positive pertussis, erythromycin allergy, or liver disease. Household contacts were not excluded if they had respiratory symptoms in the absence of a positive culture for *B pertussis*. Written informed consent was given by all study participants or their parents. The protocol was approved by the research ethics board of the Izaak Walton Killam Hospital for Children.

Randomization, Blinding, and Study Procedures

Eligible household members were allocated by the Pharmacy Department of the hospital using a table of random numbers to receive either erythromycin estolate (40 mg/kg/day in 3 divided doses for 10 days; maximum of 1 g/day) or an identical appearing and tasting placebo (Eli Lilly Canada, Inc, Scarborough, Ontario). The unit of randomization was the household; therefore, all household members were allocated to the same treatment group. Participants and study personnel remained blinded to the treatment allocation.

Five visits were made by study personnel to each participating household for collection of clinical data and specimens. At the first visit, a nasopharyngeal aspirate was obtained for culture for *B pertussis*; serum was obtained for baseline pertussis antibody levels; a questionnaire was completed to determine the presence and duration of any respiratory symptoms; and study medication was distributed. Follow-up visits for repeat culture occurred on day 7 (during chemoprophylaxis), day 14 (4 days after completion of chemoprophylaxis), and day 21 (11 days after completion of chemoprophylaxis). Serum for convalescent serology was collected at the final visit on day 28. Compliance with therapy- and antibiotic-associated adverse events were assessed by study nurses through a standardized questionnaire and measurement of medication remaining during the first two follow-up visits; the questionnaire to assess clinical symptoms was completed at all follow-up visits and was based on participant recall.

Laboratory Methods

Cultures for *B pertussis* were obtained by nasopharyngeal aspirate.[24] Secretions were rinsed from the catheter with 0.8 mL of phosphate-buffered saline containing 1% casaminoacids (Difco Laboratories, Detroit, MI).[25] Rinsed secretions were used to inoculate two Regan-Lowe plates, one with and one without cephalexin.[26] Suspicious colonies were confirmed as *B pertussis* using specific agglutinating antisera; *B parapertussis*-specific antiserum was used as a negative control (Murex, Dartford, UK).

Blood was collected by finger prick or venipuncture, and serum was separated and stored below −70°C. Immunoglobulin G (IgG) and immunoglobulin A (IgA) antibodies against pertussis toxin, filamentous hemagglutinin, pertactin, and fimbriae 2 and 3 were measured by enzyme immunoassay.[27,28] Antibody titers were expressed as reciprocal dilutions using single point, parallel line calculations.[24]

Data Analysis

Study groups were assessed for baseline comparability. Family-specific attributes such as age of the index case and number of children were compared between groups by Wilcoxon tests for continuous outcomes and Fisher's exact test for categoric outcomes. Subject-specific attributes such as the presence of preprophylaxis symptoms were compared between groups by a generalized estimating equations (GEE) analysis using the subjects within the same family as repeated measures. This allows for the possibility that measurements within the same family may be correlated.[29] Baseline antibody levels were compared by mixed model analysis of variance using family and randomization group as the factors; logarithmic conversion was used to correct for skewed data.

The primary outcome of the study was the efficacy of chemoprophylaxis in households defined by the equation:

$$\text{Efficacy} = \frac{[\text{incidence (placebo)} - \text{incidence (erythromycin)}]}{\text{incidence [placebo]}} \times 100.$$

Households were used as the unit of randomization and analysis because of the concern that the risk of second cases of pertussis within a household was dependent not only on the index case, but potentially on other household contacts. Differences in family rates of secondary infections were compared between groups by Fisher's exact test. Groups were compared in subanalyses on individual subjects using GEE. The incidence of pertussis in households was defined as the acquisition of a positive nasopharyngeal culture for *B pertussis* in any nonindex household member. Household members with a baseline nasopharyngeal culture positive for *B pertussis* (before initiation of chemoprophylaxis) were considered coindex cases, were removed from blinded randomization and treated with erythromycin estolate, and were excluded from the analysis.

A secondary, post hoc analysis was performed to assess the efficacy of erythromycin estolate in household contacts who did not already have symptoms compatible with a diagnosis of pertussis before the institution of erythromycin estolate chemoprophylaxis. Three case definitions for pertussis were used in this analysis: 1) nasopharyngeal culture positive for *B pertussis*; 2) culture positive or paroxysmal cough for ≥2 weeks; and 3) culture positive for *B pertussis* or cough for ≥2 weeks with at least one other symptom (whoop, paroxysms, vomiting, apnea, or cyanosis). The primary case of pertussis in the household (distinct from the index case described previously) was defined as the first household member meeting the case definition for pertussis with onset of disease defined as the first day of cough. Secondary cases were defined as household members who met the case definition for pertussis and in whom the first day of cough occurred ≥7 days after the primary case. For this analysis, efficacy was calculated after excluding primary cases, coprimary cases (cases with onset of cough <7 days after the primary case), and secondary cases with onset of symptoms before initiation of chemoprophylaxis.

Compliance was graded (excellent, ≥90% of doses taken; good, ≥60% but <90% doses taken; and poor, <60% of doses taken) and was tabulated for each randomization group. The actual values were compared by GEE. The proportion of subjects in each group with pertussis-like symptoms, and total number of symptoms was compared by GEE. Durations of symptoms were compared by the log rank test and Kaplan-Meier survival curves were prepared. Adverse reactions related to treatment were compared by GEE.

Mean antibody levels to each antigen for the first and second blood test were estimated by geometric means and 95% confidence intervals. Mean log-titers at the two sampling times were compared by mixed model analysis of variance using family as a random effect and randomization group as a fixed effect. Proportions achieving specified increases in antibody levels were compared GEE.

RESULTS

Study Population

In total, 152 families were enrolled into the study (Fig 1). There were 362 household members who participated; an additional 60 members were excluded because of already being treated with an erythromycin-containing antimicrobial agent (44), pregnancy (6), other contraindication to erythromycin (5), age <6 months (4), or history of pertussis (1). At least 29 other family members refused to participate for personal reasons.

A total of 73 households consisting of 170 individuals were allocated to the erythromycin group, and 79 households (192 members) were allocated to the placebo group. For the primary bacteriologic outcome, participants were considered to have withdrawn if they did not provide at least the baseline and one follow-up nasopharyngeal culture for *B pertussis*. There were 12 households in the erythromycin group in whom all members withdrew (24 members) and an additional 2 households in which 1 member each withdrew (26 [15.3%] household contacts and 12 [16.4%] com-

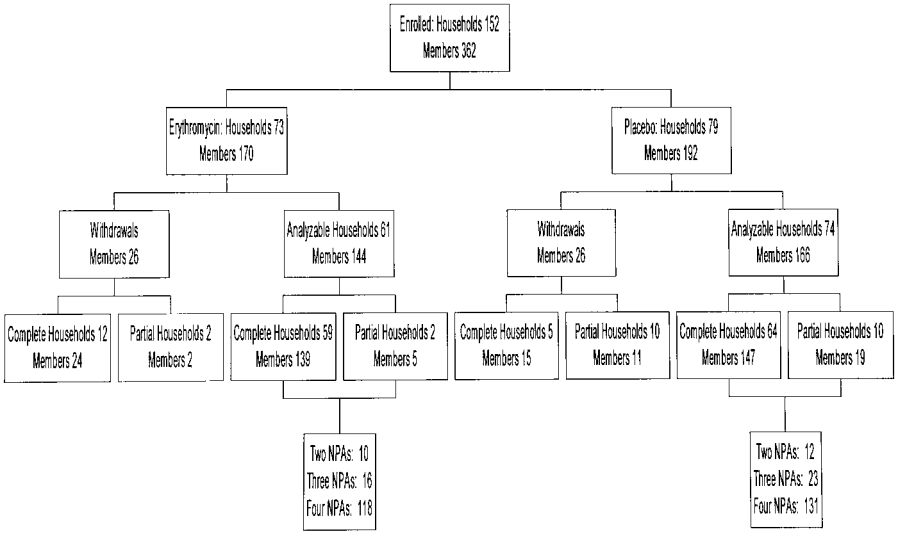

Fig 1. Distribution of households and individuals allocated to treatment with erythromycin estolate or placebo and number eligible for analysis. Details of withdrawals and specimens are included in the text. NPAs = nasopharyngeal aspirate culture specimens obtained for *B pertussis*.

plete households). There were also 26 individuals who withdrew from the placebo group comprised of 5 complete households (15 members) and 11 additional members from 10 households (13.5% of household contacts and 6.3% of complete families). Therefore, after withdrawals, there were 61 analyzable households (144 members) in the erythromycin group and 74 analyzable households (166 members) in the placebo group. Of the 144 members in the erythromycin group, 118 (81.9%) provided all four nasopharyngeal aspirates, 16 provided three specimens, and 10 provided the baseline and one follow-up. Of the 166 household members allocated to the placebo group, 131 (78.9%) provided all four specimens, 23 provided three specimens, and 12 provided the baseline and one follow-up.

The erythromycin and placebo groups were similar before initiation of treatment (Table 1). There were no differences in the number of household members or in their mean age; however, there was a trend toward a higher proportion of households in the placebo group with a child <5 years of age (29.7% compared with 14.8%; $P = .06$). The characteristics of the index case were also similar; erythromycin or placebo chemoprophylaxis in household contacts was initiated a mean of 11.7 and 12.5 days, respectively, after the onset of paroxysmal cough ($P = .7$) and 24.4 and 22.9 days after onset of any cough in the index case ($P = .23$).

Compliance and Safety

Adverse events were reported more frequently by participants in the erythromycin group than in the placebo group (Table 2). Gastrointestinal complaints predominated in both treatment groups. Compliance

TABLE 1. Baseline Demographic Comparison of Household Members and Index Cases

Characteristic	Detail	Number (%) of Households		*P* Value
		Erythromycin ($n = 61$)	Placebo ($n = 74$)	
Households				
Number of members	1	7 (11.5)	8 (10.8)	.12
	2	11 (18.0)	25 (33.8)	
	3	21 (34.4)	23 (31.1)	
	4	19 (31.1)	14 (18.9)	
	5	3 (4.9)	2 (2.7)	
	6	0	2 (2.7)	
	Mean	3	2.8	
Mean age of members	Years	26.6	24.9	.19
At least one member	<5 y	9 (14.8)	22 (29.7)	.06
	≤16 y	30 (49.2)	41 (55.4)	.83
Mean duration (in days) of symptoms in the index case before chemoprophylaxis	Cough	24.4	22.9	.23
	Paroxysmal cough	11.7	12.5	.7
Index cases				
Treatment group*	Nonparticipant	11 (18.0)	12 (16.2)	.71
	Multiple index	10 (16.4)	8 (10.8)	
	7 d	17 (27.9)	26 (35.1)	
	14 d	23 (37.7)	28 (37.8)	
Mean age	Years	5.1	4.1	.1
Number of index cases	1	41 (80.4)	55 (87.3)	.39
	2	10 (19.6)	5 (7.9)	
	3	0	3 (4.8)	
	Mean	1.2	1.2	

* Comparison of 7 and 14 days of erythromycin estolate treatment of *B pertussis* infection.[23]

TABLE 2. Incidence of Adverse Events During Treatment and Compliance With Medication in Household Contacts According to Treatment Group

Outcome	Treatment Group, Number (%)		*P* Value
	Erythromycin (n = 144)	Placebo (n = 166)	
Adverse event			
Any adverse reaction	49 (34.0)	26 (15.7)	.0004*
Nausea	18 (12.6)	8 (4.9)	.04*
Vomiting	6 (4.2)	4 (2.4)	.41
Diarrhea	29 (20.3)	14 (8.5)	.004
Abdominal cramps	8 (5.6)	1 (0.6)	.04*
Stomach ache	2 (1.4)	1 (0.6)	.66
Jaundice	0	1 (0.6)	1
Other†	3 (2.1)	5 (3.1)	.55
Compliance			
Excellent (≥90% of doses)	78 (54.2)	108 (65.1)	
Good (≥60% to <90% of doses)	45 (31.3)	45 (27.1)	.04*
Poor (<60% of doses)	21 (14.6)	13 (7.8)	

* Statistically significant; $P < .05$.
† Other reactions included fatigue (1), thirst (1), and night sweats (1) in the erythromycin group, and headache (1), constipation (1), aftertaste (1), spitting up (1), and foul smelling urine (1) in the placebo group.

was better in the placebo group than in the erythromycin estolate group ($P = .04$).

Efficacy Outcomes

Bacteriologic Efficacy

There were a total of 21 secondary cases identified; 5 in the erythromycin group and 16 in the placebo group. Positive cultures were obtained both during and after completion of the chemoprophylaxis regimen. In the placebo group, there were 9 positive cultures during treatment and 7 positive cultures after completion of treatment. In the erythromycin group, 1 positive culture was obtained during treatment and 4 posttreatment. In each group, there was 1 household with 2 secondary cases; therefore, there were 4 (6.6%) chemoprophylaxis failures in the 61 households randomized to receive erythromycin and 15 (20.3%) failures in the 74 households randomized to placebo ($P = .026$). The efficacy of erythromycin prophylaxis in preventing culture-positive pertussis in household contacts was 67.5% (95% confidence interval: 7.6–88.7).

The effect of several variables on the efficacy of erythromycin chemoprophylaxis using the primary outcome measure of a positive nasopharyngeal culture was examined. The duration of treatment of the index case (7 or 14 days) did not affect the efficacy of chemoprophylaxis. Secondary cases were not more likely to occur in households in which the index case had been treated 7 days; in fact, all erythromycin chemoprophylaxis failures were in households in which the index case was allocated to the 14-day treatment group. There was a trend toward an increased attack rate with increasing numbers of household members. In erythromycin-treated households in which >60% of doses were taken by all members, the attack rate was 0% in the 6 and 8 households with 1 or 2 contacts, respectively; 5.9% in the 17 households with 3 contacts; 13.3% in the 15 households with 4 contacts; and 0% in the 2 households with 5 contacts ($P = .109$). Using the individual rather than the household as the unit of observation, efficacy was 78.7% ($P = .045$) in household members with excellent compliance compared with 38.1% ($P = .50$) in individuals with poor compliance. The individual compliance rates for the five erythromycin chemoprophylaxis failures were 20%, 20%, 80%, 93.3%, and 96.7% of doses taken. No correlation was found between the duration of symptoms in the index case before enrollment of the household and efficacy of chemoprophylaxis (data not shown).

Clinical Efficacy

Development of respiratory tract symptoms was common in household contacts of children with pertussis (Table 3). No differences were detected for total respiratory symptoms, nasal congestion, cough, or paroxysmal cough. Significantly fewer erythromy-

TABLE 3. Presence and Duration of Symptoms in Household Contacts of Children With Culture-proven Pertussis by Treatment Group

Symptom	Number (%) Reporting Symptom			Mean Duration (Days) of Symptoms		
	Erythromycin	Placebo	*P* Value	Erythromycin	Placebo	*P* Value
Any symptom	98 (68.1)	127 (76.5)	.14	61.8	46.6	.87
Nasal congestion	83 (57.6)	93 (56.0)	.86	39.1	40.2	.96
Any cough	88 (61.1)	110 (66.3)	.45	53.8	46.4	.25
Worse at night	50 (34.7)	70 (42.2)	.32	38.6	38	.87
Paroxysmal	31 (21.5)	41 (24.7)	.55	37.1	50.5	.17
With vomiting	13 (9.0)	31 (18.7)	.03*	24.8	28.5	.71
Whoop	10 (6.9)	22 (13.3)	.08	34.9	21	.46
Apnea	1 (0.7)	4 (2.4)	.2	8	19.3	.71
Cyanosis	1 (0.7)	1 (0.6)	.91	79	15	.32

* Statistically significant; $P < .05$.

cin-treated household contacts had posttussive vomiting than did placebo-treated contacts (9.0% vs 18.7%; $P = .03$); there was also a trend toward less whoop in the erythromycin-treated group (6.9% vs 13.3%; $P = .08$). Overall duration of respiratory tract symptoms was similar in both groups.

In view of the high rates of pertussis-like symptoms in both treatment groups, a post hoc analysis was performed excluding household members in whom symptoms meeting one or more conditions of the two case definitions for pertussis began before the initiation of chemoprophylaxis (Table 4). In the remaining household contacts, using a nasopharyngeal culture positive for *B pertussis* after the implementation of chemoprophylaxis as a case definition, the secondary attack rate was 2.1% in the erythromycin-treated contacts and 5.1% ($P = .2$) in the placebo-treated contacts who were asymptomatic at the time chemoprophylaxis was begun. Using the outcome of culture-positive or paroxysmal cough for ≥2 weeks, the secondary attack rate was 4.8% in erythromycin-treated contacts, and 6.1% in placebo-treated contacts who were asymptomatic when treatment was started ($P = .6$). The same lack of effect was observed using the outcome measure of cough for ≥2 weeks with at least one other pertussis symptom. Similar results were found when the analysis was restricted to households in which the index case (the first culture-positive case) was the primary case (first symptomatic case) and when all household members were included (including those excluded or withdrawn from the study because of contraindications to erythromycin, previous treatment, and refusal to permit collection of nasopharyngeal aspirate specimens; data not shown).

Serology

Despite a low incidence of culture-positive pertussis, antibodies against *B pertussis* antigens commonly were detected in culture-negative household contacts in acute and convalescent samples. There were no differences in antibody titers or in the proportion of seronegative participants between the groups assigned to erythromycin estolate or placebo before the initiation of chemoprophylaxis. A fourfold rise in antipertussis toxin IgG antibody was demonstrated in 68.8% of placebo-recipients who developed a positive culture for *B pertussis*, and 8.9% of placebo- and 11.5% of erythromycin-recipients who remained culture-negative ($P < .001$); rates of IgA rises were 80%, 10.4%, and 10.2%, respectively ($P < .001$). Similar antibody responses were found for IgG and IgA antibodies against filamentous hemagglutinin, pertactin, and fimbriae (data not shown). Analysis of the antibody response of recipients of erythromycin estolate who developed culture-positive pertussis was not possible because of the small numbers involved.

DISCUSSION

As a result of the high secondary attack rate among household contacts patients with pertussis[12,13] and the considerable risk of morbidity among young infants,[1,5] erythromycin chemoprophylaxis of household contacts patients with pertussis is recommended in both Canada and the United States,[14,15,30,31] although it is not supported widely in in the United Kindom and Europe.[32] In the 40 years since chemoprophylaxis for pertussis was first proposed,[33] case series, poorly controlled studies, and reports of community and institutional outbreaks have been published describing both its success[16–22,34–36] and its failure.[37–41] This study is the first large randomized, placebo-controlled study assessing the efficacy of this intervention.

We found evidence of bacteriologic efficacy of chemoprophylaxis but not of clinical efficacy. Timing of the institution of chemoprophylaxis is likely an important factor in determining the clinical outcome in close contacts of pertussis. In this study, treatment of household contacts was implemented after identification of a positive culture in the index case. The mean duration of cough in the index case was 3 weeks and paroxysmal cough 11 to 12 days at the time chemoprophylaxis was initiated. Pertussis is most infectious during the catarrhal stage before the onset of the cough, which progresses over several days to paroxysms that lead to the diagnosis. Thus, household contacts may be in their incubation period at the time of chemoprophylaxis initiation, if they do not already have symptoms. This could have minimized the beneficial effect of erythromycin prophylaxis in this study. Earlier therapy (such as at the time of collection of the nasopharyngeal aspirate specimen in the index case) might improve the efficacy of erythromycin prophylaxis and shift more cases from early treatment to prevention. Similarly, rapid diag-

TABLE 4. Efficacy of Erythromycin Prophylaxis in Household Members Without Symptoms Compatible With Pertussis at the Time of Initiation of Treatment

Outcome	Case Definition					
	Culture-positive (C+)		C+ or Paroxysmal Cough ≥2 Weeks		C+ or Cough ≥2 Weeks and ≥1 Symptom*	
	Erythromycin	Placebo	Erythromycin	Placebo	Erythromycin	Placebo
Total household contacts	144	166	144	166	144	166
Secondary cases	5	16	26	42	36	53
Before prophylaxis	2	8	20	34	28	45
After prophylaxis	3	8	6	8	8	8
Postprophylaxis SAR†§	3/142 (2.1%)	8/158 (5.1%)	6/124 (4.8%)	8/132 (6.1%)	8/116 (6.9%)	8/121 (6.6%)

* Pertussis symptoms include paroxysms or vomiting with cough, whoop, apnea, or cyanosis.
† Secondary attack rate = (cases/contacts) × 100.
§ $P \geq .20$ in all three group comparisons.

nostic tests for pertussis would facilitate more timely intervention. Although chemoprophylaxis may be instituted on clinical grounds during established outbreaks, awaiting laboratory confirmation as was done in this study may be more typical under routine conditions.

The epidemiology of pertussis within the household also may have contributed to the lack of clinical efficacy of chemoprophylaxis. Many household contacts who met the case definitions for pertussis had symptoms that preceded the start of chemoprophylaxis. Indeed, some had symptoms that predated the index case. These primary, coprimary, and secondary cases with onset before chemoprophylaxis could not be expected to benefit from erythromycin treatment. However, even when these cases were excluded or when only households in which the index case was the primary case were evaluated, no benefit of erythromycin in prevention of clinical pertussis illness could be demonstrated. The long duration of the symptoms (37 to 50 days for paroxysmal cough, for example) and significant rises in antibody titers in some erythromycin recipients who did not develop positive pertussis cultures indicate that these were true cases of pertussis rather than nonspecific respiratory illnesses. In addition to these household members, some of the household contacts who received chemoprophylaxis (erythromycin or placebo) were likely already immune to pertussis from previous infections and therefore were not at risk. Substantial geometric mean antibody levels against all antigens were detected in the acute serum specimens of both groups indicating previous exposure to pertussis antigens in many of the individual household members. Because protective levels of pertussis antibodies have not been established, it is not possible to determine which household contacts were susceptible to infection and which were already protected by natural infection or immunization. The presence of IgA antibodies suggests that for many of these individuals the exposure was through natural infection.[42] Indeed, some household members may have been the source of infection for the index case during a mild or subclinical infection. High acute antibody levels and similar antibody rises in the culture-negative placebo recipients and erythromycin-successes suggest that seroconversion may have occurred before the first blood sample was obtained. A better design would have included only susceptible contacts; however, in practice as in this study, susceptibility cannot be determined, and chemoprophylaxis is administered to all household contacts.

The data from this study suggest that erythromycin chemoprophylaxis used when the index case has had paroxysmal cough for 11 to 12 days is not an effective public health tool for preventing the spread of pertussis in households, because most transmission has already occurred. We cannot determine from this study whether earlier implementation of chemoprophylaxis would have been effective in preventing secondary cases within the household or whether chemoprophylaxis had an effect on limiting spread in the community. Antibiotic-associated adverse reactions were common and in community practice may limit further the implementation of erythromycin chemoprophylaxis. Consequently, public health education for physicians and patients should be directed toward early recognition of symptoms and prompt medical intervention. Newer macrolide antibiotics with improved pharmacokinetics (once daily dosing with shorter courses) and lower rates of adverse reactions (and thus the likelihood of better compliance) may prove to be useful in the future if it is demonstrated that they are effective in preventing secondary cases. Accurate, rapid, commercially available laboratory diagnosis also would facilitate interruption of secondary spread. Until more data are available, the role of chemoprophylaxis for pertussis remains uncertain.

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