

Short course antibiotic therapy for respiratory infections: a review of the evidence

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Background. The judicious use of antibiotics entails achieving the appropriate balance between prescribing them with sufficient frequency and duration to effect a clinical cure for bacterial infections and overprescribing them, a practice that increases prescription drug costs as well as the risks of bacterial resistance, non-compliance with therapy and side effects. The recognition that the traditional 10-day or greater duration of therapy for acute otitis media, tonsillopharyngitis and sinusitis does not derive from a strong scientific or medical rationale (with the exception of penicillin therapy for tonsillopharyngitis) and the increasing awareness of the adverse sequelae of long-duration antibiotic therapy have led some clinicians to call for shortening the duration of antibiotic therapy in these infections. The soundness of this recommendation hinges on the demonstration that shortened courses of antibiotic therapy are at least as effective as traditional courses of therapy.

Synopsis. Data relevant to determining the optimum duration of therapy in acute otitis media, tonsillopharyngitis and sinusitis are reviewed in this article. The review demonstrates particularly strong justification for shortening the duration of therapy from the standard 10 days to 5 days in acute otitis media, in which numerous open label and controlled studies have shown equivalent efficacy of the two durations of regimen. A growing body of evidence indicates that tonsillopharyngitis, too, can be effectively treated with non-penicillin antibiotics given for fewer than 10 days. Although sinusitis data are less plentiful than those for acute otitis media and tonsillopharyngitis, the results available to date are encouraging in suggesting that short-

ened courses of therapy may also be appropriate for acute maxillary sinusitis.

INTRODUCTION

Nearly three of four antibiotics prescribed for outpatients are written for treatment of upper respiratory tract infections including acute otitis media, tonsillopharyngitis and sinusitis.¹ Many of these prescriptions are necessary for curbing spread of infection and preventing development of harmful sequelae; however, the widespread inappropriate prescription of antimicrobials for nonbacterial respiratory illnesses ranging from the common cold to viral pneumonia is well-documented and has been a focus of efforts to curtail unnecessary antibiotic use.² Less attention has been paid to the role of the duration of antibiotic therapy for upper respiratory infections in the judicious use of antibiotics. In fact, prescribing the appropriate duration of a course of antibiotic therapy is as important as eliminating prescriptions for nonbacterial illnesses in practicing judicious use of antibiotics for upper respiratory tract infections.

How long is enough, and how long is too much? Therapeutic courses need to be of sufficient duration to result in a clinical cure to return patients as rapidly as possible to normal functioning and to prevent the progression of disease and the development of dangerous sequelae. However, unnecessarily lengthy courses of therapy may prevent the realization of these treatment goals by heightening the risk of development of bacterial resistance and side effects and by reducing compliance with the therapeutic regimen. In addition, prolonged therapy compared with shortened therapy is associated with higher direct medical costs.

The high direct medical costs of additional days of therapy are illustrated by a United Kingdom study³ that assessed prescription antibiotic costs of 5-day *vs.* 7-day treatment courses for national 1992 to 1993 tablet and capsule prescriptions for the commonly used antibiotics amoxicillin, ampicillin, cephalexin, erythromycin, phenoxymethylpenicillin, trimethoprim and cotrimoxazole. The excess cost of 7 days compared with 5 days of therapy ranged, depending on whether generic or brand leader prices were used in the calculations, from £1.9 million to £7.2 million, or \$3.17 million to \$12.0 million. This calculation includes direct prescrip-

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tion costs but not other medical costs (e.g. those associated with physician visits for side effects of antibiotics) of prolonged therapy. The authors suggest that 5 days of therapy should be considered for uncomplicated bacterial infections in the absence of evidence that longer durations of therapy are more effective.

In addition to increasing direct medical costs, prolonged courses of therapy heighten chances of noncompliance with the therapeutic regimen. Compliance rates in tonsillopharyngitis, for instance, in which antibiotic therapy is typically prescribed for 10 days, are inversely related to duration of therapy and have been observed to be as low as 8% by the ninth day of treatment in clinical studies.^{4, 5}

Perhaps most important in this era of rapidly increasing prevalence of resistant organisms, unnecessarily lengthy course of therapy may encourage the development of antibiotic resistance. For example, a 941-children study⁶ conducted in France demonstrates that beta-lactam antibiotic treatment durations greater than 5 days compared with fewer than 5 days significantly increased the risk of pharyngeal carriage of penicillin-resistant *Streptococcus pneumoniae*.

The risk of antibiotic resistance increased not only with long duration of therapy in this study but also with administration of a low (i.e. lower than clinically recommended) daily dose of antibiotic. This finding is relevant to considerations about the appropriate duration of antibiotic therapy in the context of patients' frequent practice of administering antibiotic only until they feel better, i.e. within 2 to 5 days for upper respiratory infections such as acute otitis media and tonsillopharyngitis. Truncation of therapy may be especially prevalent in pediatric patients, whose parents conserve antibiotic suspensions to use from one respiratory infection to another. Antibiotics, particularly those in suspension, rapidly lose potency as they age, and low potency antibiotics are likely to promote the growth of resistant organisms. Thus for pediatric infections, noncompliance with a 10-day course of therapy by conserving doses for future infections may indirectly foster resistance by increasing the chances of administering insufficiently potent antibiotics (analogous to the low daily doses associated with increased risk of pharyngeal carriage of resistant *S. pneumoniae* in the French study⁶).

The idea that a 10-day course of therapy is necessary for the effective treatment of respiratory infections originated from early tonsillopharyngitis studies⁷⁻¹¹ in which parenteral and oral penicillin therapy administered for 9 to 11 days was more effective at eradicating Group A beta-hemolytic *Streptococcus* than administration for 5 or 7 days. On the basis of data from these studies, the 10-day course of penicillin therapy became the gold standard for treatment of tonsillopharyngitis

in the United States and was extrapolated arbitrarily to otitis media and sinusitis and to tonsillopharyngitis cases treated with antibiotics other than penicillin. This arbitrariness is reflected in the variation between countries in standard duration of therapy for acute otitis media. In the United Kingdom the standard duration of therapy for acute otitis media is 5 days, the length of a work week. In France the standard duration of therapy is 8 days.

The recognition that the 10-day duration of therapy for common respiratory infections does not derive from a strong scientific or medical rationale (with the exception of penicillin therapy for tonsillopharyngitis) and the increasing awareness of the adverse sequelae of long duration antibiotic therapy have led some clinicians to call for shortening the duration of antibiotic therapy in some respiratory infections.^{2, 4, 12} The soundness of this recommendation hinges on the demonstration that shorter courses of antibiotic therapy are at least as effective as traditional courses of therapy; poor efficacy of shortened therapy would negate its advantages. Data relevant to determining the optimum duration of therapy in acute otitis media, tonsillopharyngitis and sinusitis are reviewed below. The review demonstrates particularly strong justification for shortening the duration of therapy from the standard 10 days to 5 days in acute otitis media, in which numerous open label and controlled studies comparing therapeutic durations have been conducted. A growing body of evidence indicates that tonsillopharyngitis, too, can be effectively treated with non-penicillin antibiotics given for fewer than 10 days. Although sinusitis data are less plentiful than those for acute otitis media and tonsillopharyngitis, the results available to date are encouraging in suggesting that shortened courses of therapy may also be appropriate for acute maxillary sinusitis.

ACUTE OTITIS MEDIA

Acute otitis media is the most common illness for which antibiotics are prescribed to pediatric patients.¹ Although acute otitis media often is a mild, self-limiting infection, most clinicians recommend use of antibiotics to avoid suppurative complications, to prevent progression to chronic otitis media and to reduce the risk of rare but serious sequelae including meningitis, mastoiditis and bacteremia.^{2, 4} Antimicrobial therapy is directed at the most common pathogens, including *S. pneumoniae*, *Haemophilus influenzae* and *Moraxella catarrhalis*.

Bacteriologic data. Biologic support for the idea that antibiotic courses shorter than 10 days might be effective in the treatment of acute otitis media derives from pediatric studies¹³⁻¹⁵ in which tympanocentesis was used to evaluate bacteria in middle ear effusion. Middle ear effusion in these studies typically became

sterile after only 3 to 6 days of antibiotic treatment. Bacterial eradication is a key determinant of treatment success; therefore, 3- to 6-day courses of antibiotic therapy would be predicted on the basis of these data to be clinically effective in acute otitis media.

Descriptive analysis of clinical data available through early 1997. Clinical evidence supporting the efficacy of shortened courses of antibiotic therapy in acute otitis media comes from a descriptive analysis⁴ of data from open label and controlled trials¹⁶⁻⁴² published and presented through early 1997 (Table 1). This analysis,⁴ which examined the percentages of patients considered clinically cured or improved at the end of therapy, demonstrates that 2- to 5-day courses of therapy are as effective in the treatment of acute otitis media as 10-day courses for oral cephalosporins²²⁻²⁹ such as cefuroxime axetil and cefaclor, the injectable cephalosporin ceftriaxone³¹⁻³⁵ and macrolides such as azithromycin.³⁶⁻⁴² Similar results were observed for amoxicillin and amoxicillin/clavulanate,¹⁸⁻²¹ although a 5-day course of therapy was less effective than a 10-day course in children fewer than 2 years of age in

one amoxicillin/clavulanate study (Table 1).²¹ In addition to patients younger than 2 years of age, patients with tympanic membrane perforation were less likely to benefit from a shortened course of therapy compared with the traditional 10-day course.

Clinical cure data derived from acute otitis media studies conducted in one country are not always readily extrapolated to other countries. First, standards of care and antibiotic prescribing behavior vary regionally and culturally. Second, bacterial resistance patterns differ from region to region. Despite the expected influence of these regional variations, the 2- to 5-day compared with 10-day courses of therapy are similarly effective in studies conducted in a variety of countries such as the United States, France, the United Kingdom, Germany, Sweden, Switzerland and South Africa. This consistency imparts weight to the conclusion that 5-day courses of therapy are as effective as 10-day courses in acute otitis media.

In addition to regional variations in prescribing habits and resistance patterns, clinic-to-clinic variation in diagnostic criteria and techniques may influ-

TABLE 1. Clinical cure/improvement rates (expressed as percent of patients) in studies involving shortened treatment regimens for acute otitis media

Reference	Study Site, Year of Publication	Shortened Therapy (Drug, Duration)	Longer Therapy (Drug, Duration)
Penicillin, amoxicillin, amoxicillin/clavulanate			
16	Sweden, 1982*	79 (penicillin, 5 days)	76 (penicillin, 10 days)
17	Denmark, 1983	71 (penicillin, 2 days)	76 (penicillin, 10 days)
18	United Kingdom, 1982	75 (amoxicillin, 5 days)	72 (amoxicillin, 10 days)
19	United Kingdom, 1985	91 (amoxicillin, 2 days)	90 (amoxicillin, 7 days)
20	United States, 1987†	57 (amoxicillin, 1 day)	100 (amoxicillin, 10 days)
21	United States, 1998*	71 (amoxicillin/clavulanate, 5 days)	87 (amoxicillin/clavulanate, 10 days)
Oral cephalosporins			
22	United States, 1984	100 (cefaclor, 5 days)	84 (amoxicillin, 10 days)
23	United States, 1984‡	90 (cefaclor, 5 days)	94 (cefaclor, 10 days)
24	United States, 1996	69 (cefuroxime, 5 days)	70 (cefuroxime, 10 days)
			74 (amoxicillin/clavulanate, 10 days)
25	France, 1993	94 (cefprozime, 5 days)	93 (cefprozime, 8 days)
26	South America/Spain, 1993	NA	100 (cefprozime, 5 days)
			100 (cefaclor, 5 days)
27	United Kingdom, 1993	NA	95 (cefprozime, 5 days)
			95 (amoxicillin/clavulanate, 5 days)
28	France, 1994	86 (cefprozime, 5 days)	83 (amoxicillin/clavulanate, 8 days)
29	Germany, 1995	100 (cefprozime, 5 days)	100 (cefaclor, 10 days)
Injectable cephalosporins			
30	France, 1990	89 (ceftriaxone, 1 day)	86 (amoxicillin/clavulanate, 5 days)
31	Israel, 1988§	82 (ceftriaxone, 1 day)	86 (amoxicillin, 7 days)
32	United States, 1993	91 (ceftriaxone, 1 day)	91 (amoxicillin, 10 days)
33	Israel, 1994	95 (ceftriaxone, 1 day)	98 (amoxicillin/clavulanate, 8 days)
34	United States, 1994	79 (ceftriaxone, 1 day)	77 (cefaclor, 10 days)
35	United States, 1996	80 (ceftriaxone, 1 day)	92 (trimethoprim-sulfamethoxazole, 10 days)
Macrolides			
36	Switzerland, 1993	93 (azithromycin, 3 days)	97 (amoxicillin/clavulanate, 10 days)
37	Germany, 1993	99 (azithromycin, 3 days)	100 (amoxicillin/clavulanate, 10 days)
38	Multinational, 1995	93 (azithromycin, 3 days)	94 (amoxicillin/clavulanate, 10 days)
39	United States, 1996	88 (azithromycin, 5 days)	88 (amoxicillin/clavulanate, 10 days)
40	United States, 1996	88 (azithromycin, 5 days)	100 (amoxicillin/clavulanate, 10 days)
41	United States, 1996	92 (azithromycin, 5 days)	90 (amoxicillin/clavulanate, 10 days)
42	United States, 1995	99 (clarithromycin, 5 days)	99 (azithromycin, 5 days)

* Five days significantly ($P < 0.05$) less effective than 10 days if children < 2 years old.

† One day significantly ($P < 0.05$) less effective than 10 days.

‡ Five days significantly ($P < 0.05$) less effective than 10 days if tympanic membrane perforation.

§ Injectable significantly ($P < 0.05$) less effective than 7 days at 30-day follow-up.

|| Five days significantly ($P < 0.05$) less effective than 10 days.

ence the outcomes of acute otitis media studies. One review⁴³ revealed 147 unique sets of diagnostic criteria for acute otitis media among 165 pediatricians and 18 unique sets among 26 clinical trials. The consistency of the finding that 5-day treatment regimens are as effective as longer courses of therapy notwithstanding the discrepant diagnostic criteria also lends credence to the findings.

Shortcomings of some of the studies included in this descriptive analysis should be considered in interpreting the data. First, many of the trials were of open label design, a characteristic that permits patient and investigator expectations to influence the results. Second, some of the trials were small and not sufficiently powered to demonstrate a difference between durations of therapy. Third, many of the studies compared shorter courses of one antibiotic with longer courses of a second antibiotic, a study design that renders it impossible to distinguish the effect on clinical efficacy of duration of therapy *vs.* type of medication. In addition, few trials used tympanocentesis as a tool for confirming a diagnosis of acute otitis media. Trials in which diagnosis was based on clinical presentation alone are likely to have enrolled a large proportion of noninfected patients.⁴ The spontaneous improvement of noninfected patients enrolled in the trials may have inflated efficacy rates for and obscured differences between short and long course treatment groups. Finally, studies included in this descriptive analysis were identified through a review of the published literature; the analysis does not include unpublished studies that may have influenced the weight of evidence in favor of or against the efficacy of short course therapy.

Although these weaknesses should be considered in interpreting the data, there is no evidence that they systematically influence the results as they relate to efficacy of various durations of therapy. Like the more poorly designed and conducted trials, the quality trials consistently demonstrated equivalence of shortened duration compared with traditional therapy. For example Gooch et al.²⁴ compared 5- and 10-day courses of therapy with cefuroxime axetil (30 mg/kg/day) with a 10-day course of amoxicillin/clavulanate (40/10 mg/kg/day) in 719 children (491 with an evaluable outcome) from 3 months to 12 years of age. Tympanocentesis for assessment of middle ear fluid was performed in approximately one-third of the patients. Clinical cure or improvement occurred in 69, 70 and 74% of patients treated with the 5- and 10-day courses of cefuroxime axetil and the 10-day course of amoxicillin/clavulanate, respectively. Side effects were less common in both of the cefuroxime groups compared with the amoxicillin/clavulanate group.

Meta-analysis of acute otitis media trials. The results of this descriptive analysis are supplemented

by a quantitative review recently conducted by Kozyrskyj et al.^{44, 45} These researchers conducted a meta-analysis of 32 controlled clinical trials, published from 1966 through 1997, that compared the efficacy of a short course (fewer than 7 days) with that of a long course (more than 7 days) of antibiotic treatment in acute otitis media. The trials enrolled patients 4 weeks to 18 years of age with a clinical diagnosis of acute otitis media and no antimicrobial therapy at time of diagnosis. In performing their data analyses, they assigned trials to one of three groups based on the antibiotic used for the short course of therapy: trials with short-acting oral antibiotics such as cefuroxime axetil, cefaclor and penicillin V potassium; intramuscular ceftriaxone sodium trials; and oral azithromycin trials.

In trials in which short-acting oral antibiotics were used for the short course of therapy, the risk of treatment failure assessed 8 to 19 days after initiation of therapy was 7.8% greater with 5-day treatment ($n = 1549$ children) compared with 10-day treatment ($n = 1569$ children). Treatment failure rates assessed 30 days after initiation of therapy did not differ between the 5-day and 10-day groups. A similar pattern of results was observed in trials in which intramuscular ceftriaxone or oral azithromycin were used for the short course of therapy. The authors concluded that 5 days of treatment with a short-acting antibiotic is effective for uncomplicated acute otitis media in pediatric patients.

The results of Kozyrskyj and colleagues' metaanalysis of controlled trials corroborate and provide quantitative support for the descriptive analysis of open label and controlled studies. The controlled trials included in the metaanalysis were the same controlled trials included in the descriptive analysis, and the shortcomings (described above) of some of these trials apply equally to both analyses. Notwithstanding these caveats, the bulk of evidence favors the conclusion that a shortened course of antibiotic therapy is as effective as the traditional 10-day course in the treatment of uncomplicated acute otitis media.

Post-1997 studies. A trial⁴⁶ published after completion of the metaanalysis and the descriptive analysis furnishes additional substantiation for the similar efficacy of short and long course therapy. Pessey et al.⁴⁶ compared the efficacy in acute otitis media of a 5-day course of the oral cephalosporin cefuroxime axetil suspension (30 mg/kg/day) with that of amoxicillin/clavulanate suspension administered for 8 days (80 mg/kg/day) or 10 days (40 mg/kg/day) in an open, randomized, multicenter study in 716 children 6 months to 3 years of age. The clinical cure rates 1 to 5 days after completion of a 5-day course of cefuroxime axetil or an 8- or 10-day course of amoxicillin/

clavulanate were 86, 88 and 88%, respectively. In the subgroup of patients less than 18 months old, the corresponding numbers were 83, 89 and 84%, a result showing equivalent efficacy among the three treatments. These data show that the 5-day course of cefuroxime axetil is equivalent to the 8- and 10-day courses of amoxicillin/clavulanate even in the youngest children (<18 months) enrolled in the study.

Cohen et al.^{47, 48} evaluated the efficacy of 5- and 10-day courses of therapy in children 4 months to 30 months of age in 2 studies. In the first study⁴⁷ ($n = 385$), clinical success 12 to 14 days after initiation of treatment was reported among 77% of children receiving a 5-day regimen and 88% of children receiving a 10-day regimen of amoxicillin/clavulanate ($P < 0.01$). Clinical success rates 28 to 42 days after initiation of therapy were similar between the 2 groups (40% for the 5-day regimen and 46% for 10-day regimen). A similar pattern of results was obtained in a study⁴⁸ with cefpodoxime proxetil, which was associated with clinical success 12 to 14 days after initiation of therapy in 84% of children receiving 5 days of treatment and 92% of children receiving 10 days of treatment ($P < 0.01$). Clinical success rates 28 to 42 days after initiation of therapy were similar between the two groups (85% for the 5-day regimen and 84% for the 10-day regimen). In both studies the superiority of the standard 10-day regimen was apparent for children cared for outside of the home, but much less evident among children cared for in the home. The authors suggest that the small efficacy benefit of 10-day therapy for children cared for outside the home should be balanced with the benefits of shortened courses of treatment in tailoring therapy to the needs of the patient.⁴⁸

Centers for Disease Control/American Academy of Pediatrics recommendations. On the strength of data such as these, the CDC and the American Academy of Pediatrics (AAP) issued in 1998 a recommendation that the traditional 10-day course of antibiotics not be reflexively prescribed for acute otitis media.⁴⁹ Characterizing the evidence in favor of long (10- to 14-day) courses of antibiotic therapy in acute otitis media as "practically nonexistent," the authors of the CDC/AAP recommendations suggest decreasing the duration of antibiotic therapy for uncomplicated acute otitis media to 5 to 7 days.⁴⁹

Although they strongly encourage 5- to 7-day courses of antibiotics in uncomplicated acute otitis media, the CDC/AAP recommendations caution against prescribing short course therapy to patients with chronic or recurrent otitis media, underlying medical conditions or tympanic membrane perforation. Clinical trials comparing durations of therapy generally excluded these patient groups at higher risk of treatment failure than uncomplicated cases, and not enough evidence has

accumulated to date to support shortening the traditional 10-day course of therapy in these patient groups.

The CDC/AAP recommendations also warn that short course therapy may not be appropriate for children less than 2 years of age because they were underrepresented in most acute otitis media trials comparing 10-day with shorter courses of antimicrobial therapy. Results of the few studies have been conducted in children younger than 2 years have been inconsistent; some studies suggest similar efficacy of shorter compared with traditional courses of therapy, and others suggest a trend toward lower efficacy of shorter courses.^{4, 47, 48, 50} This finding has led to the suggestion that the traditional 10-day course of therapy should be prescribed in these young children.⁵⁰

The apparent reduction in efficacy of short course therapy in young children compared with older children may be an artifact of the greater tendency of very young children than older children to experience recurrent otitis media, which is associated with a high failure rate of therapy regardless of duration of therapy. In patients with more frequent bouts of acute otitis media and more prolonged recovery, new otitis media infections may be observed more often in a shortened than in a longer treatment regimen. This conjecture is consistent with data from a 1999 study comparing 5-, 7- and 10-day courses of antibiotic therapy for upper respiratory infections in 2200 children, including patients younger than 2 years (Pichichero et al., submitted for publication). Efficacy rates of the therapeutic courses did not differ as a function of age but were reduced among children who had received a course of antibiotic therapy in the previous month (Figs. 1 and 2). The previous course of antibiotic therapy could signal the occurrence of a recurrent or persistent infection.

TONSILLOPHARYNGITIS

A second pediatric respiratory infection for which

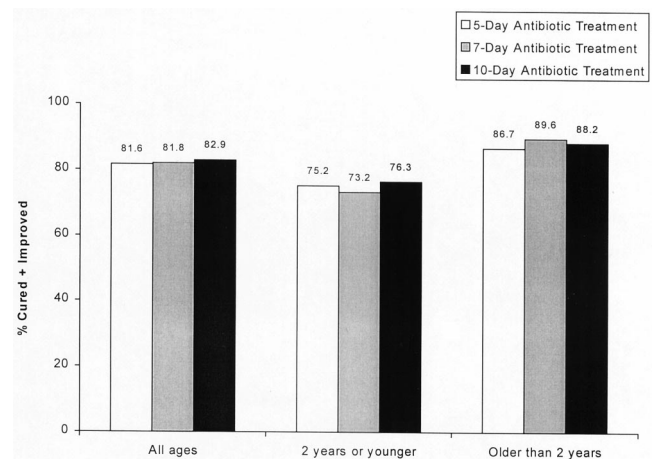


FIG. 1. Clinical efficacy of 5-, 7- and 10-day antibiotic regimens in acute otitis media according to patients' age.

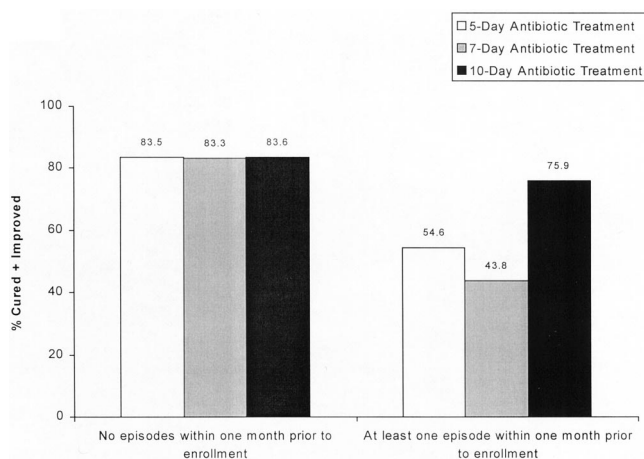


FIG. 2. Clinical efficacy of 5-, 7- and 10-day antibiotic regimens in the treatment of acute otitis media according to the number of prior episodes of acute otitis media.

shortened courses of antibiotics have been evaluated in tonsillopharyngitis. The most common bacterial cause of tonsillopharyngitis is group A beta-hemolytic *Streptococcus*, responsible for 15% of cases.⁵¹ Like acute otitis media, tonsillopharyngitis is often a mild and self-limiting infection; however, the need to prevent spread of infection and progression to complications such as rheumatic fever and toxic shock syndrome dictates the use of antimicrobials to eradicate group A beta-hemolytic *Streptococcus*.^{4, 52} The standard treatment for tonsillopharyngitis in children and adults is 10 days of penicillin therapy, a regimen based on studies conducted primarily in the 1950s and 1960s. This 10-day penicillin therapy is effective in the major-

ity of patients,⁷⁻¹¹ but failure rates of up to 25% have been observed in some countries and patient populations.⁵³⁻⁵⁶

Descriptive analysis of data available through early 1997. A descriptive analysis of data published through early 1997 suggests that courses of penicillin therapy shorter than 10 days are less effective than 10-day regimens for tonsillopharyngitis but that shorter courses of non-penicillin therapy can be as effective as 10 days of penicillin.⁴ The descriptive analysis⁴ of studies published and presented through early 1997 includes trials comparing 10 days of penicillin therapy with amoxicillin^{57, 58} (2 trials; $n = 663$), oral cephalosporins⁵⁹⁻⁶⁹ (11 trials; $n = 2606$) and azithromycin⁷⁰⁻⁷⁴ (5 trials; $n = 1479$) (Table 2). Regardless of the drug class of the penicillin comparator, the shortened course of therapy administered for 4 to 6 days was as or more effective at eradicating causative bacteria than 10 days of penicillin treatment in all studies with the exception of 2 trials^{73, 74} in which a 3-day regimen of azithromycin was used (Table 2).

Post-1997 studies. Two studies^{75, 76} published after completion of this descriptive analysis supplement this evidence by demonstrating that a 5-day course of the cephalosporin cefuroxime axetil is as effective as either a 10-day course of penicillin V or a 10-day course of cefuroxime axetil in pediatric patients with pharyngitis caused by group A beta-hemolytic *Streptococcus*. The demonstration of equivalent efficacy of 5-day course of cefuroxime axetil and a 10-day course of cefuroxime axetil is important, showing that for a given medication, 5- and 10-day courses of therapy have

TABLE 2. Bacteriologic eradication rates (expressed as percent of patients) in studies involving shortened treatment regimens for tonsillopharyngitis

Reference	Study Site, Year of Publication	Shortened Therapy (Drug, Duration)	Longer Therapy (Drug, Duration)
Amoxicillin			
57	United States, 1996	84 (amoxicillin, 6 days)	85 (penicillin, 10 days)
58	France, 1996	92 (amoxicillin, 6 days)	93 (penicillin, 10 days)
Oral cephalosporins			
59	France, 1990	97 (cefepodoxime, 5 days)	94 (penicillin, 10 days)
		80 (cefuroxime, 5 days)	
60	France, 1991	96 (cefuroxime, 4 days)	96 (penicillin, 10 days)
61	Germany, 1991	84 (cefadroxil, 5 days)	88 (penicillin, 10 days)
62	France, 1994	96 (cefepodoxime, 5 days)	94 (penicillin, 10 days)
63	United States, 1994	90 (cefepodoxime, 5 days)	78 (penicillin, 10 days)
		95 (cefepodoxime, 10 days)	
64	France, 1994	94 (cefixime, 4 days)	96 (penicillin, 10 days)
65	United States, 1995	98 (cefepodoxime, 5 days)	91 (penicillin, 10 days)
		91 (cefepodoxime, 10 days)	
66	France, 1995	88 (cefuroxime, 4 days)	87 (penicillin, 10 days)
67	Germany, 1995	83 (cefotiam, 5 days)	88 (penicillin, 10 days)
68	France, 1995	84 (cefixime, 5 days)	84 (penicillin, 10 days)
69	United States, 1996*	90 (cefdinir, 5 days)	72 (penicillin, 10 days)
Azithromycin			
70	United States, 1991	92 (azithromycin, 5 days)	96 (penicillin, 10 days)
71	United Kingdom, 1993	95 (azithromycin, 3 days)	95 (penicillin, 10 days)
72	United States, 1995*	95 (azithromycin, 5 days)	70 (penicillin, 10 days)
73	Italy, 1996†	70 (azithromycin, 3 days)	88 (penicillin, 10 days)
74	Switzerland, 1996†	65 (azithromycin, 3 days)	80 (penicillin, 10 days)

* Shortened therapy statistically superior ($P < 0.05$) to penicillin.

† Shortened therapy statistically inferior ($P < 0.05$) to penicillin.

equivalent efficacy in tonsillopharyngitis. This conclusion cannot be drawn from many of the other pharyngitis studies, which test both different durations of treatment and different drugs. In those studies the relative contributions to the results of different medicines and different durations of therapy are impossible to determine.

ACUTE SINUSITIS

Up to 1 of 20 upper respiratory infections is complicated by bacterial sinusitis,⁷⁷ most often caused by *S. pneumoniae*, *H. influenzae* and *M. catarrhalis*, the primary pathogens also responsible for acute otitis media. Recommendations for optimal treatment duration for acute sinusitis are inconsistent. The 1997 Centers for Disease Control/American Academy of Pediatrics recommendations⁷⁷ advise antimicrobial treatment for no longer than 7 days beyond the onset of substantial improvement (usually a 10- to 14-day course of treatment). The American Academy of Otolaryngology, whose specialist members may be consulted by a high proportion of patients with recurrent or chronic sinusitis, advises 21 days of antimicrobial therapy. The Canadian Medical Association guidelines recommend a 10-day course.⁷⁸

Descriptive analysis of data available through early 1997. Few studies have been undertaken to examine the optimal duration of therapy in acute sinusitis. A descriptive analysis⁴ of acute sinusitis trials published and presented through early 1997 provides preliminary evidence suggesting that ≤ 5 -day courses of therapy are as effective as ≥ 8 -day courses of therapy. Across 6 trials involving 620 patients,^{27, 79-83} clinical or bacteriologic efficacy of various classes of antibiotics was equivalent for 3- to 5-day courses compared with 8- to 10-day courses (Table 3).

Like the acute otitis media and tonsillopharyngitis trials, the sinusitis studies have limitations. First, the trials were limited to patients with maxillary sinusitis. The implications of these data for the treatment of patients with frontal, ethmoidal and sphenoidal sinusitis are unknown. Second, many of the trials did not verify clinical diagnosis of sinusitis with bacteriologic validation using sinus aspirates. Like acute otitis media, sinusitis is overdiagnosed. Spontaneous recovery

of noninfected patients in both short course and long course treatment groups would inflate efficacy rates and tend to mask between group differences in efficacy. Finally, very few children were included in the sinusitis studies.

CONCLUSIONS

The judicious use of antibiotics entails achieving the appropriate balance between prescribing them with sufficient frequency and duration to effect a clinical cure and overprescribing them, a practice that increases prescription drug costs as well as the risks of bacterial resistance, noncompliance with therapy and side effects. The evidence reviewed in this article strongly supports the reduction of the traditional 10-day course of therapy to a 5-day course for uncomplicated cases of acute otitis media in patients at least 2 years of age. This change would reduce by half the antibiotic use among older children and adults for this disease, which in the United States is the most common reason for pediatric patients to receive a prescription.

More research is needed to determine the optimum duration of therapy for acute otitis media in patients younger than 2 years of age, who account for nearly one-third of all acute otitis media patients. Although some studies suggest lower efficacy of shortened courses of therapy compared with traditional therapy in patients less than 2 years old, it would be premature categorically to eliminate these patients from consideration for short course therapy. Few patients less than 2 years old have been included in evaluations conducted to date, and the causes of higher rates of treatment failure in both shortened and traditional therapy have not yet been adequately elucidated.

The evidence demonstrating equivalent efficacy of shortened courses of non-penicillin therapy compared with 10 days of penicillin therapy for tonsillopharyngitis is also strong and consistent, although not as voluminous as that for acute otitis media. Because penicillin remains the standard for treatment for tonsillopharyngitis, short course therapy with non-penicillin agents is likely to be most relevant for community settings and regions of the country where penicillin-resistant bacterial strains are prevalent.

Although the evidence in favor of shortening the

TABLE 3. Bacteriologic eradication rates (expressed as percent of patients) in studies involving shortened treatment regimens for maxillary sinusitis

Reference	Study Site, Year of Publication	Shortened Therapy (Drug, Duration)	Longer Therapy (Drug, Duration)
79	United States, 1995	77 (trimethoprim-sulfamethoxazole, 3 days)	76 (trimethoprim-sulfamethoxazole, 10 days)
27	United Kingdom, 1993*	86 (cefprozime, 5 days)	62 (amoxicillin/clavulanate, 5 days)
80	France, 1995	96 (cefprozime, 5 days)	97 (amoxicillin/clavulanate, 8 days)
81	United Kingdom, 1996	83 (cefprozime, 5 days)	86 (amoxicillin/clavulanate, 8 days)
82	France, 1996	91 (cefprozime, 10 days)	94 (amoxicillin/clavulanate, 10 days)
83	United States, 1991	100 (azithromycin, 5 days)	100 (amoxicillin, 10 days)

* Cefprozime statistically superior ($P < 0.05$) to amoxicillin/clavulanate.

course of antibiotic therapy for acute sinusitis to 5 days or fewer is encouraging, too few data are available to date in children to justify the routine prescription of shortened courses of acute sinusitis therapy in pediatric patients. More research in children as well as in sinusitis types in addition to maxillary sinusitis is needed.

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