# Are Antibiotics Effective Treatment for Acute Bronchitis? A Meta-Analysis

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**BACKGROUND.** Most clinicians prescribe antibiotics for acute bronchitis in spite of recommendations against this practice. Because the results of individual clinical trials have been mixed, we conducted a metaanalysis to determine whether antibiotics are effective treatment for acute bronchitis.

**METHODS.** We conducted a comprehensive search to identify all trials in which patients who had a diagnosis of acute bronchitis were randomly assigned to treatment with an antibiotic or placebo. Patient-oriented outcomes of importance that were reported in at least 3 studies were quantitatively summarized.

**RESULTS.** Nine studies met the inclusion criteria, but not all trials provided data for each outcome. Patients given antibiotics were less likely to have a cough (relative risk [RR] = 0.69; 95% confidence interval [CI], 0.49 - 0.98) and be considered unimproved (RR = 0.51; 95% CI, 0.30 - 0.88) at a follow-up visit; but they were not less likely to have a productive cough (RR = 0.79; 95%

# CLINICAL QUESTION Are antibiotics effective treatment for acute bronchitis?

Antibiotic treatment for acute bronchitis is controversial. Recent studies show the majority of patients who visit a physician for acute bronchitis (65% to 80%) are prescribed antibiotics.<sup>13</sup> Experts, however, generally state that antibiotics are not indicated for acute bronchitis in patients who do not have chronic pulmonary disease,<sup>45</sup> and recent editorials have exhorted physicians to stop prescribing antibiotics for this condition.<sup>67</sup> These recommendations reflect a view that acute bronchitis is a self-limited illness caused mainly by viral pathogens. For the individual patient, unwarranted antibiotic treatment leads to unnecessary

#### Submitted, revised, October 22, 1998.

This paper was presented at the Family Health Foundation of Pennsylvania Eighth Annual Research Day, April 1997; the New York State Academy of Family Physicians Annual Congress, May 1997; the International Conference on Acute Respiratory Infections, July 1997; and the North American Primary Care Research Group 25th Annual Meeting, November 1997.

For a previous written version of this study, see Becker L, Glazier R, McIsaac W, Smucny J. Antibiotics for acute bronchitis. In: Douglas R, Bridges-Webb C, Glasziou P, Lozano J, Steinhoff M, Wang E, eds. Acute respiratory infections module of the Cochrane Database of Systematic Reviews (updated September 1, 1997). The Cochrane Collaboration; Issue 4. Oxford, England: Update Software; 1997.

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CI, 0.60 - 1.03), activity limitations (RR = 0.59; 95% CI, 0.24 - 1.44), or feel ill (RR = 0.70; 95% CI, 0.31 - 1.58). Antibiotic-treated patients had a slightly shorter duration of productive cough (weighted mean difference [WMD] = -0.56 days; 95% CI, -1.09 to -0.04), but not of overall cough (WMD = -0.94; 95% CI, -2.08 to 0.21) or activity limitations (WMD = -0.49; 95% CI, -1.07 to 0.10). Patients treated with antibiotics did not report significantly more adverse effects (RR = 1.47; 95% CI, 0.82 - 2.65).

**CONCLUSIONS.** Antibiotics may be modestly effective for a minority of patients with acute bronchitis. It is not clear which patient subgroups might benefit, and the failure of some studies to report negative findings may have resulted in overestimates of the benefits of antibiotics. Antibiotics are not necessary for every patient with acute bronchitis.

**KEY WORDS.** Acute bronchitis; antibiotics; treatment; meta-analysis. (*J Fam Pract 1998; 47:453-460*)

costs, as well as risks of adverse effects and future infection with resistant bacteria.<sup>89</sup> The increasing prevalence of resistant bacteria is thought to be related to the overprescription of antibiotics, and national efforts are under way to decrease the inappropriate use of antibiotics.<sup>10</sup>

Clinical trials of the effectiveness of antibiotics in treating acute bronchitis have had mixed results. Two descriptive reviews of these trials concluded that antibiotic therapy is generally not supported by the literature because a majority of the trials did not demonstrate antibiotics to be effective.<sup>11,12</sup> Neither review combined data from published studies into a quantitative summary or meta-analysis. Both noted that some trials did demonstrate benefits from antibiotic treatment and therefore suggested that further research was needed. Since these reviews were published, additional trials have indeed been reported.

The studies that have been published thus far have had rather small sample sizes, which can lead to type II errors. A major rationale for conducting a meta-analysis is that the power of the analysis is greater than that of smaller individual studies. Furthermore, as long as individual studies have similar design and methodological quality, a metaanalysis can provide a more accurate measure of the overall effectiveness of an intervention than qualitative reviews that tally how many studies either show or do not show a benefit.13 A meta-analysis also provides a quantitative summary estimate of treatment effect. A recently published meta-analysis of the effectiveness of antibiotics in patients who present with an acute cough did not find significant differences in the risks of productive cough or overall unimprovement after 7 to 11 days of therapy, or any differences in the risks of adverse effects.<sup>14</sup> This study did not examine the overall duration of symptoms or other potentially important outcomes.

We conducted this quantitative overview of all randomized controlled trials of antibiotic treatment for acute bronchitis to answer the question: Are antibiotics effective treatment for acute bronchitis? We specifically wanted to determine whether antibiotics: (1) lead to improved outcomes of clinical importance in otherwise healthy patients with acute bronchitis and, if so, what the magnitude of the treatment effects are; and (2) lead to increased risk of adverse effects that may outweigh any benefits in symptomatic relief.

## **METHODS**

#### **STUDY SELECTION**

We attempted to locate all randomized, controlled, blinded trials published in English that compared antibiotic therapy with placebo in patients with a diagnosis of acute bronchitis. Any trial in which patients either received the diagnosis of acute bronchitis from a physician or had a productive cough without clinical evidence of pneumonia was considered. We excluded studies that included patients with preexisting pulmonary diseases and studies that compared one antibiotic with another or an antibiotic with another active treatment, such as a bronchodilator, unless the trial also included a group of patients who received only placebo.

MEDLINE and EMBASE were searched for studies published between 1966 and 1998 using the MeSH term "bronchitis" together with the terms "randomized controlled trial," "random allocation," "double-blind method," or "single-blind method." Reference lists of relevant trials, review articles, and textbook chapters were examined; and Science Citation Index (SCISEARCH) covering the years 1989 to 1998 was searched to identify any additional studies.

Two of the authors (J.S., L.B.) used the titles and abstracts of identified citations to exclude trials that clearly did not meet the inclusion criteria. Articles that passed this initial screen were then reviewed by 3 authors (J.S., R.G., W.M.) examining only the method section of each paper, without reference to the names of the study authors, the institution, the journal, or the results to determine the study's fit with the inclusion criteria. The same 3 authors then evaluated the methodological quality of each study using an 11-point scoring system adapted from Chalmers et al.<sup>15</sup> Agreement among reviewers was calculated by the kappa statistic<sup>16</sup> and disagreements resolved through discussion and consensus.

#### DATA EXTRACTION AND STATISTICAL ANALYSIS

Three authors (J.S., R.G., W.M.) independently extracted the data from each study to avoid a single interpretation of reported data. Kappa statistics were not calculated for data extraction because some outcome variables were not categorical. We calculated the percent agreement for initial data extraction instead, and resolved differences by discussion and consensus.

After extracting data, we calculated summary outcome measures with 95% confidence intervals using software (Review Manager 3.1.1) provided by the Cochrane Collaboration. Studies were included in the meta-analysis if their outcomes satisfied the following criteria: the outcome is likely to be important to patients and was reported in at least 3 studies. Relative risks (RR) and absolute risk differences (RD) were calculated for dichotomous variables, and weighted mean differences (WMD) were calculated for continuous variables17 using DerSimmonian and Laird formulations for random effects models. Numbers needed to treat (NNT) were estimated as the inverse of the absolute risk differences. Chi-squared tests for heterogeneity of summary outcomes among trials were calculated with Cochran's Q statistic.<sup>17</sup> Statistical significance was defined a priori as P < .05.

## RESULTS

#### INCLUDED STUDIES

Our search strategy yielded 384 citations, of which 9 met our inclusion criteria. The most common reasons for excluding studies were the inclusion of patients with chronic bronchitis or the lack of a placebo group. Characteristics of the trials included in this meta-analysis are presented in Table 1.

Scores for the methodological quality of the selected studies ranged from 7 to 11. All studies were double-blinded and had standardized assessments. The differences in quality scores were due to percent of withdrawals, failure to perform an intention-to-treat analysis, and incomplete descriptions of randomization (Table 1). Agreement among reviewers regarding quality was high (k = 0.71). Agreement among the 3 reviewers for data extraction was also high (>90% initial agreement).

A total of 779 patients were enrolled in the 9 trials. All trials included patients of both sexes, with an overall majority of women (68%). Five trials included only

TABLE 1

Characteristics of	Studies Include	d in Meta-An	alysis of the Effec	tiveness of Antibiotic	s for Acute Bronchitis	
Study	Validity Score	Number of Patients in Study	Antibiotic Regimen	Method of Recording Outcomes	Outcomes Measured	Significant Differences
Stott and West, 1976 (Wales) <sup>23</sup>	10 (-1 for 2% withdrawals)	212	Doxycycline 200 mg on day 1, 100 mg qd for 6-9 days	Daily symptom log and follow-up on day 7	Day cough, night cough, "yellow spit," "clear spit," "off color," runny nose, sore throat, general aches, headache, vomit- ing, off work daily and at follow-up; clinical impres- sion at follow-up; and ill- nesses over next 6 months	Patients receiving antibiotics were less likely to have a runny nose at follow-up or recurrent upper respiratory infections over next 6 months.
Williamson, 1984 (USA) <sup>19</sup>	10 (-1 for 7% withdrawals)	74	Doxycycline 100 mg bid on day 1, 100 mg qd on days 2-7	Daily symptom log (on 10-pt scale) and follow-up on day 7-10	General well-being, bother of cough, night cough, activity limitation, feverish- ness, sputum color daily; doses of antitussives; and clinical impression at fol- low-up	Patients receiving placebo had fewer days of missed work
Scherl et al, 1987 (USA) <sup>25</sup>	7 (-1 for randomization, -3 for 20% withdrawals	39	Doxycycline 100 mg bid on day 1, 100 mg qd on days 2-7	Daily symptom log for 14 days	Cough, sputum, feverish- ness, days missed from work or normal activity, chest pain, dyspnea, side effects	None
Verheij et al, 1994 (Netherlands) <sup>22</sup>	10 (-1 for 11% withdrawals)	158	Doxycycline 200 mg on day 1, 100 mg qd on days 2-10	Daily symptom log and follow-up on day 11	Day cough, night cough, productive cough, feeling ill, impairment of activities, and side effects daily; and clinical impression and auscultatory abnormalities at follow-up	Patients receiving antibiotics had a shorter mean duration of daytime cough and were less likely to have daytime cough and activity impair- ment after 4-5 days, or feel ill at follow-up.
Brickfield et al, 1986 (USA) <sup>20</sup>	9 (-1 for randomization, -1 for 4% withdrawals)	52	Enythromycin 333 mg tid for 7 days	Daily symptom log (on 4-point scale) and follow-up on day 8	Cough, sputum, fever, rhi- norrhea, chest discomfort, earache, sore throat, work disability, feeling ill, and nausea daily; and clinical impression at follow-up	Nonsmokers who received antibiotics had better scores for cough on days 3,5,6; sputum on day 3; headache on day 5; and chest discom- fort on day 6; smokers who received placebo had better scores for headache on day 1 and chest discomfort on days 1-3.
Dunlay, 1987 (USA)21	8 (-3 for 24% withdrawals)	63	Erythromycin 333 mg tid for 10 days	Daily symptom log (present or absent, and on 5-point scale) and follow-up on day 14	Day cough, night cough, sputum production, con- gestion, sore throat, feel- ing poor, activity limitation, and use of cough/cold medications daily; and cough, sputum, and abnormal lung examina- tion at follow-up	Patients receiving antibiotics had better scores on days 6- 10 for sputum production, cold symptoms, general health, and overall symptom mean; used fewer adjunctive medications on day 10; and were less likely to have puru- lent sputum or an abnormal lung exam at follow-up.
Hueston, 1994 (USA) <sup>18</sup>	11	23	Erythromycin 250 mg qid for 10 days	Daily symptom log and follow-up visit on day 7-8	Cough, night cough, abili- ty to perform normal work, and general well- being daily and at follow- up; overall use of over- the-counter medications and side effects; and abnormal lung exam at follow-up	None
King et al, 1996 (USA) <sup>26</sup>	8 (-3 for 26% withdrawals)	91	Erythromycin 250 mg qid for 10 days	Daily symptom log for 14 days	Cough, chest congestion, use of cough medication, general well-being, sleep, and normal activities	Patients receiving antibiotics missed fewer days of work, but had more adverse effects.
Franks and Gleiner, 1984 (USA) <sup>24</sup>	8 (-3 for 19% withdrawals)	67	Trimethoprim/ sulfamethoxazole (160/800) bid for 7 days	Daily symptom log (on a 3- to 5-point scale)	Cough, night cough, spu- turn production, general well-being, fever, work disability, use of adjunc- tive medications, and side effects	Patients receiving antibiotics had lower scores for cough, night cough, temperature, and use of antihistamines or decongestants.



adults,<sup>18-22</sup> 3 included both adolescents and adults,<sup>23-25</sup> and one study included patients aged 8 and older.<sup>26</sup> The mean age across studies varied from 30 years to 44 years. All trials enrolled both smokers and nonsmokers, with 32% to 53% considered current smokers.

All trials defined acute bronchitis as an acute, productive cough without clinical evidence of pneumonia. In 3 trials, the sputum had to appear purulent.<sup>22,23,25</sup> One trial performed chest radiographs on all patients<sup>20</sup>; otherwise, radiographs were performed only if there was clinical suspicion of pneumonia. Additional exclusion criteria included apparent sinusitis,<sup>10,21,22,26</sup> otitis,<sup>26</sup> another known bacterial infection,<sup>25</sup> a chief complaint of coryza or sore throat with minimal sputum,<sup>25</sup> fever > 39.5,<sup>19</sup> and any abnormal finding on chest examination.<sup>21</sup> The duration of cough was generally any amount of time less than 2 weeks, although one trial excluded patients whose cough was present for more than 7 days.<sup>23</sup>

A single antibiotic was compared with placebo in each trial. Four trials used doxycycline,<sup>19,22,23,25</sup> 4 used erythromycin,<sup>18,20,21,26</sup> and one used trimethoprim/sulfamethoxazole.<sup>24</sup> Only 4 trials reported some measure of compliance; in 3, there were no differences in the number of pills taken in the antibiotic and placebo groups,<sup>18,21,23</sup> and in one, 94% of the patients who returned for a follow-up visit took at least one half of their medication.<sup>26</sup> Regarding cointerventions with other medications, 5 trials asked patients to record the use of nonprescription medications and included this as an outcome measure,<sup>18,19,21,24,26</sup> one restricted use to aspirin and acetaminophen but did not have patients record this,<sup>25</sup> and one reported adjunctive prescriptions but not use of over-the-counter medications.<sup>22</sup>

Results of individual trials were mixed (Table 1). Five trials had generally negative results: 3 did not detect any statistically significant improvements from antibiotic therapy;<sup>15,19,25</sup> one demonstrated improvements in only 2 minor outcomes;<sup>22</sup> and in one trial, out of 140 comparisons strati-

fied by smoking status, 6 favored antibiotics (in nonsmokers) and 4 placebo (in smokers).<sup>20</sup> In 2 trials, patients treated with antibiotics had generally better outcomes than those given placebo.<sup>21,24</sup> The remaining 2 trials had mixed results.<sup>22,26</sup>

All trials performed one or more subgroup analyses according to smoking status,<sup>18-26</sup> age,<sup>19,22,25,26</sup> severity or duration of illness,<sup>19,22,23</sup> presence of abnormal physical findings,<sup>19,22,26</sup> gross appearance or gram stain of sputum,<sup>19,24,26</sup> or Mycoplasma pneumoniae IgG/IgM serologies.<sup>26</sup> No patient subgroups were consistently found to benefit from antibiotics, although the power of any individual study to demonstrate significant differences between subgroups was limited because of small sample sizes. Only one trial found a relationship with age or severity of illness - in this study, the only patients who benefited from antibiotics were either older than 55 years or had a very frequent cough and felt ill at entry.<sup>22</sup> One study found that patients who did not have coryza or sore throat had fewer days of cough and sputum production when treated with antibiotics.25 One trial found that patients whose gram stain was abnormal returned to work more quickly if treated with antibiotics.<sup>24</sup> Although none of the trials noted a relationship between duration of illness and benefit from antibiotics, the largest negative study<sup>23</sup> excluded patients who had been coughing for more than 1 week. No trial found that smokers or patients who had purulent sputum derived any more benefit from antibiotics than patients who did not have these characteristics.

#### **META-ANALYSIS**

We found 9 outcomes that we believe are important to patients and that were reported in 3 or more trials. Six of these were dichotomous: activity limitations; feeling ill; a general clinical impression of unimprovement; the presence or absence of a productive cough at the follow-up visit; or the presence or absence of adverse effects at any time during the trial. Three outcomes were continuous: the durations of cough, productive cough, and activity limitations. Two trials reported daytime cough or nighttime cough instead of overall cough, and we included the daytime cough data with the overall cough data reported in other studies. A few authors did not explicitly report data regarding these outcomes if significant differences were not found in their own analyses. We were unable to include the data for cough from one trial<sup>26</sup> or the data for feeling ill from 2 trials.23,26

Summary statistics demonstrated a consistent trend toward improved outcomes in patients who received antibiotics, although significant differences were detected for only a few outcomes (Figure, Table 2). At the time of follow-up, patients treated with antibiotics were less likely to have a cough or be considered unimproved by the examining clinician. The estimate of the number of patients who would need to be treated with antibiotics so that one less would still be coughing at the follow-up visit is 5; to prevent one less patient from being generally unimproved, the NNT is 18. Adverse effects reported in the varjous studies included nausea, vomiting, vaginitis, headache, and skin rash. There was a nonsignificant increase in the incidence of adverse effects in patients treated with antibiotics; the NNT to produce an adverse effect is 14.

Of the 3 indicators of illness for which continuous data is available, there was a significant difference for only mean days of productive cough (Table 2).

Separate analyses were performed for trials that used doxycycline and those that used erythromycin. As compared with patients receiving placebo, patients treated with doxycycline were less likely to feel ill (according to data from one trial) or be assessed as having not improved (3 trials) at the time of follow-up, and had fewer days of productive cough (4 trials). Patients receiving erythromycin had fewer days of impaired activities than those given placebo (1 trial). Subgroup analyses based on patient characteristics were not performed because explicit data were not reported in any study.

# DISCUSSION

This meta-analysis suggests that antibiotics may possibly confer a small benefit in the management of acute bronchitis in patients without underlying pulmonary disease. However, the results must be approached cautiously for a number of reasons.

First, we were unable to combine some of the outcome measures from individual trials in summary statistics. Two trials used unique scales to rate outcomes; both of these demonstrated at least some benefits from antibiotic treatment (Table 1).<sup>2024</sup> Four studies did not explicitly report

TABLE 2

Summary Outcomes from Meta-Analysis of the Effectiveness of Antibiotics for Acute Bronchitis

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		Number of Patients	Patients with	n Outcome,	%	Number Needed to Treat
Outcome	Number of Studies		Antibiotic Group	Placebo Group	Relative Risk (95% CI)	
Cough	4	279	35	53	0.69 (0.49 - 0.98)*	5
Productive cough	5	480	24	31	0.79 (0.60 - 1.03)	20
Activity limitations	3	241	6	10	0.59 (0.24 - 1.44)	53
Feeling ill	3	251	37	45	0.70 (0.31 - 1.58)	12
Unimproved per physician	4	463	7	15	0.51 (0.30 - 0.88)*	18
Adverse effects	6	620	18	12	1.47 (0.82 - 2.65)	14

**DICHOTOMOUS OUTCOMES** 

#### **CONTINUOUS OUTCOMES**

			Weighted Mean	n Duration, days		
Outcome	Number of Studies	Number of Patients	Antibiotic Group	Placebo Group	Weighted Mean Difference, days (95% Cl)	
Cough	4	451	6.3	7.2	-0.94 (-2.08 to 0.21)	
Productive cough	4	442	3.9	4.6	-0.56 (-1.09 to -0.04)*	
Activity limitations	5	393	2.7	3.4	-0.49 (-1.07 to 0.10)	

outcomes that were not statistically significant in their own analyses. We were able to include unpublished data from 2 of these 4 trials. Therefore, the magnitude of the benefit from antibiotics noted for 2 outcomes (cough and feeling ill) may be overestimated. We were able to include data on our other outcomes from all trials that measured them.

Second, our finding of statistically significant differences between antibiotic-treated and placebo-treated patient groups may represent a type I error because we did not adjust for multiple comparisons. If we used the Bonferroni correction (significance level = 0.05 per number of outcomes per analysis), none of the outcomes would be significantly different. However, because it is likely that the outcomes are not independent, we believe that this correction would be overly conversative and feel justified in our choice of statistical significance.

Third, as we have explicitly described, the trials we have included are clinically heterogeneous in terms of selection criteria, choice of antibiotic, and outcome assessment. For this reason, we have reported detailed results of the trials separately, as well as quantitatively summarizing those outcomes reported in more than 3 trials. The differences in the characteristics of the trials represent clinical reality, and we believe that they increase the generalizability of our findings. Furthermore, in spite of the variability among trials, significant statistical heterogeneity was found for only one summary outcome (risk of feeling ill at follow-up), and homogeneity is not assumed when a meta-analysis uses random effects models to derive summary outcomes, as we have done.

In spite of these limitations, we believe that we have provided useful summary information, both qualitatively and quantitatively, that attempts to answer the question of whether antibiotics are effective in managing acute bronchitis. Unfortunately, based on the studies that have been performed thus far, the answer is not clear. Patients treated with antibiotics were less likely to continue to cough and less likely to be unimproved after 1 to 2 weeks of therapy, but significant improvements were not found for other important outcomes. Furthermore, the absolute magnitude of the benefits from antibiotic therapy was slight. Since the majority of patients (85%) who were not treated with antibiotics improved, the estimate of the number of patients who would need to be treated with antibiotics to result in one less patient not improving (18) is more than the number who would need to be treated to result in one more patient having adverse effects from therapy (14). The NNT for one less patient to still be coughing after 1 to 2 weeks of treatment (5) is more favorable. Still, the overall benefit-to-risk ratio seems slight for an individual; and the potential increase in resistant bacteria may not be worth this minimal benefit. Similarly, the only significant difference in mean duration of symptoms was of 1 half-day less of productive cough, which also seems to be minimal.

We agree, in general, with the findings of the other

overviews of the effectiveness of antibiotics in acute bronchitis.<sup>11,12,14</sup> Patients who are treated with antibiotics do not have consistently better outcomes than patients who are given placebo. Therefore, it seems clear that antibiotics should not be prescribed routinely for all patients who present with acute bronchitis. The available evidence, however, does not definitively lead to the conclusion that antibiotics are never useful. Our findings lead us to believe that there may be a minority of patients who might benefit from antibiotics. Unfortunately, the studies conducted to date have not defined that population. Subgroup analyses in individual trials did find some potentially identifiable characteristics, including patients who are older than 55,22 appear more ill,22 or do not have coryza or a sore throat.25 These findings were not consistent among all studies, however.

The effectiveness of antibiotics may be related to the infecting pathogen. The great majority of episodes of acute bronchitis in healthy individuals are presumed to be viral infections, although this has recently been questioned.27.38 Community-based studies have isolated viruses in 8% to 23% of cases.<sup>27,29,30</sup> Other pathogens implicated in acute bronchitis are Mycoplasma pneumoniae, Chlamydia pneumoniae, and Bordetella pertussis, each of which has been identified in 0% to 25% of cases in various populations.<sup>26,27,29-36</sup> Streptococcus pneumoniae, Haemophilus influenzae, and Moraxella catarrhalis have been isolated from sputum samples in up to 45% of patients with acute bronchitis,27,37 but their role is difficult to assess because of the high rates of oropharyngeal colonization in healthy individuals.<sup>38,39</sup> One study has recently shown that antibiotic therapy shortens symptom duration in patients with upper respiratory infections who have these bacteria in nasopharyngeal aspirates.<sup>40</sup> Unfortunately, there are no clinically useful criteria that accurately help distinguish bacterial from viral bronchial infections. Furthermore, even those patients whose bronchitis is bacterial in origin may not necessarily require antibiotics, as is the case with acute otitis media.41

# IMPLICATIONS FOR FURTHER RESEARCH

There have been many more studies conducted comparing the efficacy of one antibiotic with another in the treatment of acute bronchitis than comparing antibiotic with placebo. The clinical success rates (percentages of patients cured and improved) in these comparative trials have ranged from 70% to 100%, and no study has demonstrated any significant differences between antibiotics. Given the 85% spontaneous improvement rate noted in our metaanalysis, and the minimal additional benefit noted from antibiotics, further studies comparing antibiotics with one another do not seem useful. A more preferable strategy would be to evaluate other therapies and, perhaps, compare them with antibiotics. For example, two studies have shown inhaled beta-agonists to be more effective than placebo for acute bronchitis,<sup>18,42</sup> although in one study benefit was noted only for patients with objective evidence of bronchospasm.<sup>42</sup> One study has also shown that patients treated with oral albuterol were less likely to still be coughing after 1 week of therapy than patients treated with erythromycin.<sup>43</sup>

Fortunately, the Ambulatory Sentinel Practice Network is planning a large, 3-arm, multicenter trial in which 720 adults with acute bronchitis will be randomized to an antibiotic, a bronchodilator, or placebo (ASPN Newsletter Supplement, May 1998). This study should help us to more definitively determine whether antibiotics are effective treatment for acute bronchitis, and which patient subgroups, if any, derive the greatest benefit.

#### **RECOMMENDATIONS FOR CLINICAL PRACTICE**

Our meta-analysis suggests that antibiotics are, at best, of modest benefit in the management of acute bronchitis. Antibiotic treatment did lead to improvements in some outcomes, but the magnitude of these was small, and may have been overestimated. Furthermore, the number of patients who need to be treated with antibiotics to lead to symptomatic improvement is comparable to the number who would develop adverse effects from therapy. Therefore, we do not recommend the routine prescription of antibiotics for every patient who has acute bronchitis. However, our meta-analysis is not able to definitively show that antibiotics are totally ineffective. There may be a minority of patients who might benefit from antibiotic therapy, but it is not clear who these patients are. Until the results of the ASPN acute bronchitis trial and other similar trials are available, we recommend that clinicians use this overview to provide their patients with estimates of the risks and benefits from antibiotic treatment, and involve them in the decision-making about the management of this common illness.

#### REFERENCES

- Meza RA, Bridges-Webb C, Sayer GP, Miles DA, Traynor V, Neary S. The management of acute bronchitis in general practice: results from the Australian Morbidity and Treatment Survey, 1990-1991. Aust Fam Physician 1994; 23:1550-3.
- Mainous AG, Zoorab RJ, Hueston WJ. Current management of acute bronchitis in ambulatory care: the use of antibiotics and bronchodilators. Arch Fam Med 1996; 5:79-83.
- Gonzales R, Steiner JF, Sande MA. Antibiotic prescribing for adults with colds, upper respiratory tract infections, and bronchitis by ambulatory care physicians. JAMA 1997; 278:901-4.
- 4. Murray JF, Nadel JA. Textbook of respiratory medicine, 2nd ed. Philadelphia Pa: WB Saunders and Co, 1994.
- Mandell GL, Bennett JE, Dolin R. Mandell, Douglas and Bennett's principles and practice of infectious disease, 4th ed. New York, NY: Churchill Livingstone, 1995.
- 6. Gonzales R, Sande M. What will it take to stop physicians from prescribing antibiotics in acute bronchitis? Lancet 1995; 345:665-6.

- 7. Williamson HA. Treatment of acute bronchitis: there's much work to be done. Arch Fam Med 1996; 5:84-5.
- Arason VA, Kristinsson KG, Sigurdson JA, Stefansdottir G, Molstad S, Gudmundsson S. Do antimicrobials increase the carriage rate of penicillin resistant pneumococci in children? Cross-sectional prevalence study. BMJ 1996; 313:387-91.
- 9. Doone JL, Klespies SL, Sabella C. Risk factors for penicillinresistant systemic pneumococcal infections in children. Clin Pediatrics 1997; 36:187-91.
- Jernigan DB, Cetron MS, Breiman RF. Minimizing the impact of drug-resistant *Streptococcus pneumoniae* (DRSP). JAMA 1996; 275:206-9.
- Orr PH, Scherer K, Macdonald A, Moffatt MEK. Randomized placebo-controlled trials of antibiotics for acute bronchitis: a critical review of the literature. J Fam Pract 1993; 36:507-12.
- MacKay DN. Treatment of acute bronchitis in adults without underlying lung disease. J Gen Intern Med 1996; 11:557-62.
- Oxman AD, Cook DJ, Guyatt GH. User's guides to the medical literature. VI. How to use an overview. JAMA 1994; 272:1367-71.
- Fahey T, Stocks N, Thomas T. Quantitative systematic review of randomised controlled trials comparing antibiotic with placebo for acute cough in adults. BMJ 1998; 316:906-10.
- Chalmers I, Adams M, Dickersin K, et al. A cohort study of summary reports of controlled trials. JAMA 1990; 263:1401-5.
- Holman CDJ. Analysis of interobserver variation on a programmable calculator. Am J Epidemiol 1984; 129:154-60.
- Rothman KJ. Modern epidemiology. Boston, Mass: Little, Brown and Company, 1986.
- Hueston WJ. Albuterol delivered by metered-dose inhaler to treat acute bronchitis. J Fam Pract 1994; 39:437-40.
- Williamson HA. A randomized, controlled trial of doxycycline in the treatment of acute bronchitis. J Fam Pract 1984; 19:481-6.
- Brickfield FX, Carter WH, Johnson RE. Erythromycin in the treatment of acute bronchitis in a community practice. J Fam Pract 1986; 23:119-22.
- Dunlay J, Reinhardt R, Roi LD. A placebo-controlled, double-blind trial of erythromycin in adults with acute bronchitis. J Fam Pract 1987; 25:137-41.
- Verheij TJM, Hermans J, Mulder JD. Effects of doxycycline in patients with acute cough and purulent sputum: a double blind placebo controlled trial. Br J Gen Pract 1994; 44:400-4.
- Stott NCH, West RR. Randomised controlled trial of antibiotics in patients with cough and purulent sputum. BMJ 1976; 2:556-9.
- Franks P, Gleiner JA. The treatment of acute bronchitis with trimethoprim and sulfamethoxazole. J Fam Pract 1984; 19:185-90.
- Scherl ER, Riegler SL, Cooper JK. Doxycycline in acute bronchitis: a randomized double-blind trial. J Kentucky Med Assoc 1987; 85:539-41.
- King DE, Williams WC, Bishop L, Shechter A. Effectiveness of erythromycin in the treatment of acute bronchitis. J Fam Pract 1996; 42:601-5.
- Macfarlane JT, Colville A, Guion A, Macfarlane RM, Rose DH. Prospective study of aetiology and outcome of adult lower-respiratory-tract infections in the community. Lancet 1993; 341:511-4.
- Macfarlane J, Prewett J, Guion A, Gard P. Community acquired lower respiratory tract infection: bacterial infection not uncommon (letter). BMJ 1994; 308:1239.
- Stuart-Harris CH, Andrewes C, Andrews BE, Beale AJ, Gardner PS, Grist NR, et al. A collaborative study of the aetiology of acute respiratory infections in Britain 1961-4.

BMJ 1965; 29:319-26.

- Boldy DAR, Skidmore SJ, Ayres JG. Acute bronchitis in the community: clinical features, infective factors, changes in pulmonary function and bronchial reactivity to histamine. Respir Med 1990; 84:377-85.
- Foy HM. Infections caused by Mycoplasma pneumoniae and possible carrier state in different populations of patients. Clin Infect Dis 1993; 17(suppl 1):S37-46.
- 32. Grayston JT, Aldous MB, Easton A, Wang SP, Kuo CC, Campbell LA, et al. Evidence that *Chlamydia pneumoniae* causes pneumonia and bronchitis. J Infect Dis 1993; 168:1231-5.
- Falck G, Heyman L, Gnarpe J, Gnarpe H. Chlamydia pneumoniae (TWAR): a common agent in acute bronchitis. Scand J Infect Dis 1994; 26:179-87.
- 34. Thom DH, Grayston JT, Campbell LA, Kuo CC, Diwan VK, Wang SP. Respiratory infection with Chlamydia pneumoniae in middle-aged and older adult outpatients. Eur J Clin Microbiol Infect Dis 1994; 13:785-92.
- 35. Robertson PW, Goldberg H, Jarvie BH, Smith DD, Whybin LR. *Bordetella pertussis* infection: a cause of persistent

cough in adults. Med J Aust 1987; 146:522-5.

- Herwaldt LA. Pertussis in adults: what physicians need to know. Arch Intern Med 1991; 151:1510-12.
- 37. Henry D, Ruoff GE, Rhudy J, et al. Effectiveness of shortcourse therapy (5 days) with cefuroxime axetil in treatment of secondary bacterial infections of acute bronchitis. Antimicrob Agents Chemother 1995; 39:2528-34.
- Laurenzi GA, Potter RT, Kass EH. Bacteriologic flora of the lower respiratory tract. N Engl J Med 1961; 265:1273-8.
- Smith JMB, Lockwood BM. Commensal or pathogen? The growing dilemma facing the general practitioner. NZ Med J 1986; 99:242-3.
- Kaiser L, Lew D, Hirschel B, et al. Effects of antibiotic treatment in the subset of common-cold patients who have bacteria in nasopharyngeal secretions. Lancet 1996; 347:1507-10.
- Del Mar C, Glasziou P, Hayem M. Are antibiotics indicated as initial treatment for children with acute otitis media? A metaanalysis. BMJ 1997; 314:1526-9.
- Melbye H, Aasebo U, Straume B. Symptomatic effect of inhaled fenoterol in acute bronchitis: a placebo-controlled double-blind study. Fam Pract 1991; 8:216-22.

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