

programmes. Even in their own restricted terms, an intelligent marketplace should see this effort as an investment.

*The Lancet*

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## COMMENTARY

## What will it take to stop physicians from prescribing antibiotics in acute bronchitis?

Acute bronchitis, in general, refers to the acute or subacute onset of productive cough in a patient with no history of chronic pulmonary disease, and without evidence of pneumonia or sinusitis. Patients vary in the degree of purulence, fever, and associated symptoms they report. Treatment remains controversial. Over the past 20 years there have been several randomised controlled trials of the effect of antibiotics in uncomplicated acute bronchitis. Four trials reported no benefit of tetracycline, doxycycline, or erythromycin.<sup>1-4</sup> In an evaluation of methodological rigour and internal validity of all randomised controlled trials of antibiotics for acute bronchitis before 1993, the two doxycycline studies scored best.<sup>5</sup> Major endpoints included duration of cough, sputum, and loss of work. In the two trials reporting a benefit of antibiotics, erythromycin was used in one and co-trimoxazole in the other.<sup>6,7</sup> Both studies had low scores for internal validity from small sample size, possible contamination with other treatment measures, and poor assessment of patient compliance.<sup>5</sup> For example, in the trial of co-trimoxazole *vs* placebo, the investigators did not do intention-to-treat analyses.<sup>6</sup> Furthermore, the positive effects reported as significantly different from placebo were of little clinical relevance—eg, the reporting of mean symptom scores for sputum production being statistically different on the sixth day but not on the seventh or eighth days, or of a decrease in mean temperature after seven days from 37.3°C to 36.9°C.<sup>6,7</sup>

Verheij and colleagues<sup>8</sup> now report a double-blinded placebo-controlled trial of doxycycline in patients with acute bronchitis from twenty-two practices in the Netherlands. They conclude that doxycycline has clinically relevant effects in patients over the age of 55 who cough very frequently and who also feel ill. One serious problem with this conclusion is that there was a significantly greater difference (90% *vs* 77%) in the number of patients randomised to the doxycycline group who felt ill at entry to the study, and therefore were more likely to report improvement. Moreover, about 30% of all patients had abnormalities on chest auscultation. These findings suggest that some of the patients who benefited from doxycycline might have had conditions other than acute bronchitis that would benefit from antibiotic treatment—eg, atypical pneumonia or chronic bronchitis.

Despite sufficient data (now 7 randomised double-blind studies) showing no major clinical role for antibiotics in uncomplicated acute bronchitis, practitioners continue to prescribe these drugs at an alarming rate. Physician surveys indicate that 50–70% of

patients fulfilling criteria for “acute bronchitis” will leave their physician’s office with a prescription for antibiotics in hand.<sup>6,9,10</sup> This practice persists in an era when antibiotic-resistant strains of common pathogens such as *Streptococcus pneumoniae* and *Haemophilus influenzae* are emerging with disturbing sensitivity profiles.<sup>11-13</sup>

If we believe that the risks of antibiotic-resistant strains of bacteria and the risk for serious adverse side-effects outweigh the benefits of antibiotics in most patients we diagnose with acute bronchitis, then we need to focus more attention on ways of changing this prescribing habit. Contributory factors include erroneous physician beliefs—eg, when a patient’s history that “I’ve had this cough for a week, and now my phlegm has turned green” is translated into “this patient needs antibiotics”. Likewise, many physicians tend to prescribe antibiotics when fever or a smoking history is reported, or in hope of preventing potential progression to pneumonia despite the lack of data supporting these views. The patient-physician encounter is further complicated by frequent patient demands for antibiotics as their only cure. In one survey of patients in an ambulatory practice setting, as many as 60% of eligible patients refused entry to a randomised controlled trial of antibiotics because they felt antibiotics were absolutely necessary for their condition to improve.<sup>4</sup> The combination of fixed patient expectations and pressures on physicians to limit appointment times has encouraged antibiotic prescribing as the path of least resistance.

Devising a method to improve the existing pattern of managing acute bronchitis will be challenging. Merely beckoning physicians to “do no harm” is likely to fail. The optimum strategy will require efforts to educate patients as well as physicians about the natural history of this seasonal nemesis, backed up by reassurance to both parties that antibiotics will not alter the disease course. In our opinion antibiotics are never warranted in acute bronchitis. The potential benefits, at best, are negligible and the societal costs are great.

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As in the Manchester clinic, our referral pattern has also changed, with less than 10% of boys being referred from the orthopaedic team (pre-1990 it was 33%). One explanation for this change in referral pattern has been the (invaluable) development and expansion of community paediatric services, to which children are initially referred by their general practitioners, health visitor, and parents themselves. The provision of these services should (and does, in our experience) facilitate an earlier diagnosis of DMD. Finally, all mothers of the boys in whom the diagnosis had been delayed for more than 12 months stated that "no one listened to me".

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- 1 Fenton-May J, Bradley DM, Sibert JR, et al. Screening for Duchenne muscular dystrophy. *Arch Dis Child* 1994; 70: 551-52.
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## Antibiotics in acute bronchitis

SIR—In their March 18 commentary Gonzales and Sande complain that physicians still prescribe antibiotics in patients with acute bronchitis. As my colleagues and I have stated previously, we think that physicians should be very selective in their prescribing of antibiotics in these patients.<sup>1</sup> In our clinical trial of doxycycline in patients with cough, we concluded that the differences found between effects of doxycycline and placebo did not justify antibiotic treatment for all patients with an acute cough and purulent sputum.<sup>2</sup> But I doubt whether antibiotics are never warranted in patients with acute bronchitis, as Gonzales and Sande suggest. In our trial we identified two subgroups of patients (not one as Gonzales and Sande state) in which the differences between doxycycline and placebo were more evident than in the whole group—namely, patients over 54 years of age and patients who coughed very frequently and felt ill at entry.

Gonzales and Sande think that the difference in numbers of patients feeling ill at entry between the doxycycline group and the placebo group could have biased our results. However, in these two subgroups there were no differences between those receiving doxycycline and those allocated to placebo, including feeling ill. Our findings are in concurrence with those of Macfarlane and colleagues<sup>3</sup> reporting significantly more bacterial pathogens in persons over 55 with a low-airway infection than in younger patients. Gonzales and Sande also say that some of our patients might have had conditions other than acute bronchitis because 30% of all patients had abnormalities on chest auscultation. Although all participating doctors were instructed in how to exclude subjects with signs and symptoms of pneumonia and asthma, we do accept some uncertainty, consistent with standard clinical practice. However, having monitored our patients for three months after entry, we do not think that we included many patients with pneumonia or asthma. Very few physicians, especially in primary care, will request additional examinations such as radiography or bacterial tests in every patient with auscultatory abnormalities.

Whether the differences in certain subgroups of patients in our trial (4 days less coughing and 2 days less work-loss) are reasons for the physician and the patient to decide in favour of an antibiotic will depend on several personal and circumstantial factors. Therefore we conclude that in patients over 54 years of age and in those who cough very frequently throughout the day and feel ill, the advantages of

antibiotics might outweigh the disadvantages. Certainly more research should be done to confirm our findings. Until then physicians should refrain as much as possible from prescribing antibiotics in acute bronchitis.

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- 1 Verheij TJM, Hermans J, Kaptein AA, Mulder JD. Acute bronchitis: general practitioners' views regarding diagnosis and treatment. *Fam Pract* 1990; 7: 175-80.
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SIR—General practitioners who question the need for many of the antibiotics we find ourselves prescribing will be only too familiar with the dilemma described by Gonzales and Sande. Even when the doctor doubts the validity of antibiotic prescriptions in such minor conditions, 40 years of doctor behaviour are even less easily unlearned by patients than by doctors, especially when one's colleagues (both in general practice and in hospital) continue to reinforce the lesson. Furthermore, patients who are prescribed an antibiotic at a week into one episode of bronchitis frequently appear on the first day next time "to nip it in the bud, doctor", so impressive is the perceived effect of a prescribed medicine.

A suitable compromise that seems to satisfy patients and is acceptable to less therapeutically nihilistic colleagues is to give the patient an "if prescription". This is a prescription for an antibiotic that the patient is instructed not to get dispensed unless the symptoms have not improved in (say) 4 days. The doctor will suggest some measures for the symptoms and explain that most such infections will have resolved or improved within this time, and that antibiotics are only needed for those that do not resolve. The actual waiting period will depend on the severity of the illness, the duration so far, the patient's perceived readiness to accept the advice, and (not least) the doctor's nerve. Not only does this teach patients and doctors about the value of antibiotics in this condition, but it also empowers the patient, and might even reduce subsequent consultations for this condition. Prescriptions do not in themselves cause adverse effects or antibiotic resistance; it is only the administration of the drug that carries this risk.

I have used the "if prescription" in patients with otitis media and acute bronchitis. One of my partners has also taken up the idea. Anecdotally I know that some prescriptions are not dispensed. I have a controlled clinical trial planned in our practice to establish how many patients with otitis media do wait before getting them dispensed. It would be interesting to conduct a similar study with acute bronchitis.

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SIR—Although I agree with Gonzales and Sande that antibiotics are overprescribed for acute bronchitis, I am not convinced that there are sufficient data to conclude that antibiotic treatment is of no benefit. Existing studies have low power to exclude a clinically meaningful effect of antibiotics in subtypes of bronchitis, they do not address newly described atypical pathogens, and they do not include as outcomes possible long-term sequelae of acute bronchitis.

With respect to power to exclude an effect, the six randomised trials reviewed by Orr and colleagues<sup>1</sup> and cited

by Gonzales and Sande included a total of 1297 patients, and the four recent trials each enrolled an average of only 64 patients (range 52-74). As regards newly described atypical pathogens, *Chlamydia pneumoniae* is responsible for between 5%<sup>2</sup> and 25%<sup>3</sup> of acute bronchitis, depending on the geographic area. *C pneumoniae* bronchitis does not usually respond to traditional (7-10 day) courses of antibiotics but requires 3 weeks or more of continuous treatment for resolution.<sup>4</sup> Finally, untreated or insufficiently treated acute bronchitis due to *C pneumoniae* has been implicated in the development of subsequent asthma, which might have been prevented by appropriate treatment during the acute phase of respiratory illness.<sup>5</sup>

Thus, although I appreciate the concerns of Gonzales and Sande about emerging antibiotic-resistant strains and adverse side-effects caused by inappropriate antibiotic prescriptions for acute bronchitis, I think their conclusion that antibiotics are never warranted is not justified by the existing evidence. What will it take to stop physicians from prescribing antibiotics in acute bronchitis? (Or as I would state it, "what will it take to guide appropriate prescription of antibiotics in acute bronchitis?") The answer is: better data.

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