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".

Richard E Appleton, Paola Nicolaides
Regional Paediatric Neuromuscular Clinic, Royal Liverpool Children's NHS Trust (Alder Hey), Liverpool L12 2AP, UK

1 Fenton-May J, Bradley DM, Sibert JR, et al. Screening for Duchenne muscular dystrophy. *Arch Dis Child* 1994; **70:** 551–52.
2 Gardner-Medwin D. Recognising and preventing Duchenne muscular dystrophy. *BMJ* 1993; **287:** 1083–84.

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.[1] 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.[2] 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[3] 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.

Theo Verheij
Department of General Practice, State University of Leiden, PO Box 2088, 2301 CB Leiden, Netherlands

1 Verheij TJM, Hermans J, Kaptein AA, Mulder JD. Acute bronchitis: general practitioners' views regarding diagnosis and treatment. *Fam Pract* 1990; **7:** 175–80.
2 Verheij TJM, Hermans J, Mulder JD. Effects of doxycyline in patients with acute cough and purulent sputum: a double blind placebo controlled trial. *Br J Gen Pract* 1994; **44:** 400–04.
3 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:** 511–14.

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.

Arnold Zermansky
Dib Lane Practice, Leeds LS8 3AY, UK

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[1] 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%[2] and 25%[3] 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.[4] 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.[5]

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.

David L Hahn
Dean Medical Center, Arcand Park Clinic, 3434 E Washington Avenue, Madison, WI 53704, USA

1 Orr PH, Scherer K, MacDonald A, et al. Randomized placebo-controlled trials of antibiotics for acute bronchitis: a critical review of the literature. *J Fam Pract* 1993; **36:** 507–12.
2 Grayston JT, Kuo C-C, Wang S-P, et al. A new *Chlamydia psittaci* strain, TWAR, isolated in acute respiratory tract infections. *N Engl J Med* 1986; **315:** 161–68.
3 Falck G, Heyman L, Gnarpe J, et al. *Chlamydia pneumoniae* (TWAR): a common agent in acute bronchitis. *Scand J Infect Dis* 1994; **26:** 179–87.
4 Thom DH, Grayston JT. *Chlamydia pneumoniae* strain TWAR infections: descriptions, diagnosis, and treatment. *Mediguide Infect Dis* 1990; **10:** 1–4.
5 Hahn DL. Acute asthmatic bronchitis: a new twist to an old problem. *J Fam Pract* 1994; **39:** 431–35.

Vitamin K prophylaxis in high-dose chemotherapy

SIR—The complications of intensive chemotherapy include haemostatic abnormalities.[1] We find that many patients on high-dose chemotherapy for lymphoma or myeloma test positively for the prothrombin precursor PIVKA II (proteins induced by vitamin K absence or antagonism). PIVKA II is found in patients in whom the γ-carboxylation of vitamin-K-dependent clotting precursors is inhibited by antagonists such as warfarin or by nutritional vitamin K deficiency.[2] We randomised patients undergoing autologous bone marrow transplantation to receive weekly 10 mg intravenous vitamin K supplementation (Konakion) (n=9) over the four week transplant period or to receive no extra vitamin K (n=10). PIVKA II, measured by a sensitive and specific immunochemical assay, was detected in only 2 patients given vitamin K compared with 7 who did not receive supplements ($p<0.05$). Plasma vitamin K_1 levels reflect the effect of supplementation: patients whose vitamin K had dropped below the normal range after chemotherapy were maintained within or above this range after starting supplementation, in contrast to non-supplemented individuals ($p<0.01$).

Aberrations in the vitamin-K-dependent anticoagulant proteins C and S have been noted in patients receiving high-dose chemotherapy for breast cancer, and this may increase the risk of thrombosis.[3] In our patient group not receiving vitamin K supplementation the tendency toward disturbed hepatic production of haemostatic regulators was demonstrated by a fall in factor VII levels and in protein C levels shortly after bone marrow transplantation. Vitamin K administration began one week post-transplant in the group receiving supplementation when patients had previously been noted to have the lowest plasma levels. There was no significant difference in factor VII level between the patient groups at this time, but by week 3 the mean change in the supplemented group (+15%) was significantly different from that in the non-supplemented group (–17·9%) ($p<0.05$).

We conclude that the stress of high-dose chemotherapy (which apart from affecting appetite is also likely to impair the intestinal absorption and hepatic metabolism of vitamin K) may precipitate at least a temporary state of vitamin K deficiency. This vitamin-K-deficient state may be prevented by the weekly intravenous administration of 10 mg vitamin K.

**T N Elston, J M Dudley, M J Shearer, S A Schey*
Guy's Hospital, St Thomas Street, London SE1 9RT, UK

1 Ruiz MA, Marugan I, Estelles A, et al. The influence of chemotherapy on plasma coagulation and fibrinolytic systems in lung cancer patients. *Cancer* 1989; **63:** 643–48.
2 Shearer MJ. Vitamin K. *Lancet* 1995; **345:** 229–34.
3 Rogers JS, Murgo AJ, Fontana JA, Raich PC. Chemotherapy for breast cancer decreases plasma protein C and protein S. *J Clin Oncol* 1988; **6:** 276–81.

Invasive pneumococcal infections in children

SIR—Baer and colleagues (March 11, p 661) ask whether the recent increase of invasive pneumococcal infections in Finnish children might be related to the disappearance of *Haemophilus influenzae* type b (Hib) disease. The role of Hib conjugate vaccines in eliminating invasive Hib disease is indeed impressive,[1] and we share their hope that in the future pneumococcal conjugate vaccines will have a similar impact.

Baer and colleagues would, we are sure, agree that association does not prove causation. We assume that in their report of increased bacteraemic pneumococcal infections they have ruled out confounding variables such as changes in population size, paediatricians' criteria for blood cultures in febrile children, and culture techniques for pneumococci. Importantly, can we be sure that the increase is not due to an outbreak of a particular pneumococcal serotype as was recorded in Iceland several years ago?[2] That outbreak also arose in the context of Hib elimination by a vaccine programme, and so provides another possible example of upsurge in pneumococcal isolates in the Tampere region typed? Also, were carriage studies done, and did any particular pneumococcal serotype become more prevalent after the introduction of Hib vaccines? We note that another Finnish study (to which Baer and colleagues refer) showed no change in pneumococcal carriage rates among recipients of Hib vaccines. This does not support Baer's notion that Hib is being replaced by pneumococcus in the nasopharynx.

The possible replacement of one bacteria by another in the nasopharynx has long been known. In the 1950s, May showed that the isolation rate of pneumococci in adults with chronic bronchitis varied considerably from year to year and was inversely proportional to the isolation rate of *H influenzae*.[3] He speculated that a heavy growth of pneumococci might suppress *H influenzae* in culture. Later, on the basis of further data, he and Turk argued that the antagonism between these species might arise in the patient as well as in the laboratory.[4]