however, overcome many of the problems associated with relying solely on published data and some of the problems associated with relying on aggregate data and will add to the analyses that can be performed. It might therefore provide the "gold standard" to which systematic reviews should strive.[15]

Which steps in the process are the most important for improving reliability requires further testing and evidence, especially if some of these steps lengthen the time needed to conduct the meta-analysis but do not greatly improve its reliability. To this end, some of the topics for consideration would be the use of trials from which individual patient data are not available but published data are and of trials in which the individual patient data reveal problems (such as the inappropriate exclusion of some patients and the subsequent destruction of their relevant records) that cannot be rectified.

Just as different forms of health care need to be reliably assessed, so the techniques for reviewing evidence from randomised controlled trials should be empirically investigated.

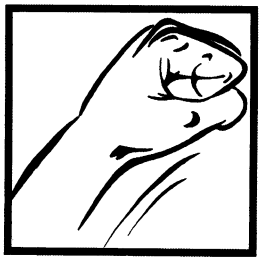
1 Peto R, Collins R, Gray R. Large scale randomized evidence: large, simple trials and overviews of trials. *Ann N Y Acad Sci* 1993;**703**:314-40.
2 Chalmers I. The Cochrane Collaboration: preparing, maintaining, and disseminating systematic reviews of the effects of health care. *Ann N Y Acad Sci* 1933;**703**:156-65.
3 Review of mortality results in randomised trials in early breast cancer. *Lancet* 1984;ii:1205.
4 Early Breast Cancer Trialists' Collaborative Group. Systematic treatment of early breast cancer by hormonal, cytotoxic or immune therapy: 133 randomised trials involving 31,000 recurrences and 24,000 deaths among 75,000 women. *Lancet* 1992;**339**:1-15. 71-85.
5 Stewart LA, Pignon JP, Arriagada R, Souhami RI, on behalf of the NSCLC Collaborative Group. A meta-analysis using individual patient data from randomised clinical trials of chemotherapy in non-small cell lung cancer. I. Survival in the surgical setting [abstract]. *Proceedings of the American Society of Clinical Oncology* 1994;**13**:336.
6 Stewart LA, Parmar MKB. Meta-analysis of the literature or of individual patient data: is there a difference? *Lancet* 1993;**341**:418-22.
7 Pignon JP, Arriagada R. Meta-analysis. *Lancet* 1993;**341**:964-5.
8 Dickersin K, Scherer R, Lefebvre C. Identification of relevant studies for systematic reviews. *BMJ* (in press).
9 Simes J. Publication bias: the case for an international registry of clinical trials. *J Clin Oncol* 1986;**4**:1529-41.
10 Gregory WM, Richards MA, Malpas JS. Combination chemotherapy versus melphalan and prednisolone in the treatment of multiple myeloma: an overview of published trials. *J Clin Oncol* 1992;**10**:334-42.
11 Advanced Ovarian Cancer Trialists Group. Chemotherapy in advanced ovarian cancer: an overview of randomised clinical trials. *BMJ* 1991;**303**: 884-9.
12 Peto R, Pike M, Armitage P, Breslow NE, Cox DR, Howard SV, *et al.* Design and analysis of randomised clinical trials requiring prolonged observation of each patient. I. Introduction and design. *Br J Cancer* 1976;**34**:585-612.
13 Hoover HC, Brandhorst JS, Peters LC, Surdyke MG, Takeshita Y, Madariaga J, *et al.* Adjuvant active specific immunotherapy for human colorectal cancer: 6·5-year median follow-up of a phase II prospectively randomised trial. *J Clin Oncol* 1993;**11**:390-9.
14 Hoover HC, Surdyke MG, Dangel RB, Peters LC, Hanna MG. Prospectively randomised trial of adjuvant active-specific immunotherapy for human colerectal cancer. *Cancer* 1985;**55**:1236-43.
15 What's wrong with the BMJ [editor's choice]. *BMJ* 1994 January 8;**308**:i.

Controversies in Management

Are antibiotics appropriate for sore throats?

Costs outweigh the benefits

P S Little, I Williamson



This is the seventh in a series of articles examining some of the difficult decisions that arise in medicine

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General practitioners prescribe antibiotics for sore throat for various reasons including to prevent complications (rheumatic fever, glomerulonephritis, sinusitis, otitis media, etc), to relieve symptoms, and for psychosocial reasons. However, the benefit is marginal and the costs are great.

Do antibiotics prevent complications?

Studies on the prevention of rheumatic fever were carried out using penicillin injections in military personnel in barracks after the second world war.[1] The attack rates were high (0·3-5%), and the results may not be generalisable to a modern community setting with lower attack rates and where the likelihood of developing rheumatic fever or glomerulonephritis is the same in those who have and have not had oral antibiotics.[2,3] The incidence of rheumatic fever has been falling since the turn of the century—well before antibiotics were discovered.[4] General practitioners in Britain have about a one in five chance of ever seeing a patient with either post-streptococcal glomerulonephritis or rheumatic fever after a sore throat.[2,3]

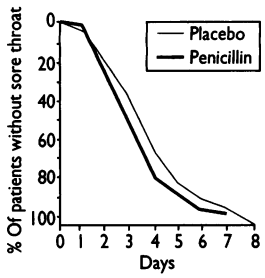
The main problem of prescribing to prevent these problems is that most patients with sore throat never attend their general practitioner.[2,3,5] Even if the benefit of oral antibiotics in the community were proved general practitioners' surgeries would need to be overwhelmed with patients or antibiotics would need to be freely available in the community to prevent such complications effectively.

Some evidence exists for a small protective effect of antibiotics on the development of otitis media and sinusitis.[1] However, these studies are old, included small numbers of complications, and were mainly conducted in institutionalised servicemen. Studies in general practice had very wide confidence intervals for the odds ratio for developing complications (greatly overlapping 1 for prevention of otitis media).[6,7] Thus it seems doubtful whether oral antibiotics prevent suppurative complications of sore throat. Even if large modern studies supported these results at least 29 subjects with sore throat would have to be treated to prevent one case of otitis media,[1] which is usually a self limiting condition.

Other reasons for prescribing

The evidence for relief of symptoms in sore throat is also marginal. Results from the few placebo controlled trials in general practice suggest there may be a small increase in the number of patients well after three days among those taking penicillin.[1] However, the largest trial (n=528) showed this benefit for only a small subgroup of the study population.[8] Furthermore, the illness was not shortened at all irrespective of initial presentation with fever, purulent tonsils, or lymphadenitis (figure).

Psychosocial factors for both the doctor and the patient are important determinants of prescribing,[9,10] and it is important to acknowlege and explore them. General practitioners probably perceive more pressure to prescribe than exists, since 41% of patients entering consultations expect a prescription but 67% leave with one.[11] Even if patients receive an antibiotic for sore throat a 10 day course would be needed to eradicate streptococci, and the evidence suggests that only half of children complete such a course.[12] An uncontrolled



Percentage of patients without symptoms after presenting to a general practitioner with sore throat and being randomised to penicillin (n=256) or placebo (n=272). Reproduced from Whitfield and Hughes[8] with permission

report of the acceptability of no antibiotic treatment in otitis media[13] and a controlled trial of no antibiotic prescription with advice in sore throat[14] indicate that most patients will find explanation and treatment of symptoms an acceptable alternative even in painful upper respiratory conditions.

Could a subgroup be targeted to improve outcome?

Given that the evidence for antibiotic prescribing in sore throat is not good for the normal range of presentations, could particular subgroups be identified? Unfortunately symptom clusters do not seem to be a good indicator of streptococcal infection or antibiotic responses, and the sensitivity and specificity of the throat swab are low—26-30% and 73-80% respectively.[15] Although a rise in streptococcal antibody titres would be definitive, the delay, cost, and inconvenience of serial titres rule out their routine use.

Costs of prescribing

The probable marginal benefit of prescribing in sore throat must be weighed against the possible costs. Routine prescribing for sore throat encourages patients' dependence and reattendance at surgery,[14] taking up valuable time of the doctor and the patient for a self limiting condition. In addition there are financial costs to the patient, surgery, and health service and side effects of antibiotic use such as allergy (3·8%),[16] and diarrhoea (10% to 60% of children).[17,18] The estimated incidence of anaphylaxis with penicillin is 1·5-4 cases per 10 000 patients with two deaths per 100 000.[16] If every case of acute pharyngitis and acute exudative tonsillitis were treated with penicillin—that is, about 500 cases per general practitioner per year[19]—in the average working lifetime a general practitioner would have roughly a one in three chance of having a patient die from anaphylaxis after treatment for sore throat. This is slightly higher than the chances of nephritis or rheumatic fever after a sore throat, neither of which have a high death rate.

We argue that the evidence for benefit of prescribing for sore throat is marginal, and the costs to the patient and health service are likely to outweigh any possible benefit. Until evidence for the use of antibiotics in sore throat comes from randomised clinical trials, general practitioners should continue to explore the psychosocial reasons behind consultations and negotiate with their patients to improve the management of the symptoms of sore throat without relying on antibiotics.

1 Del Mar C. Managing sore throat: a literature review II. Do antibiotics confer benefit? *Med J Aust* 1992;156:644-9.
2 Howie J, Foggo B. Antibiotics, sore throat and rheumatic fever. *J R Coll Gen Pract* 1985;35:223-4.
3 Taylor JL, Howie J. Antibiotics, sore throat and acute nephritis. *J R Coll Gen Pract* 1983;33:783-6.
4 White P. Changes in the prevalence of various types of heart disease in New England. *JAMA* 1953;33:783-6.
5 Banks M, Beresford S, Morrell D, Waller J, Watkins C. Factors influencing the demand for primary care in women aged 20-64 years: a preliminary report. *Int J Epidemiol* 1985;4:189-95.
6 Chappie PAL, Franklin LM, Paulett JD. Treatment of acute sore throat in general practice. Therapeutic trial with observations on symptoms and bacteriology. *BMJ* 1956;i:705-8.
7 Taylor B, Abbott GD, Kerr M, Fergusson DM. Amoxycillin and co-trimoxazole in presumed viral infections of childhood: placebo controlled trial. *BMJ* 1977;ii:553-4.
8 Whitfield MJ, Hughes AO. Penicillin in sore throat. *Practitioner* 1981;225: 234-9.
9 Howie J. Clinical judgment and antibiotic use in general practice. *BMJ* 1976;ii:1061-4.
10 Howie J, Bigg AR. Family trends in psychotropic and antibiotic prescribing in general practice. *BMJ* 1980;i:836-8.
11 Cartwright A, Anderson R. *General practice revisited: a second study of general practice.* London: Tavistock, 1981.
12 Charney E, Bynum R, Eldridge D. How well do patients take oral penicillin? *Pediatrics* 1967;40:188-95.
13 Pitts J. Shared decision making in the informed treatment of acute otitis media. *Practitioner* 1987;231:1232-3.
14 Herz MJ. Antibiotics and adult sore throat—an unnecessary ceremony. *Fam Pract* 1988;5:196-9.
15 Del Mar C. Managing sore throat: a literature review I: making the diagnosis. *Med J Aust* 1992;156:572-5.
16 Madden TA. Adverse penicillin reactions in the records of a general practice. *J R Coll Gen Pract* 1977;27:73-7.
17 Bolme P, Eriksson M. Influence of diarrhoea on the oral absorption of penicillin V and ampicillin in children. *Scand J Infect Dis* 1975;7:141-5.
18 Hoigne R, Zoppi M, Sonntag R. Penicillins. In: Dukes MNG, ed. *Meyler's side effects of drugs.* Oxford: Elsevier, 1992:600-22.
19 Hodgkin K. *Towards earlier diagnosis in primary care.* Edinburgh: Churchill Livingstone, 1978.

Careful prescribing is beneficial

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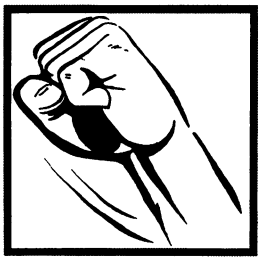

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The annual incidence of sore throat in general practice has been estimated at 100 per 1000 people per year.[1] Some doctors prescribe antibiotics for every patient presenting with a sore throat. Others use clinical scoring systems to establish the probability of group A β haemolytic streptococcal infection. They use the score result together with a knowledge of the prevalence of streptococci in the community to derive a treatment strategy.[2] Thus the management of sore throat, although essentially simple, illustrates Osler's dictum that medicine is a science of uncertainty and an art of probability.[3]

Bacteria can be isolated from 40-50% of patients with sore throat who present to general practitioners, although up to 30% of those with positive cultures may be carriers.[4] Group A β haemolytic streptococci are the most common bacterial pathogens, with *Corynebacterium diphtheriae*, and group C and group G streptococci much rarer. An increasing number of cases may be due to synergistic infection with *Staphylococcus aureus, Moraxella catarrhalis, Haemophilus influenzae*, or anaerobic organisms. Recently, evidence has emerged that some cases of non-streptococcal pharyngitis may be associated with mycoplasma and chlamydial infections.[4]

Reduction of complications

A large study of patients with acute tonsillitis in 17 European countries found that 90% were treated with antibiotics.[5] Since up to half of patients with sore throats have positive bacterial cultures, it is natural to consider such treatment for every patient. This policy is supported by a recent analysis of strategies for dealing with sore throat in which the likelihood of rheumatic fever after untreated streptococcal infection was assumed to be 37·5 times higher than that of a severe reaction to penicillin.[6]

Prevention of rheumatic fever is one of the main considerations in deciding whether to treat pharyngitis. Although now considered rare in the West, the disease remains a problem in Third World countries and even in developed ones where pockets of poverty and crowded living conditions persist.[7,8]

Since rheumatic fever is rare it is claimed that we should not give antibiotics solely to prevent it. However, no controlled studies have offered good evidence in favour of a change of policy.[9] Taking into account the low annual incidence of rheumatic fever and a 20-30% prevalence of β haemolytic streptococcal infection in people with sore throat, over 78 000 subjects would be required in a randomised trial to