prevalence of resistance of *Streptococcus pneumoniae* to common antimicrobial agents in two consecutive periods in east London.

In our first study we determined the antimicrobial susceptibilities of sequential clinical isolates of pneumococci obtained during January to September 1994. Seven (12%) of 60 isolates had reduced susceptibility to penicillin (either intermediate resistance (minimum inhibitory concentration 0.1-1 mg/l) or high resistance (minimum inhibitory concentration ≥ 2 mg/l)). In view of this high prevalence we then collected all isolates from October 1994 until April 1995 and established the minimum inhibitory concentrations for a range of antimicrobial agents and the serological type.² Seventy five isolates were obtained during this period, of which nine (12%) had reduced susceptibility to penicillin. We believe that this is the highest reported prevalence of pneumococci with reduced susceptibility to penicillin in Britain. All strains were typable and are represented in the vaccine that is currently used.

During the overall study period 16 pneumococcal strains of reduced susceptibility (12% of the 135 isolates) were collected from 16 patients. Two isolates had minimum inhibitory concentrations of penicillin of >1 mg/l but were sensitive to erythromycin. Four isolates were also resistant to at least two of the three agents commonly tested in vitro—namely, tetracycline, erythromycin, and chloramphenicol. Nine (7%) of the 135 isolates were resistant to erythromycin. The sources of the samples were predominantly sputum or respiratory samples (65 isolates), blood cultures (38), and eye (15) and ear swabs (9). Two patients yielded multiple isolates.

Our results confirm that the prevalence of resistant strains of pneumococci varies considerably in Britain and that continued monitoring of antimicrobial resistance at a local level is essential for the continuing optimal management of infections due to this organism. Many pneumococcal infections, even when caused by an organism with reduced susceptibility to penicillin, will respond to penicillin as long as adequate doses are used.³ This does not, however, apply to pneumococcal meningitis, as adequate concentrations of penicillin in the cerebrospinal fluid may not be achieved. The increasing prevalence of resistance to penicillin means that this drug will no longer be useful for empirical treatment of this condition, and it is vital that the individual susceptibilities of the causative organism are determined for each patient.

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... and Merseyside ...

EDITOR,—Alan P Johnson and colleagues report that the prevalence of resistance to penicillin in pneumococci was 3.9% in Britain in 1995.¹ In some areas, however, the prevalence is higher than this.

In 1995, 60 (7.5%) of 798 of our pneumococcal isolates were resistant to penicillin. Forty one isolates were from children (average age 2.2 years), of whom nine (22%) were infected, and 19 were from adults (average age 64), of whom 16 (84%) were infected. In total, 25 patients developed an infection: chest infection (19), eye infection (3), sinusitis (1), otitis media (1), and bacteraemia (1). Only three patients had a history of travel (to Tenerife, Turkey, and the Republic of Ireland) within the previous three months. Thirty three patients had received antibiotics in the previous three months; 20 (60%) of the prescriptions had been for penicillins or cephalosporins. In comparison, 53% of all antibiotics prescribed in this district are for these drugs.

The most common serotype was serotype 9 (335 isolates), followed by serotype 6 (223), serotype 19 (96), and serotype 23 (96) (*Streptococcus* and Diphtheria Reference Unit, Central Public Health Laboratory). Two hundred and thirty nine isolates (30%) exhibited high level resistance to penicillin (minimum inhibitory concentration >1 mg/l). Full resistance to cefotaxime occurred in only one isolate (2%) (Antibiotic Reference Unit, Central Public Health Laboratory).

The rate of resistance to penicillin in pneumococci in our district has increased inexorably since 1987, when the first resistant isolate appeared. This rise seems likely to continue.

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... and Northern Ireland

EDITOR,—Alan P Johnson and colleagues state that while the prevalence of resistance to penicillin in pneumococci in England and Wales is increasing, resistance to cefotaxime is still rare.¹ We report data from similar studies at the Northern Ireland Public Health Laboratory.

In a study of 488 consecutive routine clinical isolates of *Streptococcus pneumoniae* sent to this laboratory in 1988, only four (0.8%) were found to be resistant to penicillin (minimum inhibitory concentration ≥ 0.1 mg/l).² Subsequently, in the late 1980s and early 1990s, sporadic isolates that were resistant to penicillin were detected—on average two a year (table 1). In 1994, however, the figures increased to 3.1% and in 1995 to 10.6%, representing a 12-fold increase in the rate of isolation since 1993. A third of the isolates that were investigated further (16/42) showed high level resistance to penicillin, which usually cannot be overcome by increased doses of the drug. Of further concern is that 93% of the isolates (39/42) showed resistance to cefotaxime and by inference all cephalosporins (minimum inhibitory concentration ≥ 0.5 mg/l). This contrasts with recently reported rates of cross resistance to cefotaxime in Britain of 69%.³ Most of these pneumococcal infections would respond to the high dose schedules of intravenous cefotaxime used in hospitals, though some authors recommend that up to 24 g/day may be necessary. The pneumococci might not, however, respond to the low dose regimens of oral cephalosporins used in the community. A few isolates showed high level resistance to cefotaxime, against which even high dose intravenous regimens may fail.

A large proportion (34/42 (81%)) of the penicillin resistant pneumococci that we investigated were of serotype 9V, compared with only 10% of all the

Table 1—Number (percentage) of isolates of pneumococci that were resistant or sensitive to penicillin, Northern Ireland Public Health Laboratory, 1988-95

Year	Resistant	Sensitive
1988	4 (0.8)	484
1989	0	410
1990	4 (1.0)	400
1991	0	395
1992	0	377
1993	3 (0.9)	345
1994	12 (3.1)	372
1995	46 (10.6)	388

pneumococci in our study in 1988 and 39% in Johnson and colleagues' study. This resistant serotype is prevalent in Spain, which is a common holiday destination for young families from Northern Ireland. A clonal outbreak may be occurring in Northern Ireland after importation of penicillin resistant pneumococci by tourists returning from Spain, as was reported from Iceland in 1988.⁴ Alternatively, the pneumococci may have spread from the rest of Britain, and unrelated isolates may simply be clustered in a small number of serotypes; this is not the case with pneumococci that are sensitive to penicillin. Molecular epidemiological studies are currently under way to confirm the existence of an outbreak.

In conclusion, we agree with Johnson and colleagues that continued surveillance of antimicrobial resistance in pneumococci and the distribution of serotypes is essential, and we recommend the adoption of recent American guidelines establishing nationwide mandatory reporting of penicillin resistant pneumococci.⁵

We acknowledge the help of the Antibiotic and Streptococcal Reference Units of the Central Public Health Laboratory, London.

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Prenatal screening for carriers of cystic fibrosis should screen both partners individually

EDITOR,—Screening of pregnant women for mutations in the transmembrane conductance regulator gene for cystic fibrosis is under way in several regions. During the past few years, several papers have been published about such screening, which causes problems.^{1 2}

On the basis of a carrier frequency of 4% in the general population and a feasible rate of detection of mutations of 85%, one can calculate the proportion of couples in each category and

their residual risk of having a child with cystic fibrosis. Couples in which one partner has no identifiable mutation and the other partner is not tested have a risk of 1 in 16 100 (1/25×1/161×1/4); they represent 96.6% of the couples. Couples in which one partner but not the other has an identifiable mutation have a risk of 1 in 644 (1/1×1/161×1/4); they represent 3.3% of the couples. Couples in which both partners are carriers have a risk of 1 in 4; they represent 0.1% of the population.

As the male partner is usually tested only if the woman carries a mutation, the above calculation does not take into account all the couples in which the man is a carrier but his female partner is not. Such couples should also represent 3.3% of all the couples. Therefore, in the above calculation, 96.6% of the couples are given a low risk of 1 in 16 100 whereas the correct proportion should be 93.3%, because another 3.3% of the couples (those in whom only the man has the mutation) have a risk of 1 in 644.

One of the main objectives of screening for carriers of cystic fibrosis is to allow individuals to make better reproductive decisions. This is true for carriers but also for non-carriers. I think that both partners should be tested independently to make sure that accurate counselling is given to all couples, even if it may sometimes be difficult to explain our limitations. Furthermore, there may be a risk of stigmatisation because a larger number of women than men are being identified as carriers.

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Patients who have had fractures of the distal forearm do not lose bone as expected

EDITOR,—Women's lifetime risk of experiencing a fracture of the distal forearm is 15%.¹ Such fractures are associated with considerable pain and morbidity. They are also associated with an increased risk of vertebral fracture,² although these anatomical sites have different bone compositions, with the forearm being composed predominantly of cortical bone whereas the spine is composed predominantly of trabecular bone.

In response to the work by N F A Peel and colleagues³ we have prospectively examined rates of bone loss at the lumbar spine over five years in 1003 women (age range 45-64) who had been recruited from a general population cohort.⁴ Data on prevalent fractures of the distal forearm during the 10 years before the baseline were collected from subjects, and incident fractures were recorded during the study. Bone mineral density at the lumbar spine (L1-4) was measured with dual energy x ray absorptiometry (Hologic QDR-1000) at the baseline and at 12, 24, 36, 48, and 60 months. Short term reproducibility (the coefficient of variation) calculated with repeat measures in normal volunteers was 0.8%. Annual percentage rates of change in bone mineral density at the lumbar spine in individual subjects were calculated by linear regression analysis.

Data were available on 32 women who had sustained a fracture of the distal forearm and on 664 controls who had not. Table 1 shows characteristics of the cases and controls. Bone mineral density at the lumbar spine was reduced in the women with a fracture, and this relation was unaltered by adjustment for age. The rate of change in bone mineral density at the lumbar spine was significantly different from zero in the controls ($P < 0.001$) but not in the patients with a fracture ($P = 0.15$) and was significantly greater in the controls than in the patients with a fracture. The results were not affected by adjustment for age, weight, height, menopausal status, and use of hormone replacement therapy.

Our data confirm Peel and colleagues' findings that patients with a fracture of the distal forearm did not lose bone as expected. The data support the hypothesis that the low spinal bone mineral density of these women may be a consequence of either reduced peak bone mineral density or a period of accelerated bone loss before the menopause. This rapid loss could also affect the microarchitecture of bone and may explain the increase in forearm fractures seen at the time of the menopause. Large prospective studies in younger premenopausal and perimenopausal women will be required to clarify these findings.

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Table 1—Baseline characteristics of patients with forearm fracture and controls without fracture. Figures are means (SD) unless otherwise stated

Variable	Patients with fracture (n = 32)	Controls (n = 664)	P value
Age (years)	57.8 (5.1)	52.4 (5.7)	<0.001
Height (cm)	160.1 (6.0)	161.8 (6.1)	0.12
Weight (kg)	67.7 (12.3)	66.5 (12.0)	0.59
No (%) postmenopausal	26 (90)	392 (62)	0.002
No (%) using hormone replacement therapy	7 (22)	150 (23)	0.93
Bone mineral density of lumbar spine (g/cm ²):			
Unadjusted	0.835 (0.149)	0.991 (0.160)	<0.001
Adjusted*	0.889 (0.150)	0.988 (0.148)	<0.001
Rate of change in spinal bone mineral density (%/year):			
Unadjusted	0.62 (2.4)	-0.39 (1.7)	0.02
Adjusted†	0.38 (1.7)	-0.36 (1.7)	0.03

*Adjusted for age. †Adjusted for age, weight, height, use of hormone replacement therapy, and menopausal status.

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Definition of authorship may be changed

Peer reviewers should be identified at end of each published paper

EDITOR,—A recent meeting of academics, editors, peer reviewers, and such at the University of Nottingham concluded, not before time, that the definition of authorship in medical research should be changed.¹ Dr Drummond Rennie, deputy editor of *JAMA*, is reported to have said that "authorship" should be scrapped and authors replaced with "contributors" and "guarantors": the "film credit" approach.¹ That is right as far as it goes; it just does not go far enough. Rennie omitted from his credits the peer reviewer ("peer" is defined as an equal, a fellow, an antagonist²). This omission is ironic since reviewers formed a substantial part of Rennie's audience.

Nowadays, peer review is an integral, responsible, educative, and constructive part of medical research. It looks at the science and the originality. If these are found to be acceptable then peer review can illuminate the message. Take a simple example: say the contributors have omitted a useful reference (most of us, if we are honest, do the definitive literature search after the study instead of the other way round). Peer review should pick that up and, at its very best, should also improve content, style, layout, and readability. Peer reviewers perform these essential and thankless tasks for a pittance; they deserve better than a yearly pat on the back. (We can say this without blushing because no one has yet asked us to review anything more than our pension plans.)

If we take the cynical view, inclusion of peer reviewers in the "credits" would confirm that peer review has happened, would spread the blame, and would concentrate the mind of the reviewer, who would be as entitled as contributors and guarantors to reply to correspondence. If necessary he or she could also meet allegations of fraud, gift authorship, ghost authorship, or "jobs for the boys" (work accepted for publication not on the basis of merit but on the basis of friendship).

Peer reviewers of papers that are not accepted for publication should probably retain the privilege of anonymity (the medical researcher can always submit the study to another journal). Peer reviewers of accepted papers should not be anonymous.

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Clinicians who enter patients into randomised controlled trials should be acknowledged

EDITOR,—It is generally accepted that multicentre randomised controlled trials are important for the adequate assessment of health technologies¹ and