access, and a telephone helpline is provided during office hours. A team of dedicated scientific staff, who have the time and resources to concentrate on all aspects of anticoagulant treatment and are supervised by the consultant clinical haematologist, provide advice within the hospital and to general medical and dental practitioners, pharmacies, and social services to promote optimal control. The centralised setting facilitates audit and ensures technical and scientific back up, with easy access to a consultant haematologist when needed.

The adoption of this approach has led to a considerable improvement in control of anticoagulation. Several studies have shown that, with conventional management of anticoagulant treatment, patients' international normalised ratio is within the recommended therapeutic range for half or less of the time.^{2,3} The figure is worse in patients when they are first treated: in 47 such patients the target range was achieved only 40% (range 17-62%) of the time.³ A direct comparison of 34 of our patients taking anticoagulants long term showed that the proportion of the time for which the ratio was in the therapeutic range increased from 50.3% (0-100%) to 77.3% (60-100%) after the introduction of our integrated, proactive approach. In 38 patients the ratio was in the desired target range for 66.2% (41-93%) of the time during their first year of treatment.

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Shared care can work

EDITOR,—We welcome D A Fitzmaurice and colleagues' reference to quality assurance in their editorial on monitoring anticoagulation in primary care.¹ In 1993 we have introduced a formal shared care policy for monitoring oral anticoagulant treatment in a district where few general practitioners are prepared to manage their own patients.² This policy clearly defines areas of responsibility for the hospital, general practitioners, and community nurses.

A "yellow anticoagulant book" is used as the principal means of communication. Patients are initially seen in the clinic and are subsequently transferred to a community sampling system.

Blood samples are taken either by the district nurse or at the patient's local surgery on a date notified to the patient in his or her yellow book and to the community nurse by a computer generated letter. The samples are processed at the laboratory, results passing direct to a computer system that recommends doses and maintains the clerical aspects of the clinic, including follow up appointments and letters. It also facilitates access to a large database. All patients who are required to change their dose of warfarin urgently are telephoned, and if the international normalised ratio is >10 they are asked to attend the hospital for full assessment and administration of vitamin K. The remaining patients receive their yellow book by first class post, with a printed label stating the dose and date of the next test. General practitioners remain responsible for prescribing the warfarin tablets and ensuring that the clinic is made aware of important changes in drug treatments as well as checking the patient's yellow book for recent results and doses.

Our findings do not suggest that the lack of direct contact with a doctor is detrimental to patients in terms of serious bleeding problems or control, especially when these findings are compared with published data (table 1).^{3,5} The approximate cost per measurement of the international normalised ratio and recommended dose is less than £7.

A remote dosing system is an effective means of accommodating the recent large increase in workload, provided that all participants understand their responsibilities. The system benefits patients, who do not need to attend hospital, and general practitioners, who do not have responsibility for deciding the dose of anticoagulant or maintaining a clinic system but who do have a defined responsibility for the continuing care of the patients. The centralisation of the system allows for good quality assurance, ready availability to a database for audit, and the cost benefits of processing large numbers of blood samples.

We thank the participants in the North Nottinghamshire shared care scheme for their support and acknowledge the contribution of the Nottinghamshire Anticoagulant Working Group, especially Dr P A E Jones.

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Table 1—Comparison of manual audit of serious bleeding problems over seven months in 1991 with 12 month computerised audits in 1994-6

	1991	1994-5	1995-6
No of patients registered	577	1235	1621
No of measurements of INR requested	4635	11 010	15 426
No (%) of samples obtained in community	1390 (30)	7870 (71)	11 813 (77)
% (95% confidence interval) of INRs within therapeutic range*	NK	64 (62.9 to 65.1)	63 (61.7 to 63.7)
No (%) of INRs >10	14 (0.3)	17 (0.2)	14 (0.1)
No of serious bleeding episodes requiring fresh frozen plasma and vitamin K:			
INR >10	3	4	2
INR 6-10	NK	4	4
INR <6	NK	9	4
Total No (% of patients)	NK	17 (1.4)	10 (0.6)

INR = International normalised ratio. NK = Not known.

*Either 1.9-3.1 (target 2.5) or 2.7-4.6 (target 3.6).

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"Meteorobiology" may have a role in sudden infant death

EDITOR,—A S Douglas and colleagues conclude that seasonal variation in the sudden infant death syndrome is an unexplained epidemiological feature with the potential to be an important clue to the aetiology of the syndrome.¹ They addressed the possible role of exposure of the eyes to light. Sunlight has powerful biological effects—for example, on the metabolism of vitamin D, on the immune system, and in the aetiology of depression during the autumn and winter.

Given an epidemiological correlation between light and sudden infant death, it would be important to identify tissue changes in victims that might be influenced by exposure to light. There are some hints from earlier research. Firstly, in the older German literature there was a discussion on rickets and sudden death. But researchers into sudden infant death have found a widely varying incidence of rickets at necropsy, of 2-78%.² Secondly, Sparks and Hunsacker found altered aminergic-cholinergic synaptic markers in the hypothalamus of victims of sudden infant death, which may have led to critically disturbed sleep function in these infants.³ Thirdly, in his book on "human meteorobiology" De Rudder described the influences of weather and climate on tissues, organs, and the organism as a whole.⁴ Of special interest are the histological differences in the thyroid gland between rats exposed to light and rats living in darkness. Rats living in darkness characteristically showed an increased number of follicles with a high epithelial and low colloid content.⁴ An identical histological pattern was described by Weiler in 70% of victims of sudden infant death in his study.⁵

The hypothesis of an association between light and sudden infant death, derived from epidemiological findings, needs to be complemented by systematic histological and biochemical research. The concept of "meteorobiology" may well be fruitful.

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Prevalence of antibiotic resistance in pneumococci

Prevalence of resistance to penicillin is higher in east London ...

EDITOR,—Alan P Johnson and colleagues report that the prevalence of intermediate or full resistance to penicillin was 3.9% in England and Wales in 1995 and that the prevalence of resistance to erythromycin was 8.6%.¹ We have examined the

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

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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