Letters

Hyperglycaemia after acute stroke

Other models find that hyperglycaemia is not independent predictor

EDITOR—Christopher J Weir and colleagues conclude from their study of a cohort of 750 non-diabetic patients with stroke that hyperglycaemia (plasma glucose concentration >8 mmol/l) during the acute phase has an adverse influence on outcome and that this is independent of severity of stroke.[1] Stroke severity was assessed in a limited way using only the Oxfordshire community stroke project classification and time to resolution of symptoms (≤72 hours or >72 hours), both of which are relatively inaccurate measures. When two variables are closely correlated—for example, stroke severity and glucose concentration—the one that is most accurately measured (glucose concentration) will always emerge as the strongest explanatory variable in multiple regression even if it is, in fact, less important.[2]

We have produced a series of validated models to predict the probability of survival and disability using the 530 patients from the Oxfordshire community stroke project who were seen within 30 days of their stroke.[3] A history of diabetes mellitus and the presence of acute hyperglycaemia (glucose concentration >12 mmol/l) were two of about 20 variables that were entered into these models, in addition to several measures related to stroke severity (eye, motor, and verbal components of the Glasgow coma score; arm power; and ability to walk). Although diabetes mellitus was an adverse and independent predictor of death (relative hazard 2.01; 95% confidence interval 1.36 to 2.99), hyperglycaemia was not (1.66; 0.93 to 2.97). Neither of these variables was an independent predictor of death or disability (modified Rankin score >2) at six months.

We repeated our analyses using only the 249 patients seen within 72 hours of onset with no known history of diabetes; we redefined hyperglycaemia as glucose concentration >8mmol/l to allow direct comparison with the results of Weir and colleagues. Once more, hyperglycaemia was not an independent predictor of either death (relative hazard 1.02; 0.62 to 1.66) or death or disability (odds ratio 1.61; 0.38 to 6.75).

We would therefore disagree that hyperglycaemia is an independent prognostic factor in acute stroke. We would, however, agree that a large randomised trial of glucose control in the acute phase of stroke is necessary to clarify the clinical management of these patients. Many guidelines recommend that hyperglycaemia should be treated aggressively with insulin infusions[4]; we are not aware of a single completed randomised trial addressing this issue, and so it remains unclear whether the risks of such an approach—for example, hypoglycaemia—outweigh any possible benefits.

Carl Counsell *Clinical research fellow*
Mike McDowall *Programmer*
Martin Dennis *Senior lecturer in stroke medicine*
Department of Clinical Neurosciences, Western General Hospital, Edinburgh EH4 2XU

1 Weir CJ, Murray GD, Dyker AG, Lees KR. Is hyperglycaemia an independent predictor of poor outcome after acute stroke? Results of a long term follow up study. *BMJ* 1997; 314:1303-6. (3 May.)
2 Thelle DS. Salt and blood pressure revisited. *BMJ* 1996; 312:1240-1.
3 Counsell C, McDowall M, Slattery J, Dennis M in collaboration with the SEPIVAC and Perth Community Stroke Registries. Prediction of functional outcome following stroke using a validated model [abstract]. *Cerebrovasc Dis* 1996;6(suppl 2):50.
4 European Ad Hoc Consensus Group. Optimizing intensive care in stroke: a European perspective. *Cerebrovasc Dis* 1997;7:113-28.

May occur as result of neuroendocrine response

EDITOR—In the largest study of its kind to date, Christopher J Weir and colleagues report that early hyperglycaemia predicts mortality after stroke.[1] This investigation confirms similar findings from our group and others. The authors suggest, however, that a raised plasma glucose concentration "is not solely a stress response to neurological insult, as it predicts outcome after taking other prognostic factors into account." This conclusion is unfounded. An association, even a causative one, between glucose concentration and poor recovery does not exclude the possibility that the hyperglycaemia occurs as a result of a neuroendocrine stress response. Indeed, many measures of this stress hormone response have been correlated with poor outcome in stroke as well as in other critical illnesses.[2] Cortisol, one of the core regulators of both the stress response and plasma glucose concentration, is directly neurotoxic and inhibits recovery after brain injury.[3]

Several findings suggest that hyperglycaemia after stroke is related to stress, albeit it has prognostic effects.[4] Firstly, hyperglycaemia correlates with lesion size in most studies. Secondly, hyperglycaemia closely correlates with increases in other stress hormones. Thirdly, the rise and fall of glucose concentrations after stroke parallels the classic neuroendocrine release profile. The physiological association between concentrations of plasma glucose and blood pressure at admission is indirect at best. Therefore, the moderate statistical correlation between these two variables shown by Weir and colleagues is not surprising and certainly not evidence against a glucose response related to stress. As discussed in the paper, a correlation between early haemoglobin A_{1c} concentration and poor outcome shown by some studies is evidence that hyperglycaemia before stroke is important. This correlation, however, is much less important than the correlation with glucose concentrations after stroke, even in diabetic patients.

This clarification is not just of academic interest. Hyperglycaemia after stroke is certainly associated with poor outcome, but does it contribute to it? The authors believe that plasma glucose concentration is an independent predictor of prognosis after age, stroke type, and stroke severity have been controlled for, but they do not control for stress hormones, which are themselves related to both glucose and outcome after stroke. It may well transpire that reduction of

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Advice to authors

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When deciding which letters to publish we favour originality, assertions supported by data or by citation, and a clear prose style. Letters should have fewer than 400 words (please give a word count) and no more than five references (including one to the BMJ article to which they relate); references should be in the Vancouver style. We welcome pictures.

Letters, whether typed or sent by email, should give each author's current appointment and full address. Letters sent by email should give a telephone and fax number when possible. We encourage you to declare any conflict of interest. Please send a stamped addressed envelope if you would like to know whether your letter has been accepted or rejected.

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Letters will be edited and may be shortened.

hyperglycaemia—short of inducing hypoglycaemia—may be helpful after stroke, but, equally, the therapeutic potential of antiglucocorticoids should be investigated.

Alex Mitchell *Senior house officer in psychiatry*
Peter Kirckpatrick *Consultant in neurosurgery*
Addenbrooke's Hospital, Cambridge CB2 2QQ

1 Weir CJ, Murray GD, Dyker AG, Lees KR. Is hyperglycaemia an independent predictor of poor outcome after acute stroke? Results of a long term follow up study. *BMJ* 1997;314:1303-6. (3 May.)
2 Mitchell AJ. Clinical implications of post-stroke hypothalamo-pituitary adrenal axis dysfunction: a critical literature review. *J Stroke Cerebrovasc Dis* (in press).
3 Sapolsky RM. Glucocorticoid neurotoxicity. In Sapolsky RM, ed. *Stress, the aging brain, and the mechanisms of neuron death.* London: MIT Press, 1992:97-115.
4 Wass CT, Lanier WL. Glucose modulation of ischemic brain injury: review and clinical recommendations. *Mayo Clin Proc* 1996;71:801-12.

Participants required for trial of treatment with glucose and insulin

EDITOR—The results of the study by Christopher J Weir and colleagues on the prognostic importance of hyperglycaemia after acute stroke correspond with previous work done in Newcastle.[1 2] In our study, hyperglycaemia (blood glucose concentration >8 mmol/l) was detected in 22.8% of 200 consecutive patients with acute stroke and was associated with significantly increased mortality at four and 12 weeks; only nine of the 31 hyperglycaemic patients had a history of diabetes mellitus.[2]

Weir and colleagues performed separate analyses of results for known diabetic and non-diabetic patients. The proportion of hyperglycaemic patients was, not surprisingly, lower in the non-diabetic group (22% *v* 69%). As alluded to in the discussion section of their paper, however, glycated haemoglobin (HbA_{1c}) concentrations were not estimated and therefore some of the subjects in the non-diabetic group probably had diabetes or glucose intolerance which had been unrecognised previously. This is an important omission since hyperglycaemia may have a different effect on outcome in diabetic patients with stroke.[3] Furthermore, previous work by our group has shown raised HbA_{1c} concentrations in 33.8% of patients with acute stroke, four fifths of whom had no known history of diabetes.[2] A raised HbA_{1c} concentration >7.5% was a significant predictor of death in older patients and was likely to be associated with raised plasma glucose concentrations on admission.

There is growing evidence from clinical and laboratory studies of the detrimental effect of hyperglycaemia in acute stroke. Studies on animals have shown that coadministration of glucose and insulin at the time of experimentally induced focal ischaemia can reduce cerebral infarction after middle cerebral artery occlusion.[4] A recent trial in diabetic patients with myocardial infarction has shown that glucose-insulin treatment reduced mortality.[5] The precise time span during which hyperglycaemia occurs after stroke in humans is unknown. Consequently, the window of opportunity during which randomisation to euglycaemic treatment should take place is unclear and will need to be addressed in prospective studies. Furthermore, the safety of euglycaemic control immediately after stroke has not been formally studied in patients with acute stroke. The safety of such an intervention needs to be established before a multicentre randomised clinical trial is conducted.

We agree with Weir and colleagues that there is sufficient evidence to warrant a study of maintenance of euglycaemia in hyperglycaemic patients after acute stroke. Our group has recently obtained a grant from the Stroke Association to carry out a pilot study of the safety of glucose-insulin treatment in patients with acute stroke. We would be interested to hear from potential collaborators for a multicentre trial of this treatment.

Jonathan Scott *Medical registrar*
Janice O'Connell *Senior lecturer*
Christopher Gray *Professor*
University of Newcastle, School of Clinical Medical Sciences, Department of Medicine for the Elderly, Sunderland Royal Hospital, Sunderland SR4 7TP

1 Weir CJ, Murray GD, Dyker AG, Lees KR. Is hyperglycaemia an independent predictor of poor outcome after acute stroke? Results of a long term follow up study. *BMJ* 1997;314:1303-6. (3 May.)
2 Gray CS, French JM, Bates D, Cartlidge NEF, Venables GS, James OFW. Increasing age,diabetes mellitus and recovery from acute stroke. *Postgrad Med J* 1989;65:720-4.
3 Kiers L, Davis SM, Larkins R, Hopper J, Tress B, Rossiter SC, et al. Stroke topography and outcome in relation to hyperglycaemia and diabetes. *J Neurol Neurosurg Psychiatry* 1992;55:263-70.
4 Hamilton MG, Tranmer BI, Aver RN. Insulin reduction of cerebral infarction due to transient focal ischaemia. *J Neurol* 1995;82:262-8.
5 Malmberg K, Ryden L, Efendie S, Herlitz J, Nicol P, Waldenstrom A, et al. Randomised trial of insulin-glucose infusion followed by subcutaneous insulin treatment in diabetic patients with an acute myocardial infarction. *J Am Coll Cardiol* 1995;26:57-65.

Authors' reply

EDITOR—The suggestion by Carl Counsell and colleagues that the severity of stroke and plasma glucose concentration are closely correlated is not confirmed by our findings. There was only a weak correlation ($r=0.14$, $P<0.01$; $n=295$) between scores on the National Institutes of Health stroke scale and plasma glucose concentrations in our patients. Contrary to their statement regarding accuracy of measurement, if two strongly correlated variables were included in a multiple regression neither would have a significant independent effect. The results of the models produced by Counsell and colleagues to study the relation between hyperglycaemia and outcome in acute stroke are consistent with ours since there is a considerable overlap with our confidence intervals, both for relative hazard of death and for odds ratio of death or dependency.

A large randomised trial of glucose control in hyperglycaemic patients with acute stroke is essential. Exacerbation of infarction by hyperglycaemia after experimentally induced ischaemia was discussed in our paper. The theoretical arguments concerning cause and effect presented by Alex Mitchell and Peter Kirckpatrick are less important than the question about the clinical management of hyperglycaemia, which will be answered by the results of a clinical trial. We are pleased to note that Jonathon Scott and colleagues are performing a pilot study of glucose control in acute stroke. We are piloting a similar study and have initiated discussion with several British and international investigators to plan a multicentre trial.

Christopher Weir *MRC training fellow*
Alexander Dyker *Lecturer in stroke medicine*
Kennedy Lees *Clinical director*
Acute Stroke Unit, University Department of Medicine and Therapeutics, Western Infirmary, Glasgow G11 6NT

Gordon Murray *Professor of medical statistics*
Medical Statistics Unit, Medical School, University of Edinburgh, Edinburgh EH8 9AG

More money is needed to care for patients with cancer

EDITOR—The redistribution of NHS funding to primary care is causing severe problems in cancer units and centres. Members of clinical directorates and regional cancer centres are seeing rapidly increasing numbers of patients, often while coping with reduced budgets. The main target for budget reductions is often the money spent on cytotoxic chemotherapy. Potent but expensive new cytotoxic agents, which are generally agreed to be effective, are available. As a result of recent contract negotiations their use has in effect not been funded in many regions.

Cancer survival rates in Britain compare poorly with those in many other Western economies. Thus improvement in outcomes of cancer has been given the highest priority in the NHS.

Attention has been focused on the reorganisation of services as an efficient way to maximise benefits and provide expertise to all. Now attention should be turned to the costs of drugs and their funding. The money spent on adjuvant chemotherapy is a small part of the cost of caring for patients with cancer; Richards et al found that only 8% of the cost of the management of cancer was due to chemotherapy.[1] A comparison of the amount spent on cytotoxic chemotherapy with the amount spent on other drugs within the NHS is enlightening. The total budget for all cytotoxic chemotherapy is about £58m; in contrast, the budget for omeprazole alone is about £250m. The table shows the amount spent on different types of drugs by different specialties within the NHS.

Estimated amount spent on drugs by NHS for year ending September 1996

Type of drugs	Amount (£m)
Gastrointestinal	1038
Central nervous system	888
Cardiovascular	848
Respiratory	742
Anti-infectives	586
Dermatology	282
Cancer	167

Data from Intercontinental Medical Statistics, Pinner, Middlesex.

The old arguments about the lack of efficacy of expensive drugs no longer apply. There is direct evidence of the link between chemotherapy and outcome from two audits in Britain.[2 3] It is now accepted that adjuvant chemotherapy improves survival and that palliative chemotherapy improves quality of life in advanced cancers. The amount spent on cancer care in Britain is 10-fold less than the amount spent in the United States; Britain spends 3.5-fold less than the comparable European economies of France and Germany.

A simple way of rectifying the present situation in Britain would be for expert advisers to generate national guidelines to evaluate the cost effectiveness of new drugs for selected patients. These patients would be cared for by specialists whose academic and clinical training makes them both circumspect in using the drugs and willing to audit the outcomes.

R C F Leonard
I E Smith
R E Coleman
J S Malpas
M Nicolson
J Cassidy
A Jones
M B McIllmurray
N S A Stuart
P J Woll
J M A Whitehouse
Members of executive committee of Association of Cancer Physicians
Correspondence to: Dr Coleman, Department of Clinical Oncology, Western Park Hospital, Sheffield S10 2SJ

1 Richards MA, Braysher S, Gregory WM, Rubens RD. Advanced breast cancer: use of resources and cost implications. *Br J Cancer* 1993;67:856-60.
2 Sainsbury R, Haward B, Rider L, Johnston C, Round C. Influence of clinician workload and patterns of treatment on survival from breast cancer. *Lancet* 1995;345:1265-70.
3 Scottish Cancer Therapy Network. *Scottish breast cancer audit 1987 and 1993. Report to the chief scientist and Clinical Resource Audit Group.* Edinburgh: Scottish Cancer Therapy Network, 1996.

Cancer self help groups are underused

EDITOR—It is now established that patients with cancer are prone to psychosocial problems, and recent reviews have shown that they can benefit from taking part in self help or support groups.[1 2] The chief medical officer recommended that cancer centres and units should encourage local self help groups,[3] but only 48% of oncologists in a recent survey do so.

In a controlled study Spiegel et al showed expressive-supportive group therapy to be effective in improving mood (while the mood of control patients deteriorated), reducing maladaptive coping responses, and reducing pain.[4] The treatment group also showed improved survival, and the techniques can be taught for use in the community.[4] Although most British groups do not operate such a structured programme, they largely practise the same principle of allowing patients to discuss their problems in an atmosphere of unconditional acceptance.

There are now more than 500 self help groups for cancer, which can be contacted through Cancerlink, a charity based in London. Cancerlink has prepared good practice guidelines, which aim to improve professionals' confidence in the services.

Cunningham and Edmonds conducted an extensive literature review and concluded that most patients could gain an improved quality of life from attending a self help group.[2] A survey among the general public was recently conducted by Market and Opinion Research International.[5] In answer to the question "Which organisation if any are you aware of that can help or support people with cancer?" only 9% of respondents mentioned self help groups; most named organisations that cannot be accessed directly by the public.

As only 9% of the public are aware of self help groups and oncologists do not routinely recommend such groups to patients, more public education is required to enable more patients to benefit.

E J Watts *Consultant haematologist*
Basildon Hospital, Basildon, Essex SS16 5NL

1 Fallowfield L. Psychosocial interventions in cancer. *BMJ* 1995;311:1316-7.
2 Cunningham AJ, Edmonds CV. Group psychological therapy for cancer patients: a point of view and discussion of the hierarchy of options. *Int J Psychiatry in Med* 1996; 26:51-82.
3 Expert Advisory Groups on Cancer established by the Chief Medical Officer of England and Wales. *A policy framework for commissioning cancer services.* London: HMSO, 1995.
4 Spiegel D, Morrow GR, Classen C, Riggs G, Stott PB, Mudaliar MSW, et al. Effects of group therapy in women with primary breast cancer. *Breast J* 1996;2:104-6.
5 Watts EJ. Public awareness of a professional attitude to cancer self-help groups. *Health Trends* (in press).

Case-control study of sudden infant death syndrome in Scotland

Income level or bed sharing would confound any effect of previous use of mattress

EDITOR—Hazel Brooke and colleagues have drawn attention to the possible risk of the sudden infant death syndrome associated with "old" mattresses.[1] In their study they did not ask about mattress age or the number of previous users, only whether the mattress had been used by another infant or adult. The use of the word "old" is therefore misleading. By this definition, all adult mattresses would be considered old, as would recently bought mattresses used by one previous infant. In our study, mattress age as a continuous variable was not significant, whether mattresses totally covered with polyvinyl chloride were included or not.[2 3] When mattress age was taken as a dichotomous variable, a small but significant proportion of index mattresses were ≥4 years old; this factor became non-significant, however, when parity or family income was added in a bivariate analysis. We also asked about previous use of infant mattresses. This was not a significant factor in the univariate analysis, but, when we included infants who routinely bed shared, the risk associated with previous use became significant; the significance increased if we included instead infants who bed shared during their last sleep. Thus, distinguishing between infant and parental mattresses and what practice was adopted on the last night seems important.

Given this, one would expect that, in Brooke and colleagues' multivariate model, the factors representing income or bed sharing would confound any effect of previous use of the mattress. However, income was not measured directly and the study focused on routine bed sharing practice rather than bed sharing around the time of death. Both our study and a similar large study in New Zealand[4] showed considerable differences in the risk associated with routine practices and the practice around death. The risk associated with routine bed sharing rises twofold when practice at the time of death is considered and is an important risk factor among parents who smoke. Several other studies have shown that routine bed sharing is not significant in multivariate analysis.[2 4 5]

Given the higher incidence of the syndrome in families of lower socioeconomic status, it would not be surprising that some index infants slept on older mattresses. When analysis was restricted solely to infant mattresses, multivariate analysis showed no risk associated with greater mattress age or previous use. Our data indicate that any apparent risk associated with previous use of a mattress would be confounded by the effect of parental bed sharing for the last sleep or by the use of a suitable proxy marker for income.

Peter Blair *Medical statistician*
Peter Fleming *Professor of infant health and developmental physiology*
FSID Unit, Institute of Child Health, Royal Hospital for Children, Bristol BS2 8BJ
Iain Smith *Senior lecturer*
Nuffield Institute for Health, Leeds LS2 9PL

1 Brooke H, Gibson A, Tappin D, Brown H. Case-control study of sudden infant death syndrome in Scotland, 1992-5. *BMJ* 1997;314:1516-20. (24 May.)
2 Fleming PJ, Blair PS, Bacon C, Bensley D, Smith I, Taylor E, et al. Environment of infants during sleep and risk of sudden infant death syndrome: results of 1993-5 case-control study for confidential inquiry into stillbirths and deaths in infancy. *BMJ* 1996;313:191-5.
3 Blair PS, Fleming PJ, Bensley D, Bacon C, Smith I, Taylor E, et al. Smoking and the sudden infant death syndrome: results of 1993-5 case-control study for confidential inquiry into stillbirths and deaths in infancy. *BMJ* 1996;313:195-8.
4 Mitchell EA, Taylor BJ, Ford RPK, Stewart AW, Becroft DMO, Thompson JMD, et al. Four modifiable and other major risk factors for cot death: the New Zealand study. *J Paediatr Child Health* 1992;28(suppl):S3-8.
5 Luke JL. Sleeping arrangements of sudden infant death syndrome victims in the District of Columbia: a preliminary report. *J Forens Sci* 1978;23:379-83.

Multiple statistical comparisons used are confusing

EDITOR—We are concerned that the findings of Hazel Brooke and colleagues' study of the sudden infant death syndrome are being interpreted as providing evidence for the "toxic gas theory" of the cause of the syndrome, although the authors explicitly reject this interpretation.[1] The Department of Health's expert group on cot death theories, of which we are members, is investigating this theory, and it would be inappropriate for members of the group to anticipate the report of the group as a whole. We do

not, however, think it improper to comment on particular pieces of research that are the subject of public concern.

The authors report that sleeping on an old mattress "may be important" as a cause of the sudden infant death syndrome. There are three problems in the analysis and thus in the interpretation of the findings: firstly, the considerably different response rates both between groups and in answers to individual questions; secondly, the complexities of the statistical methods, which are not elaborated; and, thirdly, the problems of multiple statistical comparisons. Thus it is difficult to assess either the biological or the statistical significance of the results.

The authors do not explain the results in terms of the other factors measured in their study, and maybe the findings cannot be so explained. It seems essential, however, to investigate possible explanations in order to assess the plausibility of an explanation based on the toxic gas theory. At least two other explanations are possible, and it is not clear to us whether the authors' analyses excluded them. Sudden infant deaths are more common in socially deprived families, and an obvious possibility is that the use of older mattresses is associated with social deprivation; socially deprived families are also the families in which more parents smoke. We wonder whether, in carrying out their rather complex analyses, the authors could have overlooked the possible importance of such relations. It is also known that the likelihood of sudden infant death is related to sibship position. One of the variables considered by the authors is "two or more previous births," but this does not take into account the children with just one older sibling; again, the complex analyses described may have overlooked such a relation.

Of course, even if the association with the use of older mattresses is explained by an association with social deprivation or sibship position, this leaves unsettled the actual cause of the sudden deaths. But a variety of other explanations (child care practices, exposure to infection) can then be offered.

Gerald Draper *Director*
Childhood Cancer Research Group, Oxford OX2 6HJ

Walter Holland *Professorial fellow*
LSE Health, London School of Economics, London WC2 2AE

1 Brooke H, Gibson A, Tappin D, Brown H. Case-control study of sudden infant death syndrome in Scotland, 1992-5. *BMJ* 1997;314:1516-20. (24 May.)

Risk of bed sharing was not sufficiently examined

EDITOR—We are concerned by several aspects of Hazel Brooke and colleagues' study of the sudden infant death syndrome in Scotland.[1] The first, and most important, is that the risk of bed sharing was not sufficiently examined. Routine bed sharing had an odds ratio of 3.9 when analysed univariately. The authors did not, however, test the effect of bed sharing at the time of death (univariately or multivariately), even though its frequency was four times the frequency reported for bed sharing as the usual practice (8% routine bed sharing; 34% bed sharing at death).

Secondly, the multivariate modelling approach includes many variables that are highly correlated, such as social class and deprivation score, birth weight and gestational age, and number of parents smoking in the household and marital status of the mother. Others that do not overlap as conspicuously include social class or deprivation score with some behavioural factors such as smoking, maternal age, marital status, mother's education level, and current drug treatment. These cannot be treated as independent variables in a regression analysis without there being substantial collinearity problems. When these correlated variables are included in a multivariate model the estimates of coefficients for each factor become highly unstable and, therefore, make the adjusted estimates suspect.

Finally, social class or deprivation scores, or both, can rarely be modified and encompass (or mask) many behavioural and physiological characteristics. As an exercise in public health, it would be far more useful to include the meaningful components that are known to contribute to differences found within the socioeconomic levels rather than to include socioeconomic levels as an undefined, overall influence on health outcomes. Including both socioeconomic levels and factors that predict these makes it more problematic to estimate correctly the effects of the modifiable risk factors in multivariate analyses. If bed sharing is related to and predicted by such variables as these its effect will be obscured by this approach.

The important and useful information contained in this study should be strengthened by a more directed analysis of the available data.

Cindie Carroll-Pankhurst *Research associate, paediatrics*
Edward A Mortimer Jr *Professor emeritus, department of epidemiology and biostatistics*
School of Medicine, Case Western Reserve University, Cleveland, OH 44106-4945, USA
ccp@hal.cwru.edu

1 Brooke H, Gibson A, Tappin D, Brown H. Case-control study of sudden infant death syndrome in Scotland, 1992-5. *BMJ* 1997;314:1516-20. (24 May.)

Authors' reply

EDITOR—Peter Blair and colleagues claim that the term "old" mattress is misleading since we did not measure age. The condition of the mattress surely depends on the amount of soiling, the level of home hygiene, and storage conditions rather than precise age and number of previous users. We included adult mattresses in our comparisons since we were not testing a particular hypothesis on infant mattresses only. Income was not measured directly, but we believe that factors such as father's employment, social class, and deprivation score[1] provide suitable surrogates.

Bed sharing at death was significantly more common than the routine index rate and has led to suggestions that this confounded the results for old mattresses. We confirm that this is not the case by excluding bed sharers at death. The odds ratio for routine use of an old mattress becomes 2.17 (95% confidence interval 1.27 to 3.71) on univariate analysis and 2.84 (1.30 to 6.20) on multivariate analysis. Additionally, data on use of an old mattress were available for 56% of the cases at death. The odds ratio for these cases when compared with the routine control practice was 1.99 (1.14 to 3.49) after exclusion of bed sharers.

Gerald Draper and Walter Holland question our analysis. The difference in response rates between the groups was discussed in our paper, and we do not expect it to have given rise to any major biases. As regards individual questions, for most there were only a few missing responses, making any biases small. Our results are based on conditional logistic regression analyses, a standard method used for analysing matched case-control data. Multiple testing occurred in our study, as in any epidemiological study based on regression. However, we were following convention in presenting results of analyses without any formal adjustment of P values, and we believe that this is good practice.

Adjustment was made for both social deprivation and smoking in the multivariate analysis. Use of an old mattress is still highly significant when an alternative, simpler analysis is done adjusting for only these factors. After stratification for parity (0, 1, 2, or $\geq 3+$) the odds ratio for an old mattress is 2.33 (1.48 to 3.68).

Cindie Carroll-Pankhurst and Edward A Mortimer query the inclusion of many correlated variables in the multivariate analysis. There is no requirement for variables to be independent in a multiple regression analysis. Analyses using reduced sets of factors showed that the estimated coefficients remained stable, indicating that no problems associated with collinearity occurred in the multivariate analysis.

Hazel Brooke *Executive director*
Angus Gibson *Chairman*
Scottish Cot Death Trust, Royal Hospital for Sick Children, Glasgow G3 8SJ

David Tappin *Senior lecturer in community paediatrics*
University of Glasgow, Glasgow G12 8QQ

Helen Brown *Research associate*
Medical Statistics Unit, University of Edinburgh Medical School, Edinburgh EH8 9AG

1 Carstairs V, Morris R. Deprivation: explaining differences in mortality between Scotland and England and Wales. *BMJ* 1989;299:886-9.

Giving thyroid hormones to clinically hypothyroid but biochemically euthyroid patients

Supporting authors' views would be unwise

EDITOR—Gordon R B Skinner and colleagues advocated that a diagnosis of hypothyroidism in patients with suggestive symptoms should not be excluded on the basis of "normal" hormone concentrations.[1]

Furthermore, they proposed that an incremental trial of thyroxine for three months is not unreasonable in these patients.

The consensus is that patients with subclinical hypothyroidism in whom serum thyroid stimulating hormone concentrations are consistently above the usually quoted upper limit of the reference range of 5 mU/l should be treated with thyroxine; this is particularly so if the patients have antibodies to thyroid peroxidase, a history of treatment of thyrotoxicosis, or a goitre.[2] Two double blind trials in patients with subclinical hypothyroidism have shown that, after treatment with thyroxine, target organ function may improve and there may be a greater sense of wellbeing in some patients, though by no means all.[3] The most cogent reason for treatment, however, is the knowledge that a considerable proportion of patients will develop overt hypothyroidism in future years,[4] and it makes sense for the disorder to be "nipped in the bud" rather than risk loss to follow up.

Because autoimmune thyroid disease is common, it is possible that reference ranges were calculated from populations containing patients with a degree of thyroid failure and that the true upper limit for normal serum thyroid stimulating hormone concentrations may be slightly lower than 5 mU/l. There are, however, no studies of the effect of thyroxine in patients with non-specific symptoms and hormone concentrations below 5 mU/l, and, until there is objective evidence of benefit—which from clinical experience is unlikely—it would be unwise to support Skinner and colleagues' views. It is also likely that many patients would gain a placebo effect and, in the long term, "feel better" only with a dose of thyroxine that suppresses serum thyroid stimulating hormone[5]—a situation that may be associated with the development of osteoporosis or atrial fibrillation.

G J Beckett *Senior lecturer, university department of clinical biochemistry*
A D Toft *President, British Thyroid Association*
Royal Infirmary NHS Trust, Edinburgh EH3 9YW

1 Skinner GRB, Thomas R, Taylor M, Sellarajah M, Bolt S, Krett S, et al. Thyroxine should be tried in clinically hypothyroid but biochemically euthyroid patients. *BMJ* 1997;314:1764. (14 June.)
2 Vanderpump MPJ, Ahlquist JAO, Franklyn JA, Clayton RN. Consensus statement for good practice and audit measures in the management of hypothyroidism and hyperthyroidism. *BMJ* 1996;313:539-44.
3 Cooper DS, Halpern R, Wood LC, Levin AA, Ridgeway ED. L-thyroxine therapy in subclinical hypothyroidism: a double blind, placebo-controlled trial. *Ann Intern Med* 1984;101:18-24.
4 Weetman AP. Hypothyroidism: screening and subclinical disease. *BMJ* 1997;314:1175-8. (19 April.)
5 Carr D, Mcleod DT, Parry G, Thornes HM. Fine adjustment of thyroxine replacement dosage: comparison of the thyrotrophin releasing hormone test using a sensitive thyrotropin assay with measurement of free thyroid hormones and clinical assessment. *Clin Endocrinol* 1988;28:325-33.

Distinguishing hypothyroid symptoms from common non-specific complaints is difficult

EDITOR—Gordon R B Skinner and colleagues propose the apparently empirical treatment of suspected hypothyroidism in patients in whom results of thyroid function tests that fall within the normal range[1]. Nobody would argue with the assertion that the symptomatology of hypothyroidism can be non-specific, that it can be an easy diagnosis to miss, or that the rewards of replacing thyroxine in patients with proved hypothyroidism can be spectacular.

There are considerable risks, however, in the inappropriate prescription of thyroid hormone replacement to patients who do not warrant it. This has been a particular problem in the management of obesity, and correspondence with our local group of the ME Association indicates that thyroid hormone treatment is also being promoted for chronic fatigue. For this condition, certain medical practitioners are advocating the use of desiccated thyroid extract in preference to the pure thyroid hormones that are recommended in the *British National Formulary*, presumably to add an element of mystique to this unproved treatment.

Given the difficulty of distinguishing hypothyroid symptoms from common non-specific complaints such as tiredness, lack of energy, and difficulty in concentrating, Skinner and colleagues need to reassure us that their "established criteria" stand up to objective scrutiny. I agree with them that a formal clinical trial might be justified but suggest that this would be of little use unless an objective physiological outcome can be measured. In the meantime, giving thyroid hormones to patients who are biochemically euthyroid must remain dubious and potentially dangerous on both scientific and medicolegal criteria.

Gareth Williams *Professor of medicine (diabetes and endocrinology)*
University Clinical Departments at Aintree, Fazakerley Hospital, Liverpool L9 7AL

1 Skinner GRB, Thomas R, Taylor M, Sellarajah M, Bolt S, Krett S, et al. Thyroxine should be tried in clinically hypothyroid, but biochemically euthyroid patients. *BMJ* 1997;314:1764. (14 June.)

Long term treatment is being used

EDITOR—During the past six months I have become aware of an increasing number of patients with normal results of thyroid function tests who are being treated with a daily dose of up to 100 µg thyroxine—mainly as a result of publicity being given in the lay media[1] to a hypothesis put forward by Gordon R B Skinner and colleagues.[2] These biochemically euthyroid patients invariably have several symptoms that are compatible with a clinical diagnosis of hypothyroidism, but many of them also have agreed diagnostic criteria for the chronic fatigue syndrome, a condition that does involve dysfunction of the hypothalamic-pituitary axis but not hypothyroidism.

Although a short trial of low dose thyroxine may be relatively safe in these circumstances, my experience is that almost all of these patients are continuing to be prescribed thyroxine. In some cases the dose is being progressively increased. Serious cardiovascular side effects cannot be ruled out in patients with the chronic fatigue syndrome with undetected abnormalities in cardiovascular function,[3] and there is a further danger of an addisonian crisis being precipitated in those who have hypocortisolaemia. Long term unwarranted use of thyroxine will increase the likelihood of osteoporosis and lead to a risk of permanent disruption to the normal feedback mechanisms affecting the release of thyroid stimulating hormone.

In the absence of any reputable evidence to support the hypothesis that clinical hypothyroidism can exist in biochemically euthyroid patients, I believe that this entirely speculative use of thyroxine should be restricted to a carefully supervised research project with normal ethical approval. In the meantime I have sent all my information to the Department of Health in an attempt to persuade the chief medical officer to issue clear guidelines on giving thyroxine to patients with normal results of thyroid function tests. Doctors who decide to prescribe thyroxine for such an unlicensed purpose may well find themselves involved in litigation should a mishap subsequently occur.

Charles Shepherd *Medical director*
ME Association, Stanford le Hope, Essex SS17 0HA

1 Reid M. Kicking out against thyroid disease. *Glasgow Evening Times* 1997 Feb 21.
2 Skinner GRB, Thomas R, Taylor M, Sellarajah M, Bolt S, Krett S, et al. Thyroxine should be tried in clinically hypothyroid but biochemically euthyroid patients. *BMJ* 1997;314:1764. (14 June.)
3 Lerner AM, Lawrie C, Dworkin HS. Repetitively negative changing T waves at 24 hour electrocardiographic monitors in patients with chronic fatigue syndrome. Left ventricular dysfunction in a cohort. *Chest* 1993;104:1417-21.

Diagnosing pulmonary embolism

EDITOR—The letters commenting on my review on the diagnosis of pulmonary embolism merit a reply.[1,2] My first comment concerns the morbidity of anticoagulant treatment. A study by the British Thoracic Society showed a mortality of 0.1%, with serious bleeding in 6/1000 patient months.[3] Most published studies of mortality and morbidity refer to long term treatment with anticoagulants, but even recent studies of the treatment of atrial fibrillation in which the target international normalised ratio was 2-3 have shown a mortality of between 0% and 0.8% a year[4]; indeed, in the general practice study referred to by David Fitzmaurice and colleagues no deaths occurred.[5] Thus, when published guidelines or computer programs are used and a target international normalised ratio (of 2-3) is maintained, mortality and morbidity are extremely low.

My review may have seemed somewhat backward looking, but only because I was attempting to impart what is known rather than what might be. The diagnosis of pulmonary emboli has seen many false dawns in the past. Spiral computed tomography may well be that long sought non-invasive test to rival angiography. At the moment, however, a negative result of computed tomography is in many ways less

helpful than a negative result of isotope lung scanning or, indeed, an indeterminate result of scanning since we do not know the likely incidence of pulmonary embolism in these patients or what ultimately happens to them. Transthoracic cross sectional echocardiography and Doppler measurements can sometimes raise the possibility of a pulmonary embolus, but this is usually in cases in which such a finding was unexpected; these tests are unlikely ever to be first line investigations for suspected disease.

Finally, I accept John A Holemans and John F Reidy's point that pulmonary angiography has a low mortality and morbidity and that a few clinicians may be under the misapprehension that both are high. While many clinicians indeed do not request the test because it is not readily available, if we do not make concerted efforts to get angiography then it will never be made available. In patients in whom scans are non-diagnostic and who have underlying cardiorespiratory disease, for example, we should perhaps be pushing for angiography more often than we do.

A G Fennerty *Consultant physician*
Southern General Hospital NHS Trust, Glasgow G51 4TF

1 Diagnosing pulmonary embolism (letters). *BMJ* 1997;314:1550-1. (24 May.)
2 Fennerty T. Diagnosing pulmonary emboli. *BMJ* 1997;314:425-9. (8 February.)
3 Research Committee of the British Thoracic Society. Optimum duration of anticoagulation for deep vein thrombosis and pulmonary embolus. *Lancet* 1992;240:873-6.
4 Koefed BG, Gull VAL, Paterson P. Prevention of thromboembolic events in atrial fibrillation. *Thromb Haemostas* 1997;78:377-81.
5 Fitzmaurice DA, Hobbs FDR, Rose P, Murray ET. A randomised controlled trial comparing primary care oral anti-coagulant management utilising computerised decision support (DSS) and near patient testing (NPT) with traditional management. *Br J Haematol* 1996;93:S30.

Pneumococcal vaccine campaign based in general practice

Further prospective randomised controlled trial is necessary

Editor—Paula McDonald and colleagues have shown that a pneumococcal campaign based in general practice is feasible and offers the potential to increase substantially the proportion of patients at risk of pneumococcal infections who are vaccinated.[1] Unfortunately, there remains a lack of robust evidence, particularly outcome data, to support pneumococcal vaccination in all the at risk groups identified in their paper. For example, one of the studies quoted by McDonald and colleagues fails to show any evidence of a protective effect of vaccination in patients with alcohol dependence or cirrhosis, sickle cell disease, chronic renal failure, or Hodgkin's disease.[2] These conditions, however, are included in most lists of target groups for pneumococcal vaccination, including McDonald and colleagues'.

Butler et al's work also shows that the vaccine's efficacy in the conditions with a higher prevalence, such as congestive cardiac failure, may be as low as 17% or as high as 88% when confidence intervals are considered.[2] Small sample sizes make conclusions difficult to draw.

Other work has relied on the development of pneumococcal antibodies rather than reductions in morbidity and mortality. We have collated details of 40 trials and 15 other papers on this topic. The general trends show that the groups at greatest risk from pneumococcal infection are those with the most impaired immune response. This potentially limits the usefulness of pneumococcal vaccination programmes.

Fine et al have published a meta-analysis of randomised controlled trials of pneumococcal vaccination, which McDonald and colleagues did not cite.[3] They concluded that "evidence from randomized controlled trials fails to demonstrate vaccine efficacy for pneumococcal infection-related or other medical outcomes in the heterogeneous group of subjects currently labelled as high risk."

A protocol for a systematic review of the literature in relation to pneumococcal vaccination has been posted in the *Cochrane Database of Systematic Reviews*.[4] A further prospective randomised controlled trial is necessary. Such a trial will need to look at outcome measures reflecting reductions in infection, morbidity, and mortality, with subgroup analysis by underlying illness and age, to provide a definitive answer to whether McDonald and colleagues' primary care based model would save lives or waste large amounts of healthcare resources.

Neal Maskrey *Consultant in primary care development*
Martin Parkinson *Pharmaceutical adviser*
North Yorkshire Health Authority, York YO1 1PE

1 McDonald P, Friedman EHI, Banks A, Anderson R, Carman V. Pneumococcal vaccine campaign based in general practice. *BMJ* 1997;314:1094-8. (12 April.)
2 Butler JC, Breiman RF, Campbell JF, Lipman HB, Broome CV, Facklam RR. Pneumococcal polysaccharide vaccine efficacy. An evaluation of current recommendations. *JAMA* 1993;270:1826-31.
3 Fine MJ, Smith MA, Carson CA, Meffe F, Sankey SS, Weissfeld LA, et al. Efficacy of pneumococcal infection in adults. A meta-analysis of randomized controlled trials. *Arch Intern Med* 1994;154:2666-77.
4 Holden J, Fine M, Jefferson T. A systematic review of the effectiveness of pneumococcal vaccination in adults and children. In: Douglas R, Berman S, Black RE, Bridges-Webb C, Campbell H, Glezen P, et al, eds. Acute respiratory infections module. *Cochrane Database of Systematic Reviews*. Oxford: Cochrane Collaboration. [Updated 2 December 1996.]

Expert advice is unclear

Editor—Paula McDonald and colleagues' study of pneumococcal vaccination in general practice shows what might be achieved by a targeted vaccination campaign.[1] The authors state that they based their guidelines pragmatically on the best available advice. Although, like many other general practitioners, I am in favour of clinical guidelines,[2] I have some concerns about the validity and practical application of recent expert advice on pneumococcal vaccination.

The Department of Health recommends vaccination for chronic lung disease, but whether this includes chronic asthma is not clear.[3] In the same guidelines general practitioners are encouraged to give pneumococcal vaccine when immunising patients against influenza, as some practices in McDonald and colleagues' study would have preferred; patients with asthma are considered to be a target group for immunisation against influenza.[3]. In the United States, where pneumococcal vaccination is considered to be cost effective, it is recommended for asthmatic patients.[4] I find it difficult to see why a patient with severe chronic asthma should be excluded from vaccination while a patient with mild chronic bronchitis is included. The authors did not reference the expert advice on which they based the exclusion of patients with asthma from pneumococcal vaccination in this study.

Another practical difficulty is that of reimmunisation. The Department of Health advises against reimmunisation except for patients with asplenia, hyposplenism, or the nephrotic syndrome,[3] whereas a recent review suggested monitoring antibody concentrations three to four weeks after vaccination and then annually.[5] If reimmunisation was necessary then there would be resource implications for practices and perhaps also a reluctance among patients to reattend if, as this study suggests, the rate of side effects from the vaccination was over 50%.

Poor uptake of vaccine may be due to poor knowledge or attitudes among doctors as well as patients. I accept that knowledge may be constantly changing, but effective vaccination programmes in primary care will be impeded by unclear expert advice.

A N Siriwardena *General practitioner*
Minster Practice, Lincoln LN2 2JP

1 McDonald P, Friedman EHI, Banks A, Anderson R, Carman V. Pneumococcal vaccine campaign based in general practice. *BMJ* 1997;314:1094-8. (12 April.)
2 Siriwardena AN. Clinical guidelines in primary care: a survey of general practitioners' attitudes and behaviour. *Br J Gen Pract* 1995;45:643-7.
3 Department of Health, Welsh Office, Scottish Home and Health Department, Department of Health and Social Services (Northern Ireland). *Immunisation against infectious disease*. London: HMSO, 1996:169-72.
4 Fiebach N, Beckett W. Prevention of respiratory infections in adults: influenza and pneumococcal vaccines. *Arch Intern Med* 1994;154:2545-57.
5 Obaro SK, Monteil MA, Henderson DC. The pneumococcal problem. *BMJ* 1996;312:1521-5.

Datasheet for vaccine contradicts authors' recommendations

Editor—Paula McDonald and colleagues include patients with immunodeficiency and immunosuppression as target groups for pneumococcal vaccination,[1] in agreement with the Department of Health's guidelines.[2] The current datasheet for the 23-valent vaccine (Pneumovax II; Pasteur Mérieux), however, states that the vaccine is contraindicated for patients less than 10 days before or during immunosuppressive treatment.[3] As a further contraindication, the datasheet mentions patients with Hodgkin's disease who have received extensive chemotherapy or nodal irradiation, or both, whereas McDonald and colleagues specifically include patients with Hodgkin's disease as a target group.

Recommending a vaccine for groups in which it is contraindicated by the manufacturer puts prescribers in a difficult position; which advice do we follow?

Antony Walters *General practitioner*
Mayford House Surgery, Northallerton DL6 1NP

Nigel C Weightman *Consultant microbiologist*
Department of Microbiology, Friarage Hospital, Northallerton DL6 1JG

1 McDonald P, Friedman EHI, Banks A, Anderson R, Carman V. Pneumococcal vaccine campaign based in general practice. *BMJ* 1997;314:1094-8. (12 April.)
2 Department of Health, Welsh Office, Scottish Home and Health Department, Department of Health and Social Services (Northern Ireland). *Immunisation against infectious disease.* London: HMSO, 1996.
3 ABPI compendium of data sheets and summaries of product characteristics 1996-7. London: Datapharm, 1996:736-7.

Authors' reply

EDITOR—Neal Maskrey and Martin Parkinson suggest that there is not enough evidence to support the Department of Health's policy of vaccinating high risk groups. The meta-analysis of randomised controlled trials that they cite, however, provides little evidence to support or disprove their view[1]: the randomised controlled trials that included patients relevant to the Department of Health's guidelines found only four confirmed pneumococcal infections in total. Randomised controlled trials are not helpful in evaluating pneumococcal vaccine because no reliable outcome measure for pneumococcal pneumonia exists. This makes results difficult to interpret unless there is a clear difference between groups, as in the early trials in a population with a high incidence of the disease. Randomised controlled trials based on confirmed infections (bacteraemia and meningitis) require unfeasibly large numbers. The trial that Maskrey and Parkinson want to do would require 117 000 people in each risk group to show 50% efficacy against confirmed pneumococcal infections—for example, all HIV positive patients diagnosed in Britain for the next 39 years. Such a trial would be unlikely to get ethical approval, as the vaccine is already licensed for these groups.

Case-control studies and indirect cohort analysis are more powerful than randomised controlled trials in conditions with a low incidence and high morbidity. Several such studies have found evidence of efficacy of the vaccine against confirmed pneumococcal infections, including in some common at risk groups. Limited recruitment of patients has precluded definitive estimates of efficacy in some disorders, but there is a trend towards reduced efficacy in immunosuppressed patients. Pneumococcal infections, however, are serious, and costly to treat. Vaccination is cost effective in high risk conditions even if the vaccine has low efficacy and protection is short lived.[2]

We need a better test for pneumococcal infections. Meanwhile, an estimated 60-90 patients per health authority will die of pneumococcal infections annually. We can ignore this, or we can base our decisions on the best evidence available. In our view, it is reasonable to vaccinate groups known to be at high risk from pneumococcal infections if the efficacy of the vaccine is unknown but antibody response has been shown.

Recent evidence supports an age related policy for vaccination.[3 4] This would simplify the situation, which A N Siriwardena suggests is necessary, but younger patients at high risk would still need vaccinating. We listed our advisers at the end of our paper.

Finally, we have asked the manufacturer to review its datasheet regarding Hodgkin's disease. Our protocol (not published) advised on timing of vaccination, as do the Department of Health's guidelines (widely available).

Paula McDonald *Consultant in communicable disease control*
Communicable Disease Unit, Public Health Laboratory Service, Chester CH2 1UL

Ellis Friedman *Director of public health*
Alan Banks *Medical adviser*
West Pennine Health Authority, Oldham OL1 2PU

Ros Anderson *Independent pharmaceutical adviser*
Lorac Clinical Pharmacy Services, Cheadle, Cheshire SK8 1DW

Val Carman *Nurse adviser*
East Lancashire Health Authority, Nelson, Lancashire BB2 5SZ

1 Fine MJ, Smith MA, Carson CA, Meffe F, Sankey SS, Weissfield LA, et al. Efficacy of pneumococcal vaccine in adults. A meta-analysis of randomised controlled trials. *Arch Intern Med* 1994;154:2666-77.
2 Rose DN, Schecter CB, Sacks HS. Influenza and pneumococcal vaccination of HIV positive patients: a policy analysis. *Am J Med* 1993;94:161-8.
3 Sims RV, Steinmann WC, McConville JH, King LR, Zwick WC, Schwartz JS. The clinical effectiveness of pneumococcal vaccine in the elderly. *Ann Intern Med* 1988;108:653-7.
4 Makela PH. A cost-benefit analysis of pneumococcal disease. In: Mayon-White RT, ed. *The clinical impact of pneumococcal disease and strategies for its prevention.* London: Royal Society of Medicine, 1995:41-8. (International congress and symposium series No 210.)

Small audit showed that only 14% of patients were offered pneumococcal vaccine

EDITOR—Paula McDonald and colleagues' paper on the implementation of a pneumococcal vaccination campaign highlighted not only the effectiveness of such a campaign but also the pressing need for such campaigns.[1] Although the Department of Health recommends the use of pneumococcal vaccine in several high risk groups,[2] the authors found that only 17% of general practitioners offered the vaccine before the campaign.

We have found a similar poor degree of compliance with these recommendations in a group of patients with chronic obstructive pulmonary disease in East Yorkshire. Patients with this disease comprise one of the high risk groups for which pneumococcal vaccination is recommended. In a random sample of 40 patients admitted to hospital in 1995 with an acute exacerbation of chronic obstructive pulmonary disease, records were available for 28. Only four of the 28 had been offered pneumococcal vaccine by their general practitioner at any time before that admission. All these patients had symptomatically severe chronic obstructive pulmonary disease, as shown by both their admission to hospital and their average of 7.2 primary care consultations for their chest condition in the year before their admission.

The low number of patients who were offered pneumococcal vaccine contrasted greatly with the finding that 22 had been offered influenza vaccine in the year before admission. Other work has also shown relatively good rates of acceptance of influenza vaccination in high risk groups.[3] Although the sample size in our study was small, there was a striking difference between the immunisation rate with pneumococcal vaccine and that with influenza vaccine. Differences in the potential for remuneration might explain part of the difference between these rates.

McDonald and colleagues' paper suggests that further education could result in a similar proportion of high risk people receiving pneumococcal vaccine as receive influenza vaccine. We are therefore repeating our study to find out if the rate of pneumococcal immunisation has increased in the two years since the original audit. Further education and specific campaigns are needed in both primary and secondary care to increase compliance with the Department of Health's guidelines.

M J Doherty *Senior registrar in respiratory medicine*
M A Greenstone *Consultant in respiratory medicine*
R Meigh *Consultant microbiologist*
Castle Hill Hospital, Cottingham, North Humberside HU16 5JQ

1 McDonald P, Friedman EHI, Bank A, Anderson R, Carman V. Pneumococcal vaccine campaign based in general practice. *BMJ* 1997;314:1094-8. (12 April.)
2 Department of Health, Welsh Office, Scottish Home and Health Department, Department of Health and Social Services (Northern Ireland). *Immunisation against infectious disease.* London: HMSO, 1996.
3 Gene J, Espinola A, Cabezas C, Boix C, Comin E, Martin A, et al. Do knowledge and attitudes about influenza and its immunisation affect the likelihood of obtaining immunisation? *Fam Pract Res J* 1992;12:61-73.

Managing eye conditions in general practice

EDITOR—Though general practitioners' confidence in diagnosing and managing eye conditions is not high, they can expect 2-5% of all consultations to be eye related.[1] Teaching of ophthalmology at medical school is limited in duration and far removed in time from entry to general practice. Less than 5% of general practice registrars do any ophthalmology as part of vocational training (data from Joint Commitee for Postgraduate Training in General Practice), but over 70% do an accident and emergency post, usually for six months. I sent a questionnaire to all accident and emergency departments in England, asking clinical directors and general practice registrars about the amount, usefulness, and potential for improvement of any ophthalmology training received during this period.

Of 214 questionnaires sent, 104 were returned. Six per cent of new patients presenting to accident and emergency and 11% of those returning have ophthalmological diagnoses, exposing the average sen-

Eye problems most commonly seen in accident and emergency departments and general practice[4 5]

	Proportion of diagnoses (%)
General practice	
Infective conjunctivitis	44
Allergic conjunctivitis	15
Meibomian cyst	8
Blepharitis	5
Contact lens problem	4
Abrasion and foreign body	3
Stye	2
Accident and emergency	
Foreign body	29
Abrasion	15
Conjunctivitis	9
Allergy	3
Lid inflammation	3
Other trauma (combined)	15

ior house officer to 230 new eye problems over six months. All responding senior house officers said that this experience was useful and relevant to general practice. Sixty one of the 102 senior house officers (60%) had a slit lamp available, and nearly all of these considered themselves reasonably competent in its use. Seventy five senior house officers (74%) felt confident in handling most presenting eye problems. This contrasts with established general practitioners, 68% of whom admit to "some uncertainties about eyes" (10% affirm that eyes "scare me stiff").[2]

Over three quarters (78%) of all responding departments offered formal teaching in ophthalmology (although only 68% of senior house officers received it), and 78% of the clinical directors were happy to have responsibility for initial assessment and treatment of eye casualties. Both groups of respondents wished to have more liaison, teaching, and feedback from their local eye department.

The spectrum of eye disease in accident and emergency differs from that in general practice (table 1),[3 4] but there is more overlap than between general practice and an eye clinic.

This survey shows that there is much exposure to eye problems in accident and emergency departments. For most general practitioners this could be their most important period of ophthalmological training, if supervision and training are adequate. Confidence can be gained with basic eye examination and use of the slit lamp (a feasible tool in many group practices), together with a working knowledge of many common eye conditions. Simple improvements in equipment and training and involvement of specialists may improve confidence among future general practitioners. Any moves by individual hospitals to set up eye casualty units staffed by career ophthalmologists must consider the inevitable weakening of general practice training in their area.

T Manners *Specialist registrar*
Ophthalmology Department, Addenbrooke's Hospital, Cambridge CB2 2QQ

1 Featherstone PI, James C, Hall MS, Williams A. General practitioners' confidence in diagnosing and managing eye conditions: a survey in south Devon. *Br J Gen Pract* 1992;42:21-4.
2 Wilson A. The red eye: a general practice survey. *J R Coll Gen Pract* 1987;37:62-4.
3 Edwards RS. Ophthalmic emergencies in a district general hospital casualty department. *Br J Ophthalmol* 1987;71: 938-42.
4 McDonnell PJ. How do general practitioners manage eye disease in the community? *Br J Ophthalmol* 1988;72:733-6.

Medical managers

Doctors need training in management skills

EDITOR—The recent call for more doctors to be involved in the management of the NHS is to be welcomed.[1] Jenny Simpson and Richard Smith outlined the benefits of having doctors involved in management, the main thrust of the argument being that doctors have knowledge of patient care and are in a more credible and secure position to take a stand against financial priorities imposed by bureaucratic hierarchies. This position is strongly supported by Oni, who argues that only doctors should manage the NHS because doctors treat patients and are the only permanent members of staff.[2]

A paradox arises because many of the good reasons for having doctors as managers pose difficulties for them in making the transition to effective management roles in NHS hospitals. Consultants are managers of their clinical teams. Rightly, their focus and loyalty is to their patients, specialty, and royal college. When they assume a managerial role they are asked to take a more corporate view and to take decisions which may not directly benefit their patients. Consultants, as a result of their length of service in one place, may not feel able to challenge colleagues in their efforts to improve the system of delivering health care.

Few hospital consultants have been trained to think strategically about how health care is delivered across a population. As consultants become more specialised their ability to use their in depth knowledge of patient care across the breadth of hospital services diminishes.

Doctors should become managers. However, just as professional managers often lack the necessary insight into the clinical aspects of patient care, doctors without suitable training lack the insight into the more corporate function of a manager. What is key to the future success of the NHS at hospital level is a partnership approach to leadership. The skills that different groups bring to the task will ensure success. As Berwick discussed, doctors and their medical associations can either play the role of victim or become leaders in improving healthcare systems.[3] The task of the leaders is to develop the interactions of the system, not the individual elements.

Doctors are experts in the individual elements; the management challenge for us all is to develop better interactions in the corporate system.

Mike Williams *Chief executive*
Radcliffe Infirmary NHS Trust, Oxford OX2 6 HE

1 Simpson J, Smith R. Why healthcare systems need medical managers. *BMJ* 1997;314:1636-7. (7 June.)
2 Oni O. *Who should run the health service?* Abingdon: Radcliffe Medical, 1997.
3 Berwick DM. Medical associations: guilds or leaders? *BMJ* 1997;314:1564 -5. (31 May.)

BMA is also working to develop role of clinicians in management

EDITOR—Jenny Simpson and Richard Smith rightly drew attention to the unique contribution that clinicians can make to the management of the NHS.[1] The initiatives they described—to develop the intellectual base of medical management and to disseminate the knowledge and experience of enthusiasts more widely within the profession—are welcomed. These initiatives will give support to medical managers in the vital task of maintaining the confidence of clinicians, on whom their influence ultimately depends.

How disappointing, then, that Simpson and Smith do not acknowledge the contribution of the BMA in this area. The Clinical and Medical Directors Subcommittee of the Central Consultants and Specialists Committee functions within the wider representation processes for senior hospital doctors, so that differences of view as well as areas of common interest can be debated in the forum of the national craft committee. The subcommittee, which was reconstituted last year after national elections (in which 114 candidates stood for 14 seats), has already produced new guidance on developing the role of clinical directors and has almost completed the same task for medical directors. Such documents are published with the support of the consultants and are thus uniquely influential.

I hope that the new journal, *Clinician in Management*, will provide further impetus for our common efforts to ensure that medical management is increasingly seen as an integral part of the profession's clinical role.

Christopher Bayliss *Chairman*
Clinical and Medical Directors Subcommittee, Central Consultants and Specialists Committee, BMA House, London WC1H 9JP

1 Simpson J, Smith R. Why healthcare systems need medical managers. *BMJ* 1997;314:1636-7. (7 June.)

Correction

Impact of postmenopausal hormone therapy on cardiovascular events and cancer

Owing to an editorial error, one of the authors was omitted from the final letter in this cluster (13 September, pp 676-9). There should have been two authors to this authors' reply: Elina Hemminki (as given) and Klim McPherson, professor of public health epidemiology at the Health Promotion Sciences Unit (Department of Public Health and Policy), London School of Hygiene and Tropical Medicine, London WC1E 7HT.