risks of nicotine replacement treatment are likely to be much less than those of cigarette smoking for several reasons.[4] For most smokers the doses of nicotine obtained by cigarette smoking exceed those delivered by currently marketed nicotine replacement treatments. The cardiovascular effects of nicotine are more intense when delivered rapidly by cigarette smoking than when delivered more slowly, as by nicotine patches. The relation between the dose of nicotine and cardiovascular response is flat, such that the effects of cigarette smoking combined with nicotine from other sources are similar to those of cigarette smoking alone.[5] At a minimum, the risk of nicotine replacement treatment is likely to be much less than that of cigarette smoking, even in patiens with coronary heart disease. These risks are substantially outweighed by the potential benefits of the increased likelihood of stopping smoking by using nicotine replacement treatment.

With respect to the case reports, relatively few adverse cardiovascular events have been reported despite millions of patients having used nicotine patches, many of whom are presumed to be at considerable risk of acute cardiovascular events. Any middle aged or older person who has smoked long term is at increased risk of myocardial infarction or sudden death; and some of these events are bound to occur by chance in the first few weeks or months after that person has stopped smoking, whether or not nicotine patches are used.

I agree that further research into the risks of nicotine replacement treatment in patients with cardiovascular disease is needed. Meanwhile, I would much prefer my patients with coronary heart disease to use nicotine patches than to smoke cigarettes.

NEAL L BENOWITZ*
Chief

Division of Clinical Pharmacology and
Experimental Therapeutics,
Department of Medicine,
University of California, San Francisco,
San Francisco General Hospital,
San Francisco, CA 94110,
USA

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*Professor Benowitz has been a consultant to many of the pharmaceutical companies that manufacture or market nicotine replacement products, including nicotine patches.

Limitations of randomised controlled trials

EDITOR,—T C B Dehn has commented on the problems of accruing patients into randomised controlled trials, noting the understandable reluctance of patients to enter some trials ("I want the best treatment, doctor") in which the patient's outcome (for example, time to death) is the main end point and, consequently, the patient is unable to benefit from the study directly.[1] This raises a fundamental issue concerning the usefulness of randomised controlled trials in reliably identifying new clinical knowledge. Less recognised, but equally important, is inconsistent clinical enthusiasm to offer the study to all patients presenting during the study period, which results in patient selection bias.

The large bowel cancer project's randomised controlled trial recorded the presence of such an "eligible but not randomised" subpopulation, the proportion of which varied among participating clinicians.[2] Furthermore, the clinical outcome in this group differed from that in the trial's control arm, confirming the problem of selection bias. This factor, and other forms of bias, limit the value of randomised design for prospective studies.[3] If, however, we are committed to generating reliable new knowledge using the format of randomised controlled trials then the clinical scientists conducting these studies, as well as the grant giving bodies supporting them, should recognise the existence of patients who are eligible but not randomised in all such trials.

We propose two strategies to address this problem. Firstly, all patients with the diagnosis of interest in the study should be documented and followed up whether or not they become part of the randomised controlled trial. Secondly, after a positive study result has been obtained documentation should continue during the implementation phase of the new treatment to show that the expected positive outcome for the population at large does occur. Without such post-trial surveillance it is difficult to know that the predicted value of the study materialises in an unselected population. In addition, the low rates of unexpected sequelae (either complications or additional benefits) may not be recognised. This additional documentation should become part of the plans for the randomised controlled trial. Pollock concluded that consecutive audit has value in this context.[4]

The high cost of randomised controlled trials (money, resources, and professional commitment) and the trust that patients place in us when they enter such trials mandate that all efforts are geared to improving patients' care. An increased awareness of the group in randomised controlled trials who are eligible but not randomised, the need for post-trial surveillance, and the need for eventual audit will help the process of responsible implementation of new treatment. These issues not only are the responsibility of clinical investigators but should be crucial concerns for funding leaders and medical publishers.

L PETER FIELDING
Chief

Department of Surgery,
Genesee Hospital,
Rochester, NY 14607-4005,
USA

ROGER GRACE
Consultant surgeon

Oaken,
Wolverhampton WV8 2BA

ROSEMARY HITTINGER
Senior audit coordinator, surgery, NHS

Queen Elizabeth the Queen Mother Academic Surgical Unit,
St Mary's Hospital,
London W2 1NY

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Childhood antecedents of schizophrenia

EDITOR,—Andrew D Paterson is correct to point out the abundant evidence of a genetic contribution in the aetiology of schizophrenia, but I take exception to his conclusions regarding treatment.[1] He makes a basic error in assuming that just because a biological factor can be shown to be of primary importance in the aetiology of a condition then it must follow that suitable treatments must also be limited to the biological. Even if, as seems the case, environmental factors are of minimal importance in the aeriology of schizophrenia, we must not neglect the psychological and social aspects of management. We should remember, for example, that it is a simple dietary intervention that is required in phenylketonuria, an autosomal recessive disorder whose genetics are far better understood than schizophrenia.

Paterson's statement that "it is questionable whether psychotherapeutic intervention will have any influence on the expression of the disease" is surprising in the light of the fact that in his previous paragraph he quoted McGuffin *et al* as stating, "there is good evidence that psychosocial factors, such as high expressed emotion at home or life events, can hasten relapses or precipitate onsets."[2] Surely it is now time to move on from this Platonic dualism separating soul and body, mind and brain, to a medicine that recognises and treats the whole person with whatever interventions prove to be effective.

IAN JONES
Registrar in psychiatry

St Cadoc's Hospital,
Newport, Gwent NP6 1XQ

1 Paterson A. Childhood antecedents of schizophrenia. *BMJ* 1995;310:667-8.
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Palliative care in terminal cardiac failure

Hospices cannot fulfil such a vast and diverse role

EDITOR,—I agree with Sarah Jones's comments about the neglected needs of patients with terminal cardiac failure[1] and the fact that the poor prognosis is not appreciated as being the same as that in cancer.[2] Ironically, this benefits patients with cardiac failure, who are spared the taboos of cancer, its particular stresses, and the distancing of health professionals. The infrequency of requests to hospices regarding cardiac failure could reflect the ability and willingness of hospitals and primary care teams to continue care. The original need for hospices was to redress this imbalance.

Palliative care for all is an admirable goal, and palliative medicine's basic principles apply to those dying of any illness. It is naive, however, to pretend that present hospices could fulfil such a vast and diverse role.

Hospices offer intensive specialist input, historically to patients with cancer plus motor neurone disease and multiple sclerosis and more recently to those with HIV infection. Patients are seen at any time of their illness according to need, with end stage care being only part of hospices' role. Hospices' skill lies in actively controlling symptoms and providing support through day centres, outpatient visits, and short inpatient stays averaging 14 days,[3] with discharge in most cases. This does not qualify hospice doctors as specialists in the many other terminal diseases that need hospice-type care. Nor are hospices in a position to offer medium term or long term care, which is a common request for patients with non-malignant diseases. As with cancer, this would be a waste of resources, and provisions are made elsewhere.

Over three quarters of hospice beds are funded by charities and bound by mission statements, which may single out cancer for individual attention. The reason for donations must be honoured.

Palliative medicine is acknowledged to be advancing rapidly while concentrating on this specific range of patients[4]; broadening its remit would dilute the benefits of specialising and hence slow progress. The hospice philosophy provides staff with a clear approach in a stressful specialty. This may be less appropriate for diseases with

differing natural courses,[5] and their inclusion could require intolerable variations in management.

The hospice environment may seem more distressing for patients with diseases other than cancer; moreover, if such patients were treated in hospices, patients with cancer might have greater difficulties with body image and in accepting the inconsistency of more active management being given for non-malignant diseases.[5] Hospices are deliberately not generally equipped to deliver such management so that overmedicalisation of terminal care is avoided.

Presently hospices see only about half of patients with cancer, which leaves little scope for the needs of a wider population (estimated at 150% extra bed days required for patients with diseases other than cancer[6]).

Hospice-style input for non-malignant diseases remains equally important but requires appropriate provision in addition to traditional hospices. Adequate community services could also meet much of this need. Hospices offer quality rather than quantity and should not be seen as an easy and cheaper option for providing care for patients with terminal disease as if they were a homogeneous group.

CRAIG GANNON
Staff grade doctor in palliative medicine
Myton Hamlet Hospice,
Warwick

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Small numbers of patients with terminal cardiac failure may make considerable demands on services

EDITOR,—We agree with Sarah Jones that palliative care seems rarely to be offered to patients with congestive heart failure and that referral of such patients for community based hospice care is exceptional.[1] It is uncertain, however, whether the small uptake of such services that Jones reports reflects clinical need,[2] the referral practice of local doctors, or the conceptual approach of the small group of hospices surveyed. Similarly, alternative, hospital based symptomatic support may be available for these patients.

Such a palliative care programme was established in this hospital in July 1989, closely linked to a busy regional adult cardiology service. From the inception of this department, staffed by clinical nurse specialists, we have actively collaborated in the care of inpatients with a primary diagnosis of congestive heart failure whose symptoms have proved refractory to aggressive medical treatment (New York Heart Association grade III or IV). The number of such patients referred for palliative care was four in July to December 1989, seven in 1990, 10 in 1991, six in 1992, five in 1993, and five in 1994. The number requiring palliative care thus seemed to be relatively small, with a mean annual referral rate of 7 (SD 2) patients. This constituted only 1% of all referrals to the service over the above period. The patients, however, made a considerable demand on services, with a range of 1 to 25 contacts between individual patients and staff (mean 6(4)).

Most of this population had progressive heart failure due to coronary heart disease. The 37 patients were aged 28-81 (mean 68(9)), and 29 were male. As expected, they had a poor prognosis, with an average period between referral and death of 16 weeks. Only seven of this group remain alive, three have been treated in the latter half of 1994; they include our youngest patient, who made a full recovery after presenting in cardiogenic shock due to viral myocarditis.

Palliative care in the community remains largely devoted to oncology patients, which perhaps reflects the historical development and funding base of such activity. The needs of other diagnostic groups, however, seem to be increasingly recognised, albeit with some reluctance. Six of our early patients were followed up at home because a lack of provision for patients with heart failure was perceived at that time. This activity was deemed impractical 18 months after the initiation of our hospital based continuing care service because of the high inpatient workload. In contrast, over the past year three of our patients with heart failure have been supported by local hospice care or the Macmillan nurse service.

J M BEATTIE
Consultant cardiologist
R G MURRAY
Consultant cardiologist
JAN BRITTLE
Continuing care sister
TRISH CATANHEIRA
Continuing care sister
Department of Cardiology,
Birmingham Heartlands Hospital,
Birmingham B9 5SS

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Reperfusion injury after myocardial infarction

EDITOR,—Ever D Grech and colleagues omit to mention the role of the complement system in their discussion of the mechanism of reperfusion injury after myocardial infarction.[1] It has long been recognised that complement activation, which occurs on reperfusion of ischaemic myocardium (and, indeed, on reperfusion of other ischaemic tissues) is an important effector in the tissue damage that often occurs.[2,3] This has been graphically illustrated in studies in animal models of myocardial reperfusion injury, in which administration of the powerful systemic inhibitor of complement activation, soluble complement receptor type 1, dramatically reduces myocardial damage.[4,5]

It is important to emphasise the role of complement in reperfusion injury of myocardium and other tissues because the new generation of complement inhibitors now being developed for treatment offers the prospect of reducing tissue injury if given at the appropriate time. Indeed, soluble complement receptor type 1, the first of this new generation of inhibitors to reach the clinical stage, is already being assessed for its therapeutic role in myocardial infarction.

B PAUL MORGAN
Wellcome senior clinical fellow
Department of Medical Biochemistry,
University of Wales College of Medicine

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Sleep related vehicle accidents

EDITOR,—J A Horne and L A Reyner provide useful data on sleep related vehicle accidents, which were defined according to criteria that they rightly consider more likely to have resulted in underreporting than overreporting of such accidents.[1] The criteria that they used, however, although including "breathalyser/blood alcohol levels below the legal driving limit," do not eliminate the possibility that alcohol was a considerable contributory factor in the accidents studied.

Blood alcohol concentrations increase the risk of road traffic accidents at values well below the legal limit.[2] Inexperienced drivers who drink infrequently seem to be particularly vulnerable.[3] Furthermore, alcohol increases drowsiness by acting as a cerebral depressant. The times at which sleep related accidents occurred most frequently in this study, in addition to being times at which drivers may be most sleepy, are those when drivers might be predicted to be affected by consumption of alcohol. In the early hours of the morning (0100-0300) some drivers may have been returning from social functions at which alcohol was served. During 0500-0700 drivers may be travelling to work unaware that their previous night's intake of alcohol has still not been completely metabolised. In the mid-afternoon, when drivers are presumably suffering postprandial somnolence, they may also still be under the influence of alcohol consumed at lunchtime.

Horne and Reyner have made a useful contribution to the literature on road traffic accidents. But an accident should not be assumed not to be related to alcohol simply because the driver was below the legal driving limit. While sleepiness may be an important contributor to road traffic accidents, it may in turn be due to consumption of alcohol.

C C H COOK
Senior lecturer in the addictions
I P ALBERY
Research psychologist
National Addiction Centre,
Institute of Psychiatry,
London SE5 8AF

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Screening overseas students for tuberculosis

EDITOR,—As part of our programme to control a recurrence of tuberculosis we examined the implementation of the national policy of screening, at port of entry to the United Kingdom, of students and their dependants from countries where tuberculosis is prevalent. We did this by interviewing students who complied with the local requirement to attend the chest clinic for screening, sending postal questionnaires to non-attenders, and comparing our experience with that of 22 other universities and associated health authorities.

Questionnaires were completed by the interviewer for 170 students who attended the clinic. In addition, 103/213 (48%) questionnaires sent by post were returned. Of 383 students arriving in Bristol with families, 376 (98%) came from regions where tuberculosis was prevalent. Only 23 (8%) had been medically examined and 10 had had chest radiography at the airport of entry (Heathrow 83%, Gatwick 12%). A total of 170 (44%) attended our chest clinic as requested. In 149 (88%), chest radiographs were normal. In 36 (21%) Heaf tests were negative. In 20 (12%) Heaf tests were strongly