Treatment for cancer pain in France

EDITOR,—François Larue and colleagues draw attention to the persisting problem of undertreatment of cancer pain.¹ In their French multicentre study of patients (most of whom were inpatients) 30% (84/279) of patients with cancer pain received no analgesic drugs. Of those patients given analgesics, 51% (137/270) received inadequate treatment for their pain. Discrepancy between physicians' and patients' pain ratings, young age of the patient, absence of metastatic disease, and better performance status were predictors for the undertreatment of cancer pain. The authors conclude that poor assessment of cancer pain is an important factor in the undertreatment of such pain.

The observation that less "seriously ill" patients with cancer are more likely to be undertreated prompts the speculation that physicians may be overcautious about using opioids in these patients owing to an ill-founded fear of addiction. We suggest that the poor assessment of pain described by Larue and colleagues is only one part of a widespread lack of knowledge on the part of physicians about managing cancer pain.

We have analysed the prescribing patterns of German physicians in the treatment of cancer pain.² We found that only 322 of 16 630 (1.9%) patients with cancer received strong opioids. In all, 191 of 328 (58.2%) practices did not prescribe a single strong opioid to their patients with cancer in three years; 295 (31%) of the prescriptions for morphine and buprenorphine were written for an inadequate intake schedule. Few patients who were receiving strong opioids received treatment for side effects of opioids (laxatives were given to 48 (14.9%) patients and antiemetics to 49 (15.2%)). Only 75 (23%) patients receiving strong opioids also received non-opioid analgesics. We conclude that patients with cancer pain in Germany are severely undertreated.

Our data suggest that restrictive laws on prescribing strong opioids, lack of knowledge about health care providers, and prejudice against opioids impede effective management of cancer pain in Germany. While some European countries, particularly Britain and Denmark, have achieved a satisfactory level of care for patients with cancer pain, most European countries are still far behind this standard.¹⁻⁴ Further education in the management of cancer pain and the dissolution of prejudice against opioids is warranted. Govern-

ments should be forced to liberalise restrictive laws on opioids. As long as penalties of up to DM50 000 (£23 000), as in Germany, impede the prescribing of opioids, the situation for patients with cancer pain will not change. We hope that Britain does not have to introduce laws on opioids similar to Germany's as a result of the European Union.

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Strategy needed for adolescent patients with cancer

EDITOR,—The care of children with cancer in the United Kingdom has rightly been cited by many professionals as being an outstanding success, translating into year on year improvements in survival for a wide range of haematological and solid cancers. In contrast, the care of adolescents with malignant disease has been unsatisfactory for various reasons and requires a new approach.

Adolescent patients span an age range from early teenage to the early 20s. The tumour types are rare and often complex. From an organisational standpoint the care of adolescent patients is often seen as neither the preserve of adult oncologists nor the preserve of paediatric oncologists. Adult oncologists are unpractised in managing rare sarcomas and certainly untutored in the arrangements for ancillary medical, psychological, and educational support that are so important to people who are facing dangerous diseases and taxing treatment at a vulnerable time in their lives. Paediatric oncologists are often expert in treating the diseases seen in young teenagers and well versed in organisational aspects and supporting care, but they have little or no experience of epithelial tumours or some of the other tumours common in late adolescence.

The very difficulty of defining the age limits of adolescence illustrates some of the complexity of the issues that require addressing. There seems to be a good case for re-examining the divisions between cancer care for adults and children to provide an appropriate service.

An audit based on cancer registry data indicates that there may be up to 2000 new cancers diagnosed each year in the United Kingdom in people aged 15 to 25 years. If patients "graduating" from paediatric oncology services are added this number would be considerably larger. In the light of specific recommendations of the Calman report on cancer services,¹ the time is right for purchasers to recognise the needs of these patients and for interested professionals within the United Kingdom Children Cancer Study Group and the Joint

Council of Clinical Oncology to develop a national strategy for adolescent cancer units linked to major cancer centres.

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Pneumococcal vaccine for HIV patients

Patients with HIV infection should be immunised . . .

EDITOR,—We were dismayed by the article of A Jain and colleagues, which was published just as we were about to start a pneumococcal vaccine campaign in Tameside. We do not agree with the conclusions of Jain and colleagues, and we do not see how they arrived at them from the evidence they cite.

We agree that the Department of Health's policy is not being well implemented, but this is not specific to HIV infection. Failure to vaccinate has many causes, including lack of ownership of responsibility for implementing the policy, the low status and difficulty in identifying the target groups, and, until recently, limited supplies of the vaccine in the United Kingdom.

Jain and colleagues first suggest that a policy of early vaccination in HIV infection is reasonable. Later, they advise that vaccinating some or all HIV positive patients is illogical. Which piece of advice do they wish us to follow?

They seem to call for a (randomised controlled?) large clinical trial of vaccine efficacy in HIV positive patients. At this stage a more ethical (and cheaper) approach would be to carry out a retrospective cohort analysis.

They also suggest that "data from trials suggest that the vaccine works in healthy but not immunocompromised people."¹ The vaccine works less well in immunocompromised people, but it does offer some protection.^{2,3} Their comment that those who will benefit the least are being vaccinated is illogical. The desired end point of immunisation is prevention of infections, not good antibody values. There is more health gain in providing partial protection to patients whose risk of infection may be up to 600 times increased⁴ than there is in providing good protection to someone at low risk of infection.

The vaccine has not been shown to perform worse than the very low efficacy and shortened duration at which Rose *et al* estimated that it was still cost effective.⁵ We will continue to advise

Advice to authors

We prefer short letters that relate to a recently published article and we are unlikely to publish letters longer than 400 words and containing over five references. Letters may be shortened. Your letters should be typed with double spacing and include a word count. All authors need to sign the letter and provide one current appointment and address. We encourage you to declare any conflict of interest. Please enclose a stamped addressed envelope if you require an acknowledgment.

general practitioners in Tameside to vaccinate patients at all stages of HIV disease.

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... though vaccine's efficacy is unproved

EDITOR,—A Jain and colleagues elegantly reviewed published work on the efficacy of pneumococcal vaccine in HIV infection.¹ Failure of protection in the United Kingdom has been reported and the question of efficacy raised elsewhere.^{2,3} We recently conducted a postal survey of 176 consultants in genitourinary medicine in the United Kingdom on the routine vaccination of HIV positive patients with pneumococcal vaccine. Preliminary data show that only 25 of the 129 consultants who replied offer the vaccine as part of their clinic policy. Only one of the 28 consultants who replied from the London boroughs offers the vaccine routinely, which is similar to the figure obtained by Jain and colleagues.

We think that the Joint Committee on Vaccination and Immunisation of the departments of health of the United Kingdom may have been a little premature in recommending the routine use of pneumococcal vaccine in all HIV positive patients without considering the evidence for clinical efficacy in this group of patients. Some people think that vaccinations may have a deleterious effect on the progression of HIV disease, whereas others have suggested using a double dose, as advocated for other vaccines. Interestingly, most of the consultants caring for HIV positive patients in this country do not follow the recommendations. There could be medicolegal implications if an unvaccinated HIV positive patient died of pneumococcal disease. Rather than wait for such an occurrence in the present climate where standards of care prevail, the recommendation should perhaps be either withdrawn or modified to state clearly that clinical efficacy has not been proved in this group of patients. In the meantime, while the present recommendations are in force, clinicians are in a dilemma.

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Surgical bleeding and calcium antagonists

Incidence of bleeding may be lower than suggested

EDITOR,—In L E Wagenknecht and colleagues' prospective randomised placebo controlled study of nimodipine in patients undergoing cardiac valve surgery an interim analysis of 149 patients suggested that nimodipine was associated with bleeding complications leading to increased mortality.¹ In two out of three patients treated with nimodipine who died because of blood loss, however, an underlying haematological disease may have precipitated bleeding, but the authors do not comment on this.

The authors refer to a study in which various calcium antagonists were associated with an increased frequency of haemorrhagic stroke and subdural haematoma among survivors of myocardial infarction, and to a study suggesting increased blood loss from ear incisions in a rabbit model. In both studies, however, recombinant tissue-type plasminogen activator was given in combination with a calcium antagonist.

A haemodynamic and pharmacokinetic study of nimodipine in patients undergoing coronary artery surgery did not show an increased risk of bleeding in this population.² A prospective randomised placebo controlled study with nimodipine in the prevention and treatment of delayed ischaemia after aneurysmal subarachnoid haemorrhage was conducted in my unit from 1985 to 1988: nimodipine significantly reduced the incidence of delayed ischaemia.³ In particular, no haemorrhagic complications associated with nimodipine were detected. We have used intravenous nimodipine routinely in subarachnoid haemorrhage since 1988 in over 1500 cases, with no haemorrhagic complications attributed to its use.

As cardiac valve surgery differs considerably from other surgical interventions, especially with respect to pharmacological management, it does not seem appropriate to conclude that similar problems should emerge during other surgical interventions—for example, repair of an intracranial aneurysm. Furthermore, in two trials in patients with head injury, in which nimodipine was given to a total of 581 patients, no bleeding problems became apparent.^{4,5}

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Other causes for increased risk of bleeding are possible

EDITOR,—L E Wagenknecht and colleagues report an increased risk of major surgical bleeding associated with treatment with nimodipine in patients undergoing replacement of a cardiac valve.¹ In other situations nimodipine has been used in thousands of patients without any suggestion of bleeding problems. The common indication

for this drug is aneurysmal subarachnoid haemorrhage, in which it undoubtedly reduces delayed ischaemia and improves outcome. In a review of this topic, with 4555 patients receiving intravenous nimodipine and 1271 oral treatment (with a much higher dose of 360 mg/day), surgical bleeding was not mentioned as a problem, although many of the patients had surgery for an aneurysm during their treatment.² Furthermore, recurrent bleeding from ruptured aneurysms was not prominent: this complication was noted in 12% of 4489 patients receiving nimodipine or other calcium antagonists and 15% of 523 controls.³ In our experience of giving nimodipine to 140 patients, only one of 34 with recently ruptured unoperated aneurysms had a recurrent haemorrhage.

If nimodipine had an antihaemostatic effect an increase in less severe perioperative haemorrhage would also be expected. Was there a difference in the overall or median blood loss between the two groups as a whole? What other factors, such as the use of heparin, may have played a part?

Several statistical questions arise, particularly when trials are stopped early.³ How many interim analyses of data were planned, and what consideration was given to the increased risk of false positive results? The cause specific mortality from haemorrhage was not significantly associated with nimodipine (estimated odds ratio 5.2 (95% confidence interval 0.6 to 45.8)), assuming that the haemorrhage contributed significantly to death in those who both had massive haemorrhage and died: what other factors were considered to explain the difference in mortality? Also, the associations between nimodipine and mortality (odds ratio 6.5 (0.8 to 55.7)) and between nimodipine and haemorrhage (4.4 (0.9 to 21.6)) do not reach significance when the two patients with pre-existing blood disorders are excluded. Should consideration be given to another, similar trial in which such disorders are excluded?

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Conflict of interest: N Dorsch has received funding from Bayer and other companies involved in the manufacture of cerebral protective drugs, which has enabled him to address international meetings on these topics.

British aneurysm nimodipine trial reported improved clinical outcome with nimodipine

EDITOR,—L E Wagenknecht and colleagues report a randomised placebo controlled trial, in which the calcium antagonist nimodipine was assessed as a possible neuroprotective agent during cardiac surgery.¹ The trial was stopped prematurely after 149 patients had been enrolled because an interim analysis showed an excess mortality with nimodipine (eight deaths versus one). This excess mortality was strongly associated with major surgical bleeding. The authors state that this was an unexpected finding, observed in a post hoc analysis, and requires further exploration.

Relevant additional data are available from the British aneurysm nimodipine trial.² In this pragmatic trial 554 patients with suspected aneurysmal subarachnoid haemorrhage were randomly allocated to receive either oral nimodipine 60 mg every four hours for 21 days or matching placebo. A