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such an occurrence in the present climate where standards of care prevail, the recommendation should perhaps be either withdrawn or modified to state clearly that clinical efficacy has not been proved in this group of patients.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