Misuse of benzodiazepines

Specify the formulation when prescribing

EDITOR,—John Strang and colleagues comment that doctors who prescribe benzodiazepines to injecting drug users should consider the likelihood of the drugs being injected, given the degree of misuse of benzodiazepines among this population.¹ We agree that there is a considerable problem and estimate the prevalence of use of benzodiazepines by injecting drug users entering treatment at Liverpool Drug Dependency Clinic to be 44% based on a random sample of 100 (M Shaw *et al*, unpublished findings). We would go further and advocate care in prescribing benzodiazepines to all patients. A study in Liverpool of 23 people who misused temazepam intravenously showed that most obtained their supply from sources other than their general practitioner.² They most commonly obtained temazepam off the street (18 users) or from friends (13) (there was some overlap in means of supply).

To have maximal impact on reducing the prevalence of injection of temazepam and other benzodiazepines, we suggest a dual approach. We agree that a change in the regulations governing prescribing is needed to limit the general availability of temazepam capsules, the formulation most susceptible to intravenous misuse. Prescribers may not be aware that capsules may be routinely dispensed unless the prescription states the required formulation. Our clinical impression, based on experience of dealing with dispensaries in the Liverpool area, is that up to half may prescribe temazepam capsules when no formulation is specified. In view of this, we would advise general practitioners always to state the formulation required. General practitioners should also be aware that most temazepam reaches misusers from illicit sources. Vigilance should be extended to all prescriptions for temazepam as the possibility of misuse extends beyond the patient.

We share Strang and colleagues' concern that focusing solely on temazepam may draw attention away from misuse of other benzodiazepines. Similarly, there is a danger of concentrating attention on prescribing practice alone. As illicit supply will be difficult to eradicate totally, efforts should be made to reduce the mortality and morbidity associated with misuse of benzodiazepines by educating patients by using a strategy to minimise risk.

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1 Strang J, Griffiths P, Abbey J, Gossop M. Survey of use of injected benzodiazepines among drug users in Britain. *BMJ* 1994;308:1082. (23 April.)

2 Ruben S, Morrison CI. Temazepam misuse in a group of injecting drug users. *Br J Addict* 1992;87:1387-92.

Voluntary ban on prescribing is effective

EDITOR,—John Strang and colleagues report that temazepam capsules were the benzodiazepine most commonly misused by subjects who completed questionnaires at drug clinics in seven cities in

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Britain in 1992.¹ They conclude that, with regard to removing drugs from supply, "a focus on temazepam seems appropriate at present but may prove too narrow in the longer term."

Altogether 97% of the 244 general practitioners in Hull and Grimsby joined together in May 1993 to ban the prescribing of temazepam capsules as one measure to decrease availability in two urban areas that had a particular problem with intravenous misuse of temazepam. This voluntary ban resulted in a fivefold decrease in prescriptions for temazepam capsules, a further 7% decrease in all prescriptions for temazepam, and a 6% decrease in all prescriptions for hypnotics and anxiolytics.

General practitioners in the Scunthorpe and East Yorkshire districts of Humberside have now also joined the voluntary ban. The medical adviser of the family health services authority coordinated the ban, the idea having arisen from general practitioners at postgraduate education meetings in Hull and Grimsby.

General practitioners will work jointly to change their prescribing when they are convinced of the appropriateness of action to improve the quality of prescribing.

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Drug users will shift to another preparation

EDITOR,—John Strang and colleagues draw attention to an important phenomenon in drug misuse in Britain—namely, the use of injected benzodiazepines.¹ As they comment, however, focusing on temazepam capsules is too narrow a strategy to solve the problem of injection of this range of drugs. The forthcoming reports from the House of Commons Scottish Affairs Committee and the Scottish Drugs Task Force will probably focus on temazepam, and widespread voluntary bans by general practitioners in Scotland on prescribing temazepam capsules have undoubtedly attenuated the use of this drug but have shifted the problem elsewhere. In the history of drug misuse since the war individual pharmaceutical preparations causing problems have been controlled by the Home Office and restricted in this way, which has

shifted the drug users' attention to whatever is prescribed in their place.

Voluntary bans of this kind have led to increasing use of intravenous diazepam. I suspect that the authors' comment that half the injecting benzodiazepine users would be removed by the control of temazepam capsules is wrong and that most of these users would shift to another preparation. In addition, in my clinic I have observed a vast increase in oral use of benzodiazepines, particularly diazepam, some patients taking quite stunning doses of diazepam daily. The narrow view of drug injecting is common among legislators and committees taking the short view of drug misuse and among those trying to draw attention away from the deplorable lack of adequate services at both primary and secondary care levels for patients misusing all sorts of substance.

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Avoid benzodiazepines whenever possible

EDITOR,—John Strang and colleagues' survey of use of injected benzodiazepines among drug users raises the issue of whether there is any rationale for prescribing benzodiazepines to drug misusers.¹ Illicit benzodiazepines are widely available and are of the same quality as prescribed drugs. In terms of reducing harm related to drugs the only benefit to be gained by prescribing seems to be to save money.

Benzodiazepines are associated with increased hostility, aggression, and antisocial acts.² Such effects are more likely at the unorthodox doses used by drug misusers. Use of temazepam in particular is associated with violence, chaotic behaviour, and criminal activity.³ Behaviour conferring a risk of HIV infection is also significantly associated with use of temazepam, including sharing equipment, casual sexual contacts, and unprotected sex.^{3,4} The physical effects of injecting temazepam are well documented.⁵

Benzodiazepines impair learning.⁵ This is relevant because of the considerable resources invested in counselling and education, which aim to change risk behaviour and improve quality of life for drug misusers. We question whether much of this effort is wasted when patients are taking benzodiazepines.

In our practice we have gradually moved to a policy of avoiding benzodiazepines whenever possible. The reasons for this are understood by our patients, who generally are aware of the dangers of these drugs. Some patients choose to obtain benzodiazepines intermittently, as results of screening their urine show. They are given advice on reducing harm rather than a prescription, which would sanction the use of these drugs, potentially add to the black market, or convert intermittent use to regular use.

When a patient who uses drugs is dependent on prescribed benzodiazepines we convert the prescription to diazepam. We then reduce and withdraw the benzodiazepines as a priority—perhaps even increasing the use of methadone if

this seems appropriate. Other requests for benzodiazepines are refused. We commend this policy to other doctors caring for drug misusers in general practice.

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Hepatitis C virus infection

Define seropositivity

EDITOR,—Carol A Seymour's editorial¹ and the papers on hepatitis C in the same issue illustrate the problems of defining chronic hepatitis C and of identifying patients who would benefit from regular follow up in a gastroenterology clinic. We and colleagues have found that only liver biopsy reliably identifies patients with chronic infection. Kate E Ryan and colleagues rightly question the effectiveness of counselling when so little is known of the natural course of this infection.²

Liver biopsy is not a minor procedure, and scarce and expensive medical resources should be used only when the patient will benefit. The patient must be given an accurate prognosis and treatment with interferon alfa and other antivirals should be offered when appropriate, although the long term effects of such intervention on the prognosis of liver disease associated with hepatitis C are unknown.

Much of this information is not new. It has been known since the 1970s that a normal serum alanine aminotransferase activity in repeated samples taken over an extended period does not exclude the finding of non-A, non-B hepatitis on liver biopsy.^{3,4} Published studies of liver biopsies in blood donors positive for antibodies to hepatitis C virus show varying proportions with normal histological appearances and different patterns of severity of liver disease.

An accurate definition of what constitutes a specific result of a test for hepatitis C antibody is essential. We have attempted such a definition based on an algorithm devised for confirmatory testing of repeatedly reactive samples from blood donors.⁵ We found that serum that was reactive in three different enzyme immunoassays had a much greater chance of being reactive in a line immunoassay than serum that was reactive in only one or two enzyme immunoassays. Alternatively, a mean ratio of the absorbance obtained for the sample to the cut off absorbance for these assays of > 3.00 was associated with a much increased chance of a positive result for viral RNA by the polymerase chain reaction, confirming that strong reactivity by enzyme immunoassay is more likely to be specific. Samples from only two of 172 blood donors with viraemia failed to react in all three enzyme immunoassays; the viruses in these two cases were antigenic variants uncommon in our population of blood donors.

Our definition of a specific result of a test for hepatitis C antibody is reactivity in three different enzyme immunoassays, with a mean ratio of the absorbance obtained for the sample to the cut off absorbance greater than a minimum derived under

standard conditions from a group of people known to be positive, and reactivity in a line immunoassay. This definition excludes serum with low concentrations of specific antibody such as that from patients with resolving infection, who are unlikely to have viraemia or to need medical intervention.

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- 1 Seymour CA. Asymptomatic infection with hepatitis C virus. *BMJ* 1994;308:670-1. (12 March.)
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Psychosocial impact similar to that of HIV infection

EDITOR,—Over four fifths of injecting drug users seen by our community drug team are positive for hepatitis C virus and find coping with the knowledge of this difficult, given the uncertain implications of such a diagnosis. Counselling such clients is difficult as clear guidelines on the epidemiology, infectivity, and prognosis of asymptomatic hepatitis C are lacking.¹ We have been concerned recently about instances when patients were denied ordinary care because they were positive for the virus. One of our clients, a former injecting drug user in her 20s who receives maintenance treatment with low dose methadone, was refused treatment by her dentist after she disclosed to him that she was positive for the virus. On referral to an NHS dental clinic she was placed on a waiting list despite the urgency of her dental condition as she had to be given an appointment at the end of an afternoon so that adequate precautions could be taken.

We agree with Kate E Ryan and colleagues that disclosure of the fact that a patient is positive for hepatitis C virus can have serious psychosocial implications,² which may mimic those associated with positivity for HIV. The issues of counselling people at risk, consent to testing, and confidentiality of results need to be addressed urgently.

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Treatment with interferon reduces viraemia

EDITOR,—Carol A Seymour's editorial on the management of chronic hepatitis C¹ has initiated an interesting discussion, with some doctors advocating a policy of no intervention.² Although the natural cause of chronic hepatitis C is still a matter for debate, at least a fifth of infected patients are likely to develop cirrhosis or a hepatocellular carcinoma, or both.³ We still do not know

how to identify those patients who are at risk of developing permanent liver damage, but liver function tests are clearly of little value.

Most hepatologists would agree that patients with fibrosis or chronic active hepatitis with bridging necrosis proved by biopsy are probably at high risk of developing cirrhosis (by analogy with chronic hepatitis B). Formal studies to confirm this in hepatitis C, however, have not been published. A liver biopsy therefore provides some information regarding the likely prognosis and, in our view, is essential in patients with abnormal serum transaminase activities.

Identifying patients who are at high risk of developing progressive disease is of value only if we can offer treatment. High dose interferon reduces viraemia to undetectable levels (an analysis with the polymerase chain reaction) in up to a quarter of treated patients.⁴ We do not know whether this represents a permanent cure, but data showing prolonged normalisation of results of liver function tests in these patients indicate that this is probable. Studies combining interferon and oral antiviral agents are under way, and recent results suggest that these new treatment regimens may "cure" 43% of treated patients (L Chemelle *et al*, Vth international symposium on viral hepatitis, Madrid, 1994). Hence we are in a position to offer patients treatment that may considerably improve their prognosis.

Although there is still legitimate debate regarding the optimal management of patients with chronic hepatitis C, the current discussions should not be used as an argument for therapeutic nihilism: without intervention many patients with this disease will die. In our view Seymour's advice is sound: patients with chronic hepatitis C should be referred to centres skilled in managing this disorder so that they can benefit from the latest management options.

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Hepatitis B and medical student admission

Admission should be based on merit

EDITOR,—*BMJ* was right to publish an editorial on hepatitis B and medical student admissions and to lend its authority to the case for screening of students after admission.¹ The editors contributed the slightly provocative subtitle and amended some of the text after my last sight of it (unwisely in my opinion) in the interests, presumably, of making a more hard hitting message. As a means of engendering controversy where there was room for informed and balanced debate, this has been a journalistic "success" and has elicited a predictably nettled response from Peter Richards and Frank Harries, who are provoked to tilt at the person ("the luxury of opinion without responsibility") and the journal ("irresponsible"), without producing a substantive argument in support of the Committee of Vice-Chancellors and Principals' guidelines.² This contrasts with letters published simultaneously from the BMA medical students