studies[1] were criticised for including only data on fertile subjects.[2] When we analysed the data for our population of fertile donors separately we observed similar significant relations to those described for the whole population. Eccersley speculates that the observed effect may be the consequence of smoking and drinking being more common among undergraduates. We are unable to confirm this: among our donor population 65% of the students compared with 63% of the non-students drank, while for smoking the comparable figures were 29% and 30% respectively. We also saw no evidence of smoking being more common in any one birth cohort group, with 28% of men born before 1959 smoking compared with 26% of those born after 1970.

Gillian Raab suggests that we failed to take account of the possibility that higher sperm counts in older men may be due to longer periods of abstinence. We were aware of this possibility, and although we did not separately record duration of abstinence, all donors received the same instructions. Whether compliance differed with age is unknown. Longer abstinence is known to produce increases in both sperm concentration and ejaculate volume.[3] We thus looked for relations between ejaculate volume and age or year of birth but found none. Other workers have failed to show any effect of age on sperm concentration, whether or not abstinence is taken into account,[4] and a recent study found no influence of fertility status on sperm concentration, ejaculate volume, or duration of abstinence.[5] This raises the issue of whether self reported abstinence is reliable and itself free from the influence of age. We are carrying out studies to identify independent biochemical markers for abstinence, unrelated to the classical variables of semen quality.

The evidence on changing semen quality is based on retrospective studies with intrinsic shortcomings.[1 6] In view of the potential seriousness of these findings, however, large, properly structured prospective studies of semen quality are urgently needed, in which confounding factors such as frequency of ejaculation and geographical location[5] are carefully monitored. Such studies are being carried out under the auspices of the European Union.

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Extrapyramidal signs should be sought more often in Alzheimer's disease

EDITOR,—Yoav Ben-Shlomo and colleagues restate the rarity of the existence of the amyotrophic lateral sclerosis-parkinsonism-dementia complex in areas other than the Pacific focus.[1] Colleagues and I have reported on a patient who had amyotrophic lateral sclerosis and dementia but in whom tremor was absent and the bradykinesia that was present was attributed to severe motor paralysis.[2] Parkinsonism was therefore not diagnosed. In the light of experience since, however, I realise that we did not properly seek rigidity. It is now my practice to test for rigidity in both elbows and both wrists by rapidly flexing and extending these joints (which should hopefully be fully relaxed) 50 times or until cogwheel rigidity is felt. An observer of the examination can usually see this phenomenon simultaneously with its becoming apparent to the examiner. Fifty times is an arbitrarily chosen figure.

This method, for which I do not claim originality, recently enabled the demonstration of rigidity in these joints after an average of only 12 passive movements. The patient was a 65 year old woman with a five year history of progressive dementia of the Alzheimer type. Investigations, including modern imaging techniques, had not shown alternative explanations for the symptoms. There was no tremor, bradykinesia, or postural instability. The glabella tap sign was present.

The papers that state the criteria for diagnosing extrapyramidal signs do not precisely describe how to elicit muscular rigidity.[3 4] Possibly, searching more often for the physical sign described will reduce the wide variation in the reported frequency of extrapyramidal signs in patients with Alzheimer's disease.[5]

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Directly observed treatment for tuberculosis

Could be provided by community pharmacists supervising consumption of methadone

EDITOR,—Increasing rates of tuberculosis are cause for concern.[1] Since increasing rates are reported in homeless people and those with HIV infection, intravenous drug users are at risk. While there is no evidence of high rates of tuberculosis in British drug users, rising rates have been reported in other European countries.[2] Britain needs effective strategies for prevention and for treating those affected. A drug user with an unstable lifestyle is unlikely to comply with six months of oral antituberculous chemotherapy. Strategies to improve compliance will be crucial in ensuring that those affected are properly treated.

The provision of methadone for harm reduction in drug users has grown rapidly in the past decade. There is good evidence of its efficacy in reducing heroin use, injecting behaviour, and criminal activity, and this form of treatment is well established.[3] Most people who are prescribed methadone in Britain collect it daily or weekly from community pharmacists and consume it without supervision. Several treatment services include the option of daily supervised consumption of methadone in clinics staffed by nurses, pharmacists, and drug counsellors. In the methadone maintenance clinic at Maudsley Hospital we have offered, in one particular case, combined antituberculous chemotherapy and methadone maintenance for over a year. This treatment, which followed a long period of non-compliance, has resulted in effective treatment of the tuberculosis and has averted legal detention procedures on public health grounds.[4]

The services in place for one population that is at risk from the new wave of tuberculosis provide an infrastructure capable of effectively providing direct observation of antituberculous chemotherapy. Community pharmacists have expressed widespread willingness to supervise the consumption of methadone, and this offers potential for the expansion of this existing infrastructure (JS *et al*, unpublished findings). Drug services have long experience of dealing with a poorly compliant population in all settings. The combination of treatment for drug dependence and treatment with antituberculous drugs offers a particularly good opportunity of improving compliance and should be explored before the blunt instrument of the law is resorted to.

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Treatment strategies will need to be changed because of drug resistance

EDITOR,—Dale I Morse notes that the emergence of multidrug resistant *Mycobacterium tuberculosis* has been one of the spurs to supervised chemotherapy.[1] Other aspects of treatment protocols are equally important in controlling the emergence of drug resistance. Currently, the *British National Formulary* recommends that standard treatment for tuberculosis should be with three drugs (isoniazid, rifampicin, and pyrazinamide). Indications for adding a fourth drug include previous default from treatment and immigration from areas of the world with a high prevalence of drug resistance. The upsurge in tuberculosis in Britain, however, is mainly due to increasing poverty, not immigration.[2] Resistance to one or two drugs is not thought to be an important problem in Britain despite experience in other developed countries.[3]

In this infectious diseases unit we reviewed the sensitivities of 360 sequential positive cultures of *M tuberculosis* to first line antituberculous treatments (isoniazid, rifampicin, pyrazinamide, ethambutol, and streptomycin). Infected patients had presented between 1990 and 1994 to either this postgraduate teaching hospital or a nearby district general hospital. Less than 10% were known to be HIV seropositive. Forty nine isolates were resistant to at least one antituberculous drug.