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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1 Auger J, Kunstmann JM, Czyglik F, Jouannet P. Decline in semen quality among fertile men in Paris during the past 20 years. *N Engl J Med* 1995;332:281-5.
2 Sherins RJ. Are semen quality and male fertility changing? *N Engl J Med* 1995;332:327-8.
3 Blackwell JM, Zaneveld LJD. Effect of abstinence on sperm acrosin, hypoosmotic swelling, and other semen variables. *Fertil Steril* 1992;58:798-802.
4 Schwartz D, Mayaux MJ, Spira A, Moscato M-L, Jouannet P, Czyglik F, *et al*. Semen characteristics as a function of age in 833 fertile men. *Fertil Steril* 1983;39:530-5.
5 Fisch H, Goluboff ET, Olson JH, Feldshuh J, Broder SJ, Barad DH. Semen analyses in 1,283 men from the United States over a 25-year period: no decline in quality. *Fertil Steril* 1996;65:1009-14.
6 Carlsen E, Giwercman A, Keiding N, Skakkebaek NE. Evidence for decreasing quality of semen during past 50 years. *BMJ* 1992;305:609-13.

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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1 Ben-Shlomo Y, Whitehead A, Smith G. Parkinson's, Alzheimer's, and motor neurone disease. *BMJ* 1996;312:724. (23 March.)
2 Lowenthal MN, Schneiderman K, Brami J-L, Galinsky D. Senile dementia and motor neurone disease: a lesson in coping. *Isr J Med Sci* 1985;21:767-8.
3 Gibb WRG, Lees A. The relevance of the Lewy body to the pathogenesis of idiopathic Parkinson's disease. *J Neurol Neurosurg Psychiatry* 1988;51:745-52.
4 Gibb WRG. Accuracy in the clinical diagnosis of parkinsonian syndromes. *Postgrad Med J* 1988;64:345-51.
5 Hamill RW, Caine E, Eskin T, Lapham L, Shoulson I, McNeill TH. Neurodegenerative disorders and aging. Alzheimer's disease and Parkinson's disease—common ground. *Ann N Y Acad Sci* 1988;515:411-20.

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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1 Morse DI. Directly observed therapy for tuberculosis. *BMJ* 1996;312:719-20. (23 March.)
2 Advisory Council on the Misuse of Drugs. *AIDS and drug misuse update*. London: HMSO, 1993.
3 Ball JC, Ross A. *The effectiveness of methadone maintenance treatment: patients, programs, services and outcome*. New York: Springer-Verlag, 1991.
4 Stewart GH, Nelson S. Tuberculosis in the United Kingdom. *BMJ* 1996;312:775-6. (23 March.)

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.

Seventeen were resistant to isoniazid, three to rifampicin, two to ethambutol, 19 to streptomycin, and six to both isoniazid and streptomycin. Two patients had tuberculosis that was resistant to at least three drugs, of whom one repeatedly defaulted from the clinic while the other was a Nigerian with his first presentation of pulmonary tuberculosis. The pattern of drug resistance was similar to that in a previous study, but the incidence has more than doubled since that study.[4]

Mycobacteria were detectable on sputum examination in 159 patients. Thus within the local urban community there is great potential for transmission of *M tuberculosis* that is resistant to one drug. In addition, patients may well receive what is effectively two-drug treatment on diagnosis, which will accelerate the emergence of drug resistance. Since multidrug resistance is the result of the sequential acquisition of resistance to single drugs,[5] treatment strategies must be altered as resistance to single drugs becomes more common and not when multidrug resistance is established. If our findings are confirmed elsewhere, British policies for treating tuberculosis will need to be revised soon. Four-drug empirical treatment of tuberculosis should then become normal practice, pending definitive results from drug sensitivity tests of the organism being treated.

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1 Morse DI. Directly observed therapy for tuberculosis. *BMJ* 1996;312:719-20. (23 March.)
2 Bhatti N, Law MR, Morris JK, Halliday R, Moore-Gillon J. Increasing incidence of tuberculosis in England and Wales: a study of the likely causes. *BMJ* 1995;310:967-9.
3 Frieden TR, Sterling T, Pablos-Mendez A, Kilburn JO, Cauthen GM, Dooley SW. The emergence of drug-resistant tuberculosis in New York City. *N Engl J Med* 1993;328:521-6.
4 Medical Research Council Cardiothoracic Epidemiology Group. National survey of notifications of tuberculosis in England and Wales in 1988. *Thorax* 1992;47:770-5.
5 Heym B, Honore N, Truffot-Pernot C, Banerjee A, Schurra C, Jacobs WR Jr, *et al.* Implications of multidrug resistance for the future of short-course chemotherapy of tuberculosis: a molecular study. *Lancet* 1994;344:293-8.

Strategic plans for vascular services have not been put into effect

EDITOR,—The media have recently focused on deaths resulting from the non-availability of intensive care. They see but the tip of the iceberg. The problem with paediatric intensive care beds, we are told, is "distribution rather than numbers."[1] The problem with accident and emergency services, we are told by the Audit Commission, is that they need to be centralised.[2] Advice such as this, however pertinent, is unlikely to be taken: the NHS is currently strangled by its own structure.

The need to rationalise those acute services that depend on round the clock availability of specialist staff and expensive resources becomes daily more obvious. The reorganisation of the NHS into independent trusts, the purchaser-provider split, and short term administrative contracts have placed road blocks in the way of strategic regional planning. Nowhere is this better shown than in the provision of vascular services.

In 1993 a report, *Vascular Surgery Services*, was prepared by a working party of the National Medical Advisory Committee.[3] Taking into account a wide body of evidence, especially quality and economic issues, the report recommended that the 20 hospitals providing vascular surgery in Scotland be centralised into six major and three intermediate units. Recommendations included that emergency services should be provided by surgeons specialising in vascular work, vascular surgeons should not work single handedly, on site intensive therapy units were essential and renal dialysis desirable, and the service should include specialist radiological and laboratory support.

What has happened in the intervening years? The distribution of vascular services has not changed. Singlehanded vascular surgeons continue to be appointed. Surgeons with no interest in vascular work are still obliged to participate in emergency rotas. Vascular services continue to lack the support of an intensive therapy unit. Renal failure, which is a common complication of vascular surgery, still necessitates interhospital transfer of ill patients. Radiology and laboratory support is deficient in many units, while elsewhere expensive diagnostic facilities are duplicated in adjacent hospitals.

Charters and guidelines are not the answer. Where are the administrative mechanisms, and what are the incentives to bring common sense, economy, efficiency, and quality into the acute services?

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1 Stibby S, Hatherill M, Marsh MJ, Murdoch IA. Paediatric intensive care: the problem is distribution rather than numbers. *BMJ* 1996;312:773. (23 March.)
2 Audit Commission. *By accident or design: improving A & E services in England and Wales.* London: HMSO, 1996.
3 Working Group of the National Medical Advisory Committee. *Vascular surgery services.* Edinburgh: HMSO, 1993.

Evidence for efficacy of topical acyclovir in recurrent herpes labialis is weak

EDITOR,—In a letter responding to my editorial about the value of acyclovir in recurrent herpes labialis[1] P-J Lamey says that the benefit of topical acyclovir has never been truly evaluated.[2] I agree. In my critical appraisal of the evidence for the efficacy of topical acyclovir I found that the trials that had been carried out had generally been of poor methodological quality and of weak power to detect treatment effects.[3] Even if reliable thermographic methods have now been developed to confirm the prodromal stage of recurrent herpes labialis, properly conducted studies of efficacy and effectiveness still need to be done in primary care.

Shortly after the publication of my original review I approached the makers of topical acyclovir and suggested that they were the logical partners to produce placebo ointment for a randomised double blind trial in primary care, but they were unwilling to help. I also note that most of the papers supporting the use of topical acyclovir have come from departments of dentistry and oral medicine rather than from general practice. I still maintain that evidence for the efficacy of topical acyclovir in recurrent herpes labialis is weak.

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1 Worrall G. Acyclovir in recurrent herpes labialis. *BMJ* 1996;312:6. (6 January.)
2 Lamey PJ. Topical acyclovir is beneficial in recurrent herpes labialis. *BMJ* 1996;312:975. (13 April.)
3 Worrall G. Topical acyclovir for recurrent herpes labialis in primary care. *Can Fam Physician* 1991;37:92-8.

Neonatal circumcision and penile cancer

Evidence that circumcision is protective is overwhelming

EDITOR,—As chairman of the American Academy of Pediatrics' Task Force on Circumcision[1] and a reviewer on the topic for the American Cancer Society,[2] I am amazed at the claim by Paul M Fleiss and Frederick Hodges that no link exists between circumcision and penile cancer.[3] In an incredible example of selective medical amnesia the authors ignore evidence that has accumulated in the past 64 years. They discredit Wolbarst's study in 1932 without mentioning the data.[4] Wolbarst reviewed 1103 cases of penile cancer in the United States and found that all occurred in uncircumcised men and none in Jewish men, even though 33 cases would have been expected because Jewish men constituted 3% of the population. Wolbarst cited confirming figures from Europe and noted that Moslems, who also circumcise boys, are protected against cancer. This landmark study served as the stimulus for five future series that were published in refereed journals in the next 50 years[2] but are apparently unknown to Fleiss and Hodges (although Hodges, a known lay anticircumcisionist, says that he is a medical historian).

In a classic review in 1935 Dean analysed 120 cases of penile cancer reviewed at what is now Memorial Sloan-Kettering Cancer Center in New York City.[5] All of these cases occurred in uncircumcised men. None occurred in Jewish men, although more than a third of other inpatients with cancer at the facility were Jewish. Dean concluded that "prophylactic treatment of cancer of the penis consists in circumcising all male infants." In four later, separate series 139 cases in Illinois were reviewed in 1946; 100 in Roswell Park, New York, in 1972; 156 in Michigan in 1973; and 77 in Cleveland in 1986. Of these 592 cases at five institutions renowned for treating cancer, none occurred in men who had been circumcised as newborn infants, although most newborn male infants in the United States were circumcised.

Since 1935, about 50 000 cases of penile cancer have been reported in the United States (annually, about 750-1000 cases and 200 deaths), only 10 of which occurred in men who had been circumcised as newborn infants. This yields a ratio of 5000:1 for the incidence of penile cancer in uncircumcised to circumcised men—overwhelming evidence.

As Kochen and McCurdy pointed out, the low incidence of penile cancer in the United States is misleading because it has been calculated by combining circumcised men (in whom the incidence is essentially zero) with uncircumcised men (in whom it is 2.2/100 000).[6]

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1 Schoen EJ, Anderson G, Bohon C, Hinman F Jr, Poland RL, Wakeman EM, American Academy of Pediatrics. Report of the task force on circumcision [published erratum appears in *Pediatrics* 1989;84:761.] *Pediatrics* 1989;84:388-91.
2 Schoen EJ. The relationship between circumcision and cancer of the penis. *CA Cancer J Clin* 1991;41:306-9.
3 Fleiss PM, Hodges F. Neonatal circumcision does not protect against penile cancer. *BMJ* 1996:312:779-80. (23 March.)
4 Wolbarst AL. Circumcision and penile cancer. *Lancet* 1932;i:150-3.
5 Dean AL Jr. Epithelioma of the penis. *J Urol* 1935;33:252-83.
6 Kochen M, McCurdy S. Circumcision and the risk of cancer of the penis: a life-table analysis. *Am J Dis Child* 1980;134:484-6.