that measurement of the plasma methadone concentration provides important information for clinicians and should be a routine part of substitute prescribing.

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Pregnant women taking methadone should be warned about withdrawal symptoms in babies

EDITOR,—Methadone maintenance programmes are established in Britain, and Michael Farrell and colleagues' review provides a reminder of the many benefits to opiate users.[1] It does not, however, mention the potentially serious neonatal withdrawal syndrome, which occurs in many babies born to mothers using methadone. The likelihood of withdrawal effects is only weakly related to the maternal methadone dose but is probably related to the speed with which concentrations decrease in the baby.[2,3]

My district does not have an excessive problem with drug misuse, but since 1 January 1993, 12 babies have been admitted to the neonatal unit with a diagnosis of neonatal withdrawal. These admissions accounted for roughly 5% of our special care cot days. The table shows the maternal drug use immediately before delivery. We admit babies only when they seem to be experiencing serious withdrawal; until that point they are monitored with their mothers in the postnatal wards, and some babies never require admission.

After admission one baby, whose mother was taking only 5 mg of methadone a day, was not thought to have the withdrawal syndrome and was not treated. The remaining 11 babies required treatment with chlorpromazine for a median of 28 days; the median duration of admission was 31 days (table). There was no correlation between the methadone dose and the duration of treatment. Many mothers said that they had not expected their baby to suffer such prolonged withdrawal effects. Even when clear withdrawal symptoms were no longer apparent, both staff and parents found these babies demanding, sometimes for several months.

By improving the mother's ability to care for her baby and reducing her exposure to the risks of illicit use of intravenous heroin, a methadone maintenance programme produces many benefits to the baby, and many paediatricians support the continuation of methadone programmes for users of intravenous heroin. For many drug users pregnancy is a stressful time that may not be suitable for active weaning from methadone.

Those involved in running methadone maintenance programmes should warn pregnant drug users that their baby will need to be observed for withdrawal symptoms for at least three days and may develop a withdrawal syndrome lasting for many weeks. This may provide an incentive for further controlled reductions in the dose of methadone. Even when the methadone dose has been reduced to very low levels, drug using mothers must be warned that prolonged admission to hospital is sometimes necessary if their baby develops serious withdrawal.

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Patients on methadone often continue with injected heroin

EDITOR,—The tentativeness of Michael Farrell and colleagues' conclusions in their review of methadone maintenance programmes suggests that the premise and execution of the programmes should be re-examined before the American policy is adopted elsewhere.[1] With reasonable doses of methadone, programmes are plagued by a high rate of early drop outs and frequent and disabling use of non-opiate depressants. With larger doses the use of stimulants is added to the problems. The findings that demand explanation, however, are the frequent continued use of injected heroin by subjects receiving a strong opiate in huge doses and the poor long term results—that is, the failure of subjects to re-enter a life free of the tyranny of compulsive drug use in numbers greater than that predicted by the usual maturation process.

Orally ingested methadone provides the "late," depressant effects of "their" drug but not the "rush." It is the total body orgasm or explosive relief of anxiety at the instant of injection that makes injected heroin so regularly the vehicle of compulsion. With methadone, the patient feels no physical withdrawal but experiences continued anxiety from the withdrawal of the major pharmacological reward. Patients, uninformed by dispensers of methadone who are unappreciative of their state, seek relief from their anxiety by negotiating larger and larger doses of methadone or by using alcohol or whatever prescription sedative they can get or, of course, heroin.

Massive doses of methadone will increase the prevalence of heroin free urine, but tolerance is not absolute and the patient will become less and less functional. If the goal of the programme is control of the user—that is, a reduction in real and nominal criminal activity—the course will be judged satisfactory. It cannot, however, be called treatment.

A programme that congregates compulsive drug users is inherently damaging. These patients are often in unending psychological withdrawal and are vulnerable to any clue or suggestion of drug use. Group therapy or the mere sight of some former dealer or companion can be irresistibly pornographic. The car parks and even the waiting rooms where the programmes are run become marketplaces for drugs. Dispersed dispensing is an attractive idea when compared with the centralised treatment required in the United States.

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Maternal drug use immediately before delivery, age of baby at presentation, duration of admission, and duration of chlorpromazine treatment for the 12 babies of drug misusers admitted

Case No	Methadone dose (mg)	Other drugs taken	Age at presentation (days)	Duration of admission (days)	Duration of chlorpromazine treatment (days)
1	5	—	0	16	10
2	5	—	0	7	—
3	10	—	2	29	107
4	10	—	2	13	11
5	10	—	2	34	28
6	10	Diazepam, cocaine	0	47	44
7	38	—	0	60	61
8	45	—	1	31	56
9	60	—	0	37	10
10	—	Crack cocaine	0	16	11
11	—	Pethidine	2	14	12
12	—	Pethidine	2	12	40

We don't know whether heroin or methadone produces more withdrawal symptoms in babies

EDITOR,—Minerva summarised the study we performed in infants with neonatal abstinence syndrome.[1] This summary was misleading as it stated that withdrawal symptoms are more likely in infants whose mothers have been taking methadone than in those whose mothers have been taking heroin. This was not a finding in our study, and, although our study can be compared with others in which mothers had been taking heroin, no meaningful comparison can be made about the relative incidence of withdrawal symptoms in infants of mothers who have taken methadone and heroin owing to the small numbers of patients in each of these studies.

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Glasgow has an innovative scheme for encouraging GPs to manage drug misusers

EDITOR,—The Advisory Council for the Misuse of Drugs has concluded that general practitioners should participate more in the care of drug misusers.[1] Michael Farrell and colleagues express pessimism about this occurring owing to general practitioners' resistance to prescribing opiate substitutes,[2] though they cite a report showing that clinics for such prescribing may be operated successfully in general practice.[3] We report an innovative method of more widely implementing this strategy.

During the recent past a number of general practitioners in Glasgow recognised that it was preferable for drug misusers to attend clinics expressly designed for their care. Greater Glasgow Health Board acknowledged and developed this initiative by creating the general practice drug misuse clinic scheme. The scheme, including payments to participating general practitioners, is being funded by the health board through its primary care development fund. The objective of

the scheme is to reduce drug related harm to health.

After discussions between general practitioners and the health board clinical standards were defined and a review body appointed to supervise the administration of the scheme. General practitioners seeking approval have to agree to register from five to 20 patients with opiate dependence and a current or recent history of injecting drugs; to provide a drug counsellor at clinics; to attend educational meetings; to use oral methadone mixture as the only opiate substitute treatment; not to prescribe dihydrocodeine or temazepam; to arrange for methadone to be consumed under the supervision of a local community pharmacist; and to complete contact forms for every consultation, and a six monthly opiate treatment questionnaire[4] for each patient, to allow evaluation of the scheme.

The scheme started on 1 May last year, and during the first six months 42 general practitioners were approved and 759 patients registered. This represents 9% of the estimated population of injecting drug misusers in Glasgow and 6% of principals in general practice. The results of evaluation are awaited, but the scheme seems to be popular with general practitioners and patients. It provides an opportunity for raising the standard of management in general practice of this potentially difficult group of patients while compensating general practitioners for the costs of doing so.

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Auditing incidents of exposure to blood

EDITOR,—Ruth R White and Elisabeth J Ridgway highlight variations in the management of reported sharps injuries in Mersey Regional Health Authority.[1] The management of common conditions, especially when there is believed to be room for variation, is a good topic for audit. The North Thames (East) Regional Occupational Health Audit Group, which has representatives from all the occupational health units in the region, recently audited the management of reported incidents of exposure to blood.

Of the 17 occupational health units, 15 participated in the audit. All were involved in the management of reported exposure to blood in some way; four were not responsible for the initial management. Only one unit ran an out of hours service for such incidents; for several others this was provided by another department. Eleven units routinely stored a sample of blood from the staff member involved. The policies about approaching source patients to request tests for bloodborne viral infections varied considerably: for hepatitis B surface antigen this was routine in four units and done in high risk cases in eight; for HIV antibody it was routine in three units and done in high risk cases in eight; and for antibodies to hepatitis C it was routine in only one unit, with four other units requesting testing in some cases. Prophylactic procedures for hepatitis B and HIV infection after sharps injuries also varied. Hepatitis B specific immunoglobulin was given more widely than is recommended by the Public Health Laboratory Service,[2] including in circumstances in which the status of the source patient was not known (two units).

At the Royal Free Hospital all known source patients are approached for testing for hepatitis C antibodies, although this goes beyond recent guidelines from the Public Health Laboratory Service.[3] We have found hepatitis C antibodies in 14% of source patients in reported incidents of exposure to blood, with a quarter of these infections being previously unknown.[4] The decision whether to test source patients routinely for hepatitis C virus and other bloodborne viruses will depend on the rates of infection in each hospital and the resources available for counselling and testing. Many occupational health units in our region do not have access to testing for hepatitis C antibodies in source patients.

The audit exercise in the region has been helpful, allowing units to compare their practices and providing support for units requesting additional resources. The level of provision of occupational health care varies too much at present to allow the development of formal guidelines that all can follow, but we hope that this may be possible in the future.

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Treatment of myocardial infarction and angina

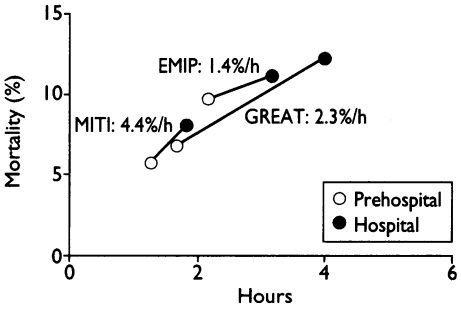
Review underestimated the benefit of early thrombolysis

EDITOR,—In their article on the treatment of myocardial infarction and angina John McMurray and Andrew Rankin perpetuate a serious error, underestimating the benefit of earlier thrombolysis in acute myocardial infarction.[1] Their figure 1 shows the loss of benefit within five weeks to be 1·6 per 1000 patients per hour of delay and is reproduced from the overview by the Fibrinolytic Therapy Trialists' Collaborative Group of all randomised trials of more than 1000 patients.[2] The graph shows the absolute reduction in mortality with thrombolytic treatment by delay from onset of symptoms to randomisation.

The severity of infarction, however, is negatively related to the delay by the patient, which constitutes a major portion of the time from onset of infarction to thrombolysis. The outcome of myocardial infarction treated at different times therefore depends on the balance between greater severity of infarction with earlier presentation and greater efficacy of thrombolysis with earlier administration. Thus the benefit of earlier thrombolysis is underestimated when based on subgroup analyses of placebo controlled clinical trials in which patients are treated as they present.

The magnitude of the benefit of earlier thrombolysis can be determined only by a trial in which patients are randomly allotted treatment on presentation or after a delay. The three largest trials of this design are the European myocardial infarction project,[3] the myocardial infarction triage and intervention study,[4] and the Grampian region early anistreplase trial.[5] Mortality at one month is reduced with prehospital thrombolysis by 1·7% absolute (P=0·03) when the results of all three trials are combined, though was not significantly reduced in any one of the trials.

The figure shows mortality at one month plotted against median times to the start of thrombolytic treatment in groups in whom it was started before and after admission to hospital; the lines linking the two groups represent gradients of benefit.



Mortality at one month plotted against median time at which thrombolytic treatment was started in prehospital and hospital groups in three trials. Figures in graph are benefit gradients. EMIP=European myocardial infarction project. MITI=Myocardial infarction triage and intervention study. GREAT=Grampian region early anistreplase trial

Although none of the comparisons is significant and there are large confidence intervals around each point, the figure gives three rough estimates of the magnitude of the time dependent benefit that are consistent with each other. Perhaps the best way to average these gradients is to draw the line of best fit between the six points: the resulting slope is 2·3% an hour. Over the period one to four hours from the onset of symptoms 23 more lives would be saved per 1000 patients treated per hour of earlier treatment. Giving confidence intervals for this estimate would give a spurious impression of reliability. Although tentative, this is so far the best estimate of the size of the time effect; it is more than 10 times that of the Fibrinolytic Therapy Trialists' Collaborative Group and substantially greater than that given in McMurray and Rankin's article.

Follow up of the Grampian region early anistreplase trial shows a separation of the survival curves, so that the reduction in mortality with prehospital thrombolysis is twice as great at one year as at one month. The true benefit of earlier thrombolysis may therefore be even greater than the estimate at one month given above.

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