audit office makes all the telephone calls a good relationship has been built up with the hospital staff, and it seems unlikely that many cases are missed.

On the basis of this telephone information two forms are sent to the consultant surgeon: one is for the surgeon, and his or her secretary passes the other, with the case notes, to the appropriate anaesthetist. In three successive six month periods we acquired similar numbers of deaths in surgical wards (about 600), of which around half occurred perioperatively.

The advantage of this system is that it does not depend on the medical records and that follow up calls to staff are made, and forms reach surgeons, soon after the patient's death, when the case is readily recalled. The medical records, however, are needed subsequently by the surgeon and anaesthetist to complete the forms.

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1 Clark L, Doyle P, Duran E, Kishore P. Effective audit: reporting to the national confidential enquiry into perioperative deaths. *BMJ* 1992;304:1472-4. (6 June.)

EDITOR,—L Clark and colleagues' report on the effectiveness of computer and manual systems for identifying perioperative deaths clearly shows the problems entailed in collecting such data over a long period and highlights potential implications with regard to large scale underreporting.

In line with the request from the National Confidential Enquiry into Perioperative Deaths that all reports for the period 1 April 1991 to 31 March 1992 should be submitted by 30 June we have used the patient administration system for a retrospective analysis of deaths during this period (in addition to using the routine manual system in operation). The hospital information department supplied the data, and a simple computer program was written to eliminate all those cases that did not fit the confidential inquiry's criteria.

The table shows that the patient administration system proved the most effective method of reporting cases, recording a third more deaths than the manual system. Assuming that the computer system and manual system in tandem discover all deaths in hospital, the manual system found 64% of all cases eligible for reporting to the National Confidential Enquiry into Perioperative Deaths whereas the computer system found 86%. The computerised search proved preferable in terms of saving the time of the local reporter and assistants.

Although the computer proved the best system, the 15% of deaths that were missed (compared with the 50% reported by Clark and colleagues) is still rather high, and further attention needs to be given to improving the system by which patients' details are entered into the computer. This is shown by

our analysis of the 28 cases missed. For 13 of the patients picked up by the manual system we could not find any apparent reason for their omission from the patient administration system; eight patients were emergency admissions who died within 24 hours; three patients were operated on outside the district and transferred to Brighton; and four patients were admitted under physicians but passed on to a consultant surgeon for an endoscopic procedure. This last group highlights a problem with using the information kept in the patient administration system because the admitting doctor is the only indicator of the person who performed the procedure, and this potentially can lead to unreliable data for those patients who, for example, have an endoscopic procedure that could be done by a consultant surgeon or physician. Fortunately, our endoscopy unit uses its own clinical information system, which can clarify who performed the procedure.

Experience in Brighton shows that it is not necessarily true that hospital information systems cannot be used to replace a manual system. The main drawback at the moment seems to be not the extent of completeness of the records in the patient administrative system (although there is scope for improvement) but, firstly, the fact that a data item required by the National Confidential Enquiry into Perioperative Deaths—the name of the anaesthetist—is omitted and, secondly, that you have to assume that the operating surgeon was also the named consultant at admission.

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EDITOR,—We were disappointed to read the paper by L Clark and colleagues because of the false emphasis that its title and some of the discussion give to the National Confidential Enquiry into Perioperative Deaths.¹ The material reported has nothing to do with the inquiry. The paper was shown to us in March 1989, when we were still finalising systems for reporting. The authors were then students in community medicine and were commissioned to investigate various systems of notification of death in hospital that might be useful if Lewisham and North Southwark Health Authority was to participate effectively with us. They studied only the first six weeks of the first year of the national inquiry but now draw invalid conclusions as if the data still apply to the rest of the country.

The authors' hospital reporting system was indeed unsatisfactory, but some of those in the remainder of the country were much superior and have improved further since the inquiry began. Our local reporters work hard in conjunction with

medical records and medical audit staff to achieve this, and the profession should be grateful for their efforts.

Both our reports (1989 and 1990) comment in clear terms about the imperfections of hospital information systems, and this report does not add anything to what is already known except that 21% of dead patients' records were (in 1989) lost in Guy's and Lewisham Hospitals.

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AUTHOR'S REPLY,—I regret that those who have done so much to establish surgical audit were disappointed by our paper. It was because of our belief in the importance of the National Confidential Enquiry into Perioperative Deaths and other emerging audit systems that we submitted the paper for publication even though the fieldwork was two years old. Two points that we made, critical to any audit system, are still relevant and will remain so for the foreseeable future.

Firstly, whatever system is used to ascertain cases for audit needs to be validated and revalidated at intervals or cases will be missed and audit performance will deteriorate. Secondly, when considering installing or improving hospital information systems doctors and managers should ensure that the system is capable of capturing and delivering the clinical information needed for medical audit.

I trust that our paper will remind doctors reporting to the confidential inquiry, or involved in other audit systems, or audit their own performance from time to time to ensure that the high standard set by the inquiry is maintained.

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Misuse of temazepam

EDITOR,—In their letter on intra-arterial injection of temazepam Roy N Scott and colleagues state that the gel used in temazepam capsules is insoluble in water.¹ This is incorrect. All macrogols are highly soluble in water, forming clear solutions. In the anhydrous state the macrogols used in the temazepam gel fill formulation range in appearance from viscous clear liquids through white, soft paraffin-like masses to hard crystalline wax-like substances. When these are blended together a stiff gel is produced. All these ingredients are, however, water soluble, and so is the resultant gel.

In the capsule temazepam is dissolved in this macrogol blend; experimental work has shown, however, that when this formulation is mixed with a small volume of water (as Scott and colleagues describe) the temazepam is precipitated out, being practically insoluble in water (maximum solubility less than 0.01%). Both Scott and colleagues and M Adiseshiah and colleagues refer to suspensions, fine particulate matter, and blockade of vessels by microemboli.^{1,2} It is the temazepam particles rather than the formulation's excipients that are likely to initiate the microemboli. This applies to any solid form of temazepam for oral dosing.

Scott and colleagues refer to the Home Office having requested withdrawal of liquid filled capsules and then suggest that manufacturers responded by substituting the liquid fill capsule by the gel formulation. In fact, before the Home Office's action Farmitalia Carlo Erba and R P Scherer had initiated an extensive reformulation

Performance of manual system and patient administration system in identifying deaths eligible to be notified to National Confidential Enquiry into Perioperative Deaths

Month	Manual system	Patient administration system	Matched cases	Cases eligible for National Confidential Enquiry into Perioperative Deaths
April 1991	13	16	12	17
May	16	15	10	21
June	9	13	7	15
July	8	7	2	13
August	11	16	9	18
September	7	9	5	11
October	10	18	8	20
November	8	13	7	14
December	8	16	8	16
January 1992	10	11	7	14
February	10	16	10	16
March	13	14	10	17
Total	123	164	95	192

programme aimed at making temazepam soft gels more resistant to misuse. Thus when the Home Office made its concern known the two companies were able, in consultation with the Home Office and the Medicines Control Agency, to replace the original liquid filled soft gelatin capsule with the gel filled product in a short time.

It is important to note that ischaemic damage has also been reported after intra-arterial injection of the contents of a liquid filled temazepam capsule. Hudson *et al* reported focal rhabdomyolysis in a 28 year old woman after injection of 80 mg temazepam from a liquid filled capsule into the femoral artery.³ Moreover, the development of an intravenous injection of temazepam for therapeutic use was abandoned because it was impossible to produce a formulation that did not cause unacceptable damage to the veins.⁴⁶ The venous damage found during the testing of these formulations was clearly due to the temazepam rather than any particular excipient(s).

In reformulating the liquid filled capsule to a gel filled product the options considered were deliberately constrained to exclude any harmful substances that might smack of a punitive approach to preventing misuse.⁷ This was one of the reasons why the familiar macrogols, used previously in the liquid filled capsule, were chosen as solvents; these excipients also had the advantage of posing no new problems regarding stability.

In conclusion, though we agree that serious risks are associated with inadvertent intra-arterial injection of the gel fill of temazepam capsules, the evidence indicates that these risks are probably due to the intrinsic physicochemical properties of temazepam rather than to any particular formulation.

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1 Scott RN, Going J, Woodburn KR, Gilmour DG, Reid DB, Leiber DP, *et al*. Intra-arterial temazepam. *BMJ* 1992; **304**:1630. (20 June.)
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EDITOR,—We agree with Roy N Scott and colleagues that the “abuse resistant” gel filled capsules of temazepam are widely misused intravenously and cause serious morbidity.¹ We are currently reviewing the clinical range of admissions of intravenous drug users to the regional infectious diseases unit. Data are available on 117 intravenous drug users admitted 170 times during October 1987 to September 1991. Overall, 57 of the admissions were of drug users who had previously injected temazepam. Twenty of the drug users (13 male, seven female; mean age 25.8 years) were admitted 33 times within four weeks of injecting temazepam; this represents 19% of the 170 admissions during the study.

The table shows the principal discharge diagnoses for those who had recently injected temazepam. Local complications of injection were common (24 admissions), particularly deep vein thrombosis, cellulitis or thrombophlebitis, and abscesses. The more dramatic arterial complications described by Scott and colleagues¹ and M

Adisheshiah and colleagues² were rare, but we recently admitted two other patients with tissue necrosis associated with extravasation of temazepam. One patient required debridement of gangrenous scrotal skin,³ and the other developed necrosis of the muscles of his upper arm.

Primary discharge diagnosis for patients admitted after intravenous misuse of temazepam in preceding four weeks

Diagnosis	No
Deep vein thrombosis	13
Cellulitis or thrombophlebitis, or both	6
Hepatitis B	5
Groin abscess	3
Other superficial abscess	1
Tissue necrosis	1
Miscellaneous	4
All diagnoses	33

Thirty nine per cent (13/33) of admissions after recent intravenous use of temazepam were for deep vein thrombosis compared with 8% (11/137) of admissions unrelated to recent use of temazepam ($\chi^2=19.07$, $p<0.001$; odds ratio 7.4 (95% confidence interval 2.7 to 21.0)). The association between deep vein thrombosis and a history of misuse of temazepam at any time was also highly significant (31% (18/57) *v* 5% (6/113); ($\chi^2=19.45$, $p<0.001$; odds ratio 8.2 (2.8 to 25.2)). All those admitted with deep vein thrombosis had injected into the groin, so the association with temazepam may simply reflect injecting behaviour or referral bias. Fifty six per cent (32/57) of admissions of those who had misused temazepam were of people who had injected into the groin, compared with 15% (17/113) of those who did not misuse temazepam ($\chi^2=29.22$, $p<0.001$; odds ratio 7.2 (3.3 to 16.2)), suggesting that misuse of temazepam leads to more injecting into the groin and an increased risk of deep vein thrombosis. The role of these factors is now being examined in greater detail.

The introduction of gel filled capsules has not prevented intravenous misuse of temazepam⁴ and is associated with severe morbidity. We believe that all liquid and gel filled capsules of temazepam should be withdrawn as they have the greatest potential for misuse. Rescheduling temazepam tablets and elixir, in addition to other short acting benzodiazepines, under the Misuse of Drugs Act should also be considered. We have recently given evidence to this effect to the Advisory Council on the Misuse of Drugs.

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2 Adisheshiah M, Jones DA, Round JM. Intra-arterial temazepam. *BMJ* 1992;**304**:1630. (20 June.)
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4 Rubens S, Morrison C. Temazepam abuse in a group of drug injectors. *Br J Addict* (in press).

EDITOR,—Temazepam is the most prescribed anxiolytic in Britain. Its misuse has been associated with misuse of other drugs, including opiates.¹ We studied 79 drug misusers in east London, of whom 55 were white men and 24 white women with a mean age of 30. The study showed that those who injected temazepam also injected opiates and most of those who injected opiates also injected temazepam. Temazepam was used to increase the

effect of the opiate and to relieve the symptoms of other drugs. Although stiff gel capsules, supposed to be resistant to misuse, were introduced in November 1989, anecdotal evidence from our sample suggests that the content of the capsules can be heated in a spoon and injected. Roy N Scott and colleagues also report this method of misusing temazepam.²

Temazepam was never the drug of first choice among our sample of drug users. In most cases heroin was the drug of both first and second choice. Sixty eight of those surveyed had injected heroin, and an additional eight had snorted or smoked it. Over half had injected cocaine. Sixty seven had taken benzodiazepines by various routes. Fifty two had taken heroin or methadone in the previous week, and 31 had taken benzodiazepines. Twenty of those taking benzodiazepines had used temazepam, and it was the only benzodiazepine that was injected. Men were more likely than women to inject temazepam. Four of those injecting temazepam did so daily and eight injected it two or three times a week. Five injected it once a week. Thirteen injected 11-30 mg, but six took over 80 mg at a time. Benzodiazepines were obtained “on the street” and from doctors, with two thirds of prescriptions originating from general practitioners. Seventy one respondents got syringes from chemists or needle exchange schemes. One third of respondents reported withdrawal symptoms from benzodiazepines.

Stark *et al* reported a myth among drug takers that HIV infection is avoided when temazepam rather than heroin is injected.¹ In our sample women were much less likely to inject temazepam and less likely to perceive themselves to be at risk of AIDS. No differences were found between men and women in the injection of other drugs.

The study highlights the need for better information on beliefs about high risk behaviour and drug use.

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2 Scott RN, Going J, Woodburn KR, Gilmour DG, Reid DB, Leiber DP, *et al*. Intra-arterial temazepam. *BMJ* 1992;**304**:1630. (20 June.)

Second brain tumour after treatment for pituitary adenoma

EDITOR,—When assessing the risk of second brain tumours after conservative surgery and radiotherapy for pituitary adenoma M Brada and colleagues found five cases (two of glioma, two of meningioma, and one of sarcoma) among 334 patients, and they compared this incidence with the population rates in South Thames region.¹ We believe that they are correct to state that further controlled studies are required to quantify more accurately the risk of second (radiogenic) tumour. Their series did not include a cohort of similar patients not receiving irradiation. Furthermore, they did not mention Jones’s recent review of radiation oncogenesis in relation to the treatment of pituitary tumours, which outlined some of the pitfalls of dealing with rare tumours.²

W Jones studied 332 consecutive patients with pituitary adenoma irradiated at St Bartholomew’s Hospital by a uniform megavoltage technique over the 21 years 1961-81 and reviewed in the same centre over seven to 27 years (median 11). Jones found no instance of sarcoma or meningioma