doctor has passed this test he or she is accepted to have the equivalent experience of a senior house officer who qualified in Britain. In fact, even before 1975 such doctors had to be assessed for professional competence and skill and English language by designated regional assessors for overseas medical graduates. Moreover, no such doctor would be accepted for any form of registration by the General Medical Council unless his parent medical school was recognised by the council.

The very fact that the same problem is now being faced by such doctors who are trained wholly in Britain, and that the ability to speak good English is not a condition for doctors who come from European countries, tends to suggest that the problem is discrimination because of prejudice and nothing else. Indeed, only when the medical profession accepts that such discrimination exists will the necessary steps be taken to eradicate it.

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Potentially dangerous ampoule confusion

SIR,—Dr Clifford Hawkins's letter (3 January, p 54) prompts me to mention another potentially lethal similarity between ampoules.

Atropine is often required during anaesthesia to correct a bradycardia. Multiple doses of suxamethonium, heavy hyoscine premedication followed by halothane anaesthesia, the oculocardiac reflex, or the use of vecuronium or atracurium may all cause a bradycardia of less than 40 beats/min, when rapid treatment with atropine 0·3-0·6 mg intravenously may be indicated.

Most anaesthetic drug cupboards are arranged alphabetically, and thus atropine 0·5 or 0·6 mg/ml and adrenaline 1 in 1000, 1 ml tend to be close neighbours.

In my experience of 15 hospitals these drugs have come in identically styled beige packaging and identical glass ampoules. The printing on the ampoules is black in both cases, although the style is different. In an emergency it is still all too easy to pick up the wrong box and inject the wrong drug, with probable dire results.

In these circumstances a different printing style is insufficient safeguard. At present we decorate the adrenaline boxes copiously with red ink, but could not the labelling on the ampoules or, even better, the glass itself be coloured red? Such a precaution would not obviate the responsibility of the doctor to check the label but merely provide additional security in emergencies.

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Cost of anaesthetic drugs and clinical budgeting

SIR,—Drs J R Lethbridge and J Secker Walker underestimate the nature of the problems facing an anaesthetist managing a clinical budget today (13 December, p 1587).

They say that the cost of some anaesthetic drugs has risen at a faster rate than inflation, yet at the time the paper was being prepared for publication the cost of what has now become the standard inhalational anaesthetic agent in the United Kingdom, enflurane, has doubled, as has the price of the more rarely used agent isoflurane, resulting in a very large increase in our department's expenditure on volatile agents.

Secondly, they point out that newer relaxants are more expensive than their older equivalents, but they have ignored the potential change in practice resulting from the introduction of a new intravenous induction agent. Studies undertaken at Lewisham Hospital when propofol was being evaluated for clinical use indicated that this was a unique induction agent, and after its release for general use it has become our preferred induction agent for day care. On a dose for dose basis it is roughly twice the price of thiopentone sodium.

Lewisham University Hospital has pursued a policy of maximum effective monitoring of patients during anaesthesia and now provides endtidal monitoring, blood pressure monitoring, and electrocardiographic monitoring at all anaesthetic sites in the hospital. However, pulse oximeter monitoring demonstrations have indicated that pulse oximetry is now mandatory for anaesthetic practice since it provides, non-invasively, an accurate analogue for arterial oxygen tension and arterial blood flow. To equip our department with satisfactory ear oximeters will require £30 000. We are undertaking a study on budgeting techniques (PACTS) because we believe that clinical activities must be budgeted if the level of service provided is to be known and defended. Our administrative colleagues are strongly resisting the provision of a capital element in the "zero based" budget we are trying to develop.

If anaesthetic departments are to be strictly held to budgets and allowances not made for pharmacological, technological, and commercial "drift" then inevitably basic services to patients will have to be sacrificed since our ability to control these three variables is limited.

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SIR,—Dr J W O'Higgins (10 January, p 124) points out that while the total caseload in 1979-80 and 1984-5 remained about the same, we bought more halothane and suxamethonium in real terms (13 December, p 124). As he points out, one explanation is that stocks bought do not necessarily relate exactly to financial years. Suxamethonium is bought in batches of 1000 ampoules (200×5) and halothane in quantities of 144 bottles. Hence a purchase of halothane on 30 March would show as belonging to the previous 12 months.

Another major factor is undoubtedly that, although the total number of cases was about the same in the period studied, the case mix altered quite considerably. There was a reduction in the number of chair dental cases and an increase in general surgical throughput.

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Adverse reaction monitoring using cohort identification

SIR,—The spontaneous adverse reaction reporting scheme using yellow cards sent to the Committee on Safety of Medicines (CSM) is generally accepted to be an effective and inexpensive method of surveillance. The scheme is essentially an early warning system which generates evidence that needs corroborating. Although more reports are being sent year by year, the use of the scheme by doctors still needs to be improved, as does the quality of the reports they submit. These reports provide the only realistic way of monitoring the entire range of medicines throughout their market lives.

Nevertheless, there is a real need for cost effective postmarketing surveillance schemes to augment the yellow card system. Such a scheme could, for example, be established within the health service by introducing integrated patient record linkage regionally or nationally; observers at any point within such a system could then relate the use of a medicine to one or more aspect of a patient's history—and this would certainly enhance the value of the yellow cards.

Other proposals have been suggested by the Grahame-Smith Working Party, including postmarketing surveillance of cohorts of 10 000 patients. This does not go far enough, however, as such numbers could detect a risk only of the order of 1 in 1000. As most product licence applications for new chemical entities are already supported by data on about 3000 patients, the working party recommendations would be unlikely to increase the chance of detecting new hazards and certainly not by the order of sensitivity needed. Recent adverse reactions judged sufficient to cause the withdrawal of products have had considerably lower incidences than 1 in 10 000 patients treated. Furthermore, the development of the Grahame-Smith postmarketing surveillance proposals would be expensive and so serve to divert resources away from the ultimate goal of record linkage, which admittedly would itself be expensive.

I suggest, therefore, the introduction of a cheaper interim measure which would involve the identifying of FP10 prescription forms for all marketed new chemical entities relating to, say, 50 000 to 100 000 patients. This would not be difficult as all such forms are sent to the Prescription Pricing Authority. Then, if the yellow card reports from doctors showed an association between an adverse reaction and a new chemical entity a special follow up form could be sent to all the doctors who had prescribed this particular drug. Information would be requested on whether any of these patients had experienced the specific adverse reaction.

The use of this scheme of "cohort identification" would enable both the numerator and denominator to be obtained for any adverse reaction which the CSM chose to pursue. The sensitivity of the method would depend solely on the size of the cohort initially identified and the response of the prescribing doctors to the questions sent to them.

The scheme does not introduce any new ethical problems; prescriptions are already identified at the Prescription Pricing Authority for the prescription event monitoring scheme operated by Professor W H W Inman at Southampton and the two systems should exist side by side. Although they both use FP10 data, they are different: prescription event monitoring is proactive and geared to identifying unexpected events, while cohort identification would be reactive, geared to determining the incidence of an identified adverse drug reaction and covering a much larger number of patients receiving the medicine under surveillance.

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Adverse drug reactions checklist

SIR,—The checklist you published (3 January, p 38) requires something more than simple coincidence in time to make an adverse reaction probable: rechallenge or immunological investigations. The ethics of rechallenge, however, need thorough discussion.

When a side effect of a drug is suspected an adverse reaction after rechallenge is probable. The

severity of the reaction, however, is unpredictable. The following two cases illustrate some problems related to rechallenge and the scientific necessity to confirm adverse reactions.

Case 1—In 1977-8 an excess of cases of leucopenia caused by rifampicin were detected in North Karelia: Rimapen caused 11 cases of leucopenia in 140 patients treated for tuberculosis (7·9%), a much higher incidence than normal (0·08%).[1] We decided to change the rifampicin preparation and prospectively study the frequency of leucopenia with Rimactan. The study was intended for internal use at the department for pulmonary diseases and was carried out in 1979-80. One patient out of 132 developed leucopenia. Our conclusion was to go on using Rimactan. This policy, however, was not accepted by the medical director of the hospital, who emphasised that there was no published evidence of an excess of side effects of Rimapen. Under these circumstances I felt obliged to publish our observations to avoid further unnecessary adverse reactions. To ensure the part played by rifampicin in two uncertain cases of leucopenia I rechallenged the patients with daily rifampicin three and three and a half years after the suspected rifampicin induced leucopenias. One patient reacted with a 'flu like syndrome and subsequently with renal failure and haemolysis on the ninth day of rechallenge despite careful precautions and informed consent. The possibility of such a severe side effect had been estimated as practically non-existent on the basis of the only seven previous cases, of which most had occurred during intermittent treatment or irregular drug intake. Seven haemodialyses were required and renal function returned to normal in three months.[2] In 1982-3 a randomised study with Rimapen and Rimactan was performed. In contrast to the previous study no differences in frequency of leucopenia caused by the drugs were detected.[3]

Case 2—In 1980 the first long acting theophylline preparation, Euphyllin Retard, was introduced in Finland. Since 1976 we had had difficulties in treating a 52 year old woman for severe bronchial asthma. She was steroid dependent, had maximal bronchodilating medication, and had to maintain a strict diet free of salicylate, preservative, and food colouring. She received Euphyllin Retard in November 1980 and reacted with an asthma attack after the third tablet. She noticed that the drug tasted of vanilla, which had earlier caused asthma symptoms. The adverse reaction was suspected to have been caused by vanillin (0·24 mg in the coating) and it was reported to the manufacturer. The company, however, refused to remove the vanillin in the coating without a more detailed case report. Therefore rechallenge with Euphyllin Retard and double blind challenge tests with vanillin and lactose as placebo were performed in May 1982. Unexpectedly the patient reacted with bronchospasm to both substances. Therefore the tests were repeated with vanillin and cellulose as placebo in October 1982. Bronchospasm occurred after vanillin but not after cellulose. As a result of the study the manufacturer removed the vanillin compound from the drug in June 1983.[4] During the rechallenges with Euphyllin Retard and with vanillin and lactose the patient suffered her only asthma attacks during that year.

I describe these two cases as a warning. In my opinion recommendations for rechallenges are questionable. They may even be in discordance with the Helsinki Declaration. Careful ethical consideration is necessary. Rechallenges should not be a scientific necessity. Rechallenge is almost the same as the deliberate harming of the patient. Should it be allowed at all except when there is no therapeutic alternative?

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1 van Assendelft AHW. Leucopenia caused by two rifampicin preparations. *Eur J Respir Dis* 1984;65:251-8.
2 van Assendelft AHW. Renal failure and haemolysis caused by rifampicin. *Tubercle* 1986;67:234-5.
3 van Assendelft AHW. Leucopenia in rifampicin chemotherapy. *J Antimicrob Chemother* 1985;16:407-8.
4 van Assendelft AHW. Bronchospasm caused by vanillin and lactose. *Eur J Respir Dis* 1984;65:268-472.

The debasing of medicine in the Soviet Union

SIR,—Those who have written on the above subject in your journal seem to have at least one thing in common: they are all against sin. The question, then, is not whether abuses have occurred in medicine in the Soviet Union but how we should respond to the situation. We can, and at times perhaps should, act as Old Testament prophets, denouncing evil when we see it. Sometimes, however, we may prefer to think of ourselves as a curious and variable mixture of saint and sinner and consider it to be more appropriate to sit down with our Soviet colleagues as equals and friends to discuss, among other things, what actions are unacceptable in medical practice. This method may be slow, but, as Dr A Haines has pointed out (17 January, p 180), it can produce results.

I have been on two medical visits to the Soviet Union in recent years and each time have been impressed by the open, thoughtful, and courteous atmosphere in which our discussions were held. Certainly, there are great cultural differences between us, but these may be due as much to historical as political factors, as Ms Caroline White (13 December, p 1524) suggested. Is it not just possible that, were the Royal College of Psychiatrists to explore these differences with its opposite number in the Soviet Union, it might prove more fruitful than pursuing its present policies?

Since Dr G A Low-Beer's letter was published (7 February, p 373) we have heard that a number of dissidents are being released. If our response to this action is generous and positive perhaps it may encourage the government of the Soviet Union to increase the pace of democratisation and strengthen the hand of Mr Gorbachev against those in the Soviet Union who feel threatened by his more liberal policies.

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Doppler studies in the growth retarded fetus

SIR,—Is it possible to go a stage further regarding the work of Dr G A Hackett and colleagues (3 January, p 13) and consider the part played by the abdominal para-aortic bodies, including the organs of Zuckerkandl, in the control of selective vasoconstriction in the hypoxic fetus?

Why are these bodies clustered down the aorta and found (among other places) very close to the origin of the inferior mesenteric artery, near but less close to the superior mesenteric artery, and near the origins of the umbilical arteries? These bodies are mature and functioning in utero at a time when the adrenal medulla, which will in due course be secreting mainly adrenaline, is immature. As Dr Hackett and coworkers state, in fetal hypoxia circulatory adjustments occur to protect the fetal brain, myocardium, and adrenal glands. The abdominal para-aortic bodies are obviously distal to the main arterial vessels to the brain and heart but also seem to be just distal to the main sources of arterial supply to the adrenal glands.

Do these very vascular but poorly innervated structures, which secrete noradrenaline in response to fetal hypoxia, release this catecholamine into the venous circulation, whence it is distributed after passage through the heart, or can these organs release noradrenaline directly into arteries or at least to affect nearby arteries? If noradrenaline can be secreted directly to affect the local arterial tree this would explain the Doppler findings in the aortas of some growth retarded fetuses and their increased risk of necrotising enterocolitis. The direct action of noradrenaline on the gut, causing smooth muscle relaxation and sphincter contraction, might also explain the troublesome abdominal distension and feed intolerance experienced by some growth retarded babies. Are the para-aortic bodies the basic reason why any baby can develop necrotising enterocolitis?

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Telling the patient

SIR,—Your (understandably) anonymous contributor (14 February, p 437) suggests, in describing her obstetric tragedy, that the consultant's apparent reluctance to discuss this with her was somehow the result of his defence society's advice. The defence societies make a substantial effort to encourage members to provide understandable explanations and to apologise when things may have gone wrong. No obstacle is placed in the way of the provision of a prompt, sympathetic, and above all truthful account of what has occurred.

This advice has been given prominence in recent publications by all of the defence societies and even in *Hansard*. I hope that such publicity will help to lay this unfounded impression to rest.

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WHO not amused

SIR,—In its Christmas competition of 1985 the *Lancet* invited readers to plan the expenditure of £1m yearly, for five years, in the best interest of health care in one or many lands.[1] This humanitarian concern was in the true spirit of Christmas. The *BMJ*'s Christmas competition "WHO's kidding" was certainly not.[2]

One of the *Lancet*'s prizewinning entries was a proposal to eradicate guineaworm disease, which still exists in some 21 countries.[3] Within weeks of the publication of this proposal the World Health Organisation's parliament adopted a resolution that committed all countries and the director general to action. This prompt response shows the influence of good medical journalism on the work of the organisation.

The diagram which was the topic of the *BMJ*'s facetious competition was an honest effort, by one of my staff, to use an analogy from physics to try to understand the forces that would impart movement into the field of health promotion. Debate on this public health problem resulted, in November 1986, in the Ottawa Charter for Health Promotion.[4] The World Health Organisation would welcome suggestions from your readers on how to put the charter into action. One example of such collaborative action, which is of particular relevance to the United Kingdom, is the Healthy Cities project. In European cities and Third World villages the World Health Organisations's scarce resources are being directed towards specific measures to improve people's wellbeing.

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2 Anonymous. WHO's kidding. *Br Med J* 1986;293:1643.
3 Anonymous. Christmas challenge. *Lancet* 1986;i:750-1.
4 World Health Organisation. *Ottawa charter for health*. Canada: Canadian Public Health Association, 1986.