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AUTHORS' REPLY,—Our study showed significantly higher concentrations of gonadotrophin in oophorectomised women treated with the 0·05 mg oestradiol patch than in those given a 50 mg oestradiol implant. As stated in our paper, we think that the lower gonadotrophin concentrations in the implant group were due to the higher oestradiol concentrations observed. Unpublished data from this group of patients at 12 months show significantly different oestradiol concentrations: a mean (SE) in the patch group of 224 (43) pmol/l and in the implant group 544 (42) pmol/l (95% confidence interval for difference between means −443 to −197, $p<0·0001$). As stated by Stevenson *et al*, patches have been shown to prevent postmenopausal bone loss, as have implants,[1] but it has also been observed that percentage increase in bone density correlates with plasma concentrations of oestradiol,[2] and so treatments resulting in higher oestradiol concentrations may be more effective in preventing this long term consequence of the menopause.

This suggests that Eliot *et al* may not be correct in their assertion that serum oestradiol levels greater than 120 pmol/l provide no additional effect. We agree that implants should not be forced on postmenopausal women who are keen to have patches and vice versa.

Reid and Ganger question the ethics of our study. Delaying treatment ensured that all women had equivalent baseline hormone profiles before starting oestrogen replacement; given that one of the aims was to compare hormone profiles, this was a necessary part of the study design. They also question the doses used in this study: we did not set out to compare equivalent doses, but rather, the recommended starting doses. Careful reading of Chetkowski *et al*'s findings reveals that transdermal oestradiol significantly decreased gonadotrophin levels in a dose dependent manner.[3] Kamel's paper referred to administration of the 0·2 mg oestradiol patch immediately after oophorectomy; suppression of gonadotrophins was not maintained.[4] Our study showed that the 0·05 mg patch did not suppress gonadotrophin release after oophorectomy (mean concentration of follicle stimulating hormone after oophorectomy, 37·3 IU/l; after four months' treatment, 53·4 IU/l). Although there is no evidence from studies on the long term benefits of the 0·05 mg patch compared with the 50 mg implant, our study shows that there are differences in gonadotrophin concentrations which we suggest are due to differences in oestradiol concentrations and which may be reflected in the long term benefits of oestrogen replacement therapy.

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1 Savvas M, Studd JWW, Fogelman I, Dooley M, Montgomery J, Murby B. Skeletal effects of oral oestrogen compared with subcutaneous oestrogen and testosterone in postmenopausal women. *BMJ* 1988;**297**:331-3.
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Midwifery and body fluid contamination

EDITOR,—Josaphat J Kabukoba and Pam Young contend that current practices to prevent the skin of staff being contaminated by mothers' body fluids during delivery are inadequate and that staff may be at risk of contracting viral diseases while practising obstetrics in the United Kingdom.[1] This has enormous implications for medical and paramedical staff practising in developing countries, especially in sub-Saharan Africa, where one in 40 adult men and women are estimated to be infected with HIV.[2]

Recently, we have seen three nurses with HIV infection probably acquired occupationally while they were working in obstetric and accident and emergency departments in Africa. The first patient was a white missionary nurse who had never had sexual intercourse but had worked for many years in general nursing and midwifery. The second was an African nurse from Zambia whose only sexual contact was her husband, who was HIV negative. She had worked in an accident and emergency department, although she may have received a blood transfusion. The third patient was a white nurse who had worked for two years in Zambia but denied having had sexual intercourse during that time. She had also worked as a midwife but had had vaccinations and minor ophthalmic surgery while in Zambia.

Kabukoba and Young found that the incidence of broken skin among doctors and midwives examined immediately after they performed obstetric procedures was 23%. Furthermore, 34% of the assistants, of whom 35% did not wear gloves, were shown to be contaminated with body fluids immediately after vaginal deliveries. This has important implications for those working in developing countries, as highlighted by the above cases. Staff doing high risk work should be encouraged at the very least to wear gloves to prevent or minimise the risk of transmission of HIV and hepatitis B virus.

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1 Kabukoba JJ, Young P. Midwifery and body fluid contamination. *BMJ* 1992;**305**:226. (25 July.)
2 Gibb DM, Newell ML. HIV infection in children: epidemiological and diagnostic aspects. *International Journal of Sexually Transmitted Diseases and AIDS* 1992;**3**:235.

EDITOR,—A R Smyth and colleagues[1] may have misunderstood our paper on midwifery and body fluid contamination.[2] We did not discuss HIV infection across intact skin. This issue followed on after the discussion of the finding that 23% of staff had broken skin on their hands and arms. These skin breaks may be portals of entry for the virus, which may then be picked by Langerhans cells.

The studies quoted by Smyth *et al* report follow ups of single exposure incidents of health workers to infected body fluids.[3,4] Obstetric staff have a cumulative risk during their long careers. With the rising prevalence of HIV it is not difficult to see that midwives and doctors face different risks from people having a single exposure. Any similarity to smoking and lung cancer?

We stated that the purpose of the study was to assess current methods of protection as issued by the royal colleges. We gave details of the methods of protection in use for the procedures mentioned and the levels of protection provided by these methods. Contamination even among surgeons doing caesarean sections who were "maximally" protected was 30%. Therefore the conclusion that the methods in use are inadequate is sound.

We will soon be publishing details of a new type of protection. A waterproof armsleeve with a watertight seal between it and the glove has been shown to reduce contamination to less than 5%. This is the answer to not only manual removal[5] but also to all other procedures on the labour ward and theatre when spillage of blood is expected.

The risk of HIV infection may be small, but we do not know how small. Also it is constantly changing as prevalence changes. Authorities and staff must ensure that risks are kept to the minimum by adopting appropriate practices and methods, or we may, as suggested by Fernando *et al*,[6] be too late.

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1 Smyth AR, Symth RL, Hart CA. Midwifery and body fluid contamination. *BMJ* 1992;**305**:474. (22 August.)
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Day surgery for cataracts

EDITOR,—Hugh F Thomas and Roger Humphry confuse the issue of the advantages of day surgery when they fall into the trap of assuming the advantages of local anaesthesia over general anaesthesia.[1] With current anaesthetic agents it is possible to provide general anaesthesia while still offering early ambulation and feeding, with a low incidence of nausea and vomiting, and of coronary and embolic complications and less need for postoperative nursing care.

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1 Thomas HF, Humphry R. Day surgery for cataracts. *BMJ* 1992;**305**:536-7. (5 September.)

Cardiorespiratory distress after sumatriptan given by injection

EDITOR,—Sumatriptan is a serotonin-1 (5HT-1) agonist that treats migraine by inducing cerebral vasospasm and is used to treat migraine and cluster headaches.[1,2] A recent report suggested that coronary vasospasm may be induced in susceptible patients.[3] We report two cases which show that serious ventricular arrhythmias may also be induced by this drug.

In the first case, a 42 year old woman who had suffered from migraine for many years and who had no previous cardiac history apart from mild hypertension (treated with Moduretic) collapsed within three minutes of receiving a first subcutaneous injection of sumatriptan. She was found to be in coarse ventricular fibrillation when the ambulance staff arrived seven minutes later. Sinus rhythm was regained by a single 200 KJ DC shock, and no further arrhythmias occurred. Subsequent investigations showed a normal 24 hour ambulatory electrocardiogram, an equivocal exercise stress test, and a 40% stenosis of the left anterior descending artery on cardiac catheterisation.

In the second case, a 67 year old man who was a life long migraine sufferer and who had had

rheumatic fever in 1944 and mitral valve repair for incompetence in 1985 was admitted in ventricular tachycardia without angina. He had started taking sumatriptan 30 days before admission. Each of the eight injections had been followed by "hot surges in the throat," and four of these were followed by a definite sensation of palpitation (up to 160 beats per minute). He required DC cardioversion and amiodarone to correct the arrhythmia.

A previous drug point showed that subcutaneous sumatriptan could produce ST elevation in susceptible subjects,[3] and a recent study has shown that vasospasm in patients with minor coronary artery stenosis can precipitate ventricular tachycardia and fibrillation.[4]

Our first patient would almost certainly have died without the prompt arrival of the ambulance service. The timing of her ventricular tachycardia in relation to the sumatriptan injection and the lack of previous or subsequent problems strongly suggest that sumatriptan induced her arrhythmia.

The second case is less clear in that there was a previous history of cardiac surgery, but eight separate administrations of the drug produced similar symptoms, which were shown to be due to ventricular tachycardia on hospital admission.

Thus we suggest that subcutaneous sumatriptan should be administered with caution and that, ideally, the first dose should be given while the cardiac rhythm is being closely monitored.

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1 Sumatriptan Cluster Headache Study Group. Treatment of cluster headaches with sumatriptan. *N Engl J Med* 1991;**325**: 322-6.
2 Subcutaneous Sumatriptan International Study Group. Treatment of migraine attacks with sumatriptan. *N Engl J Med* 1991;**325**:316-21.
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EDITOR,—Concern has been expressed about the apparently high frequency of reactions after injection of sumatriptan to relieve migraine.[1,2] We intend to follow up at least 10 000 patients, identified by means of prescriptions, for about six months by using prescription event monitoring; we report here on the 1881 patients for whom questionnaires (green forms) have so far been returned.

The most commonly described symptoms include tightness in the chest; discomfort or pain radiating into the shoulders, arms, neck, or throat and sometimes accompanied by dyspnoea; palpitations; and an alarming sense of impending doom. A few doctors have written or telephoned to express their concern in addition to completing the prescription event monitoring forms.

In 25 of the 1881 patients the common factor has been tightness in the chest, with onset within one to 60 minutes after the injection; descriptions of this have varied from mild and tolerable in the light of the benefit obtained to severe and terrifying. Four of these patients also had dyspnoea. In a further eight patients the symptoms could have been confused with those of an anginal attack. Two patients experienced bronchospasm. One other patient, a comparatively healthy asthmatic woman aged 26, died suddenly; at postmortem examination the findings were entirely consistent with death from asthma and the relation to an injection has not yet been confirmed. Three patients developed tachycardia and two developed palpitations. Finally, one patient suffered an instantaneous syncopal attack after the first but not the second of two injections. Only five of these 42 reactions were said to have been reported to the Committee on Safety of Medicines.

To be recorded in a prescription event monitoring study patients have to visit their doctor's surgery and complain about an event and the doctor has to enter it in the notes. Up to six months later the event then has to be considered to be sufficiently important to be transcribed on to a green form. Most events reported are not trivial. The incidence of this type of reaction in the series so far is 2·2%, which is unprecedented in numerous prescription event monitoring studies of more than half a million patients. Although we have seen no evidence of an unacceptable risk associated with sumatriptan in otherwise healthy patients, we believe that this drug should be prescribed cautiously for patients with a history of ischaemic heart disease, arrhythmia, or asthma.

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1 Willett F, Curzen N, Adams J, Armitage M. Coronary vasospasm induced by subcutaneous sumatriptan. *BMJ* 1992;**304**:1415. (30 May.)
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⁂ We sent these letters to Glaxo for reply

EDITOR,—Reports such as these cases of Dr Curtin and colleagues are taken seriously by the company, and we have followed up both cases.

Although the second patient experienced intense palpitations shortly after several injections, symptoms did not develop until after the third dose and did not occur consistently after injection. Similar attacks were recorded at times that were unrelated to treatment—in particular, the only documented episode of ventricular tachycardia occurred some six days after the last dose of sumatriptan. This protracted time lapse calls into question a direct causal relationship.

This patient had a history of rheumatic mitral valve disease, in which there is an established relationship with ventricular arrhythmias.[2] Underlying cardiac disease may therefore be a relevant aetiological factor.

In the first patient, a close temporal relationship was apparent, and the positive results of the exercise test and angiography support the authors' hypothesis of vasospasm superimposed on underlying coronary artery disease. The significance of hypertension in a woman of this age is unclear.

The reported occurrence of ventricular fibrillation is naturally of concern. Nevertheless, it constitutes an isolated event not otherwise identified in the entire clinical development programme or in subsequent international postmarketing experience, encompassing the treatment of an estimated 3 million attacks of migraine.

We appreciate the concern generated by this case report and are taking active steps to modify our prescribing information appropriately, in addition to continued investigation and close safety monitoring.

The preliminary data from Inman and Kabota's unit reports an incidence of adverse events which, although higher than for other drugs, is nonetheless entirely consistent with our own findings in clinical development. The potential for these symptoms is set out clearly in the sumatriptan data sheet; however, their nature and the associated use of an autoinjector will undoubtedly stimulate reporting. It is unlikely that previous prescribing events monitoring (PRM) studies with other drugs have been undertaken in comparable circumstances.

It should be emphasised again that, other than in exceptionally rare circumstances, there is no relation between the chest symptoms described and cardiac dysfunction. Furthermore, our extensive database shows no evidence of acute asthma or bronchospasm, though it is possible that the chest tightness sometimes reported by patients may have been misinterpreted as being of asthmatic origin.

We therefore strongly refute Inman's comments regarding the need for particular caution in asthma; these seem to be based on a single death from asthma, in which the relationship to medication is unknown. In contrast, we emphasise our contraindication to the use of sumatriptan in patients with ischaemic heart disease and related cardiac disorders.

The "distress" referred to in the title of the letter is a reflection of the understandable anxiety associated with the chest symptoms reported. This clearly highlights the need for adequate explanation and advice at the time of prescribing.

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1 Kligfield P, Hochreiter C, Kramer H, Devereux RB, Niles N, Kramer-Fox R, *et al.* Complex arrhythmias in mitral regurgitation with and without mitral valve prolapse. *Am J Cardiology* 1985;**55**:1545-9.

Medical reports for courts

EDITOR,—Anthony Joseph's suggestions about "neutral" medical reports for courts[1] are based on prejudice. He alleges that "the dismal results" of the adversarial method "include a tendency to miscarriage of justice (often appallingly serious, as many recent appeal cases in the English courts have shown) and suppression of truth." The fact is that these cases were the product of distortion and suppression of evidence by the police. The legal system as such—that is, the conduct of the prosecuting lawyers and the process of trial at first instance—bears no responsibility.

In my opinion the notion that the evidence of the neutral expert is of higher quality than that produced by opposing experts subject to cross examination is naive. Why should it be so? Joseph says it promotes suppression of inconvenient facts. Plainly, inconvenient records may disappear. They will always do so from time to time. It is a fact of life unaffected by legal procedure. But an expert acting for a party adversely affected by the unavailability of documents will surely probe as intensely to ascertain their whereabouts (and in my opinion more so) as will the "neutral" expert.

The merits of the competing systems in relation to medical evidence may be capable of resolution by research. Let Joseph apply his mind to the appropriate methodology. As a mere lawyer, I am incapable of doing so.

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1 Joseph A. Medical reports for courts. *BMJ* 1992;**305**:479. (22 August.)

EDITOR,—J S Price identifies medicolegal reports in litigation arising from personal injury as potentially harmful to patients and believes that the system needs reform.[1] Price notes patients' distress at being evaluated by contemptuous doctors whom they perceive as being paid by the insurance companies to prove that they are malingering. But I doubt whether having the courts request and pay for reports would help.

The problem lies less in the arrangements for producing reports than in the product. If only the arrangements were altered patients could still face opinionated "psychogenic dismissal"[2] by the same