in the hope that a ground swell of resistance will cause the politicians to think again.

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Torsade de pointes induced by sotalol

SIR,—Drs R Krapf and M Gertsch (15 June, p 1784) make an important point about the arrhythmogenicity of the β blocking drug sotalol, which has additional class III (Vaughan Williams) antiarrhythmic properties. They concluded that the arrhythmogenic effect may be due to a prolonged QT interval and that clinicians should be aware of sotalol's arrhythmogenicity when QT prolongation occurs. Therefore they suggest strict and early control of the QT interval when starting treatment.

In a recent study on patients with coronary artery disease and arrhythmias induced by exercise we observed an increase in the number and severity (assessed by the Lown score) of ventricular premature beats. After a pretreatment stress test (without any antiarrhythmic medication) 25 patients received sotalol by mouth 160 mg twice daily; they were reinvestigated at a further stress test two weeks later. Although two thirds of our patients made outstanding improvements at the second stress test, in three ventricular arrhythmias worsened (a twofold to fourfold increase in the numbers of ventricular premature beats). Two also showed a deterioration in the Lown score without demonstrable electrocardiographic changes.

The degree of deterioration agrees well with the percentage of aggravation described by Lown's group for any antiarrhythmic drug in clinical application.[1] Worsening of arrhythmias was recorded in 15% of those given propranolol and 7% of those given metroprolol. Only six out of 20 patients who deteriorated on quinidine also had prolongation of the QT interval; and out of the 722 patients studied by Velebit *et al* only these six had aggravation of ventricular premature beats corresponding to electrocardiographic changes.[1]

Clinicians should therefore be aware of drug induced arrhythmogenicity (including potentially fatal complications) in about 10-15% of patients receiving any antiarrhythmic drug, even when the QT interval is normal.

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1 Velebit V, Podrid P, Lown B, Cohen BH, Graboys TB. Aggravation and provocation of ventricular arrhythmias by antiarrhythmic drugs. *Circulation* 1982;65:886-94.

SIR,—In the patient described by Dr R Krapf and Professor M Gertsch (15 June, p 1784) torsade de pointes was induced by sotalol despite therapeutic sotalol concentrations. The patient was also receiving maprotiline 75 mg daily throughout. The authors state that "the temporal association indicates that digoxin and maprotiline did not have a role."

Tricyclic antiaepressants are known possible causes of prolonged QT syndrome and torsade de pointes,[1] and it seems logical that sotalol should not be given in combination with such agents. Although maprotiline (Ludiomil) is not a tricyclic but a tetracyclic antidepressant, it has a similar mode of action and, to quote the *Physician's Desk Reference*, "its pharmacological similarity to tricyclic anti-depressants requires that each reaction be considered when administering Ludiomil."[2] *Martindale: The Extra Pharmacopoeia* states that maprotiline requires similar precautions to those of amitriptyline, which "should be used with caution in patients with cardiovascular disease."[3] It would therefore seem that the concomitant treatment with maprotiline may have played an important part in the genesis of torsade de pointes in the patient described. As far as can be ascertained in published reports there has been only one case of torsade de pointes induced by sotalol in the absence of any other factor prolonging the QT interval.[4]

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Relation between recurrence of cancer of the colon and blood transfusion

SIR,—Professor Neil Blumberg and colleagues (6 April, p 1037) showed a significant association between recurrence of colorectal cancer and perioperative blood transfusion. We reviewed 109 patients who underwent resection of carcinoma of the colon and rectum in 1977-84 without adjuvant treatment. Sixty patients (55%) had received transfusions. There was no significant difference in the age, sex, stage of disease, degree of tumour differentiation, or length of follow up between these patients and those who had not received transfusions. Of the 55 patients with right sided (caecum, ascending, and transverse colon) carcinomas, 37 (67%) had received transfusions whereas only 26 of 54 patients (48%) with left sided tumours had received blood ($\chi^2=4{\cdot}08$, 1 df, $p<0{\cdot}05$).

Recurrent disease was diagnosed in 29 patients (27%), 18 of 63 (28%) who had received transfusions and 11 of 46 (24%) who had not ($\chi^2=0{\cdot}29$, 1 df, $p>0{\cdot}5$). Cumulative percentages of patients surviving without recurrence were calculated by a life table method.[1] Although there was no significant difference at any interval of follow up, patients who had not received transfusions had a marginal disease free survival advantage (table).

Cumulative percentages of patients free from disease after resection of carcinoma

	Time after operation (years)				
	1	2	3	4	5
Patients given transfusions	85·4	66·2	58·6	56·3	49·6
Patients not given transfusions	91·1	77·0	71·8	61·6	55·9

No significant association was found between transfusions and recurrence for any stage of disease or location of tumour, but each analysis consistently showed a slightly longer interval free from disease for patients who had not received transfusions.

Blood transfusions given before transplantation resulted in significant prolongation of renal allograft survival, probably as a consequence of immune suppression induced by transfusion. Conclusions from transplant studies, however, may not necessarily apply to cancer: tumours, which are often antigenic, have been present in patients with cancer for some time before transfusion, whereas transplant recipients are given transfusions before receiving the antigenic stimulus of a renal allograft. Although allogeneic blood given before transplantation of an immunogenic tumour significantly accelerates tumour growth in rats,[2] our recent studies in mice show that transfusions given at the time of or after tumour transplantation are not associated with increased tumour growth (unpublished data).

An association between recurrence of cancer and blood transfusions could be due to immunological manipulation or may be fortuitous. For example, Blumberg's patients who had received transfusions were more likely ($p<0{\cdot}05$) to have received cytoreductive treatment, presumably for residual and perhaps more aggressive disease. Thus blood transfusion could be simply an index of either less successful or more difficult surgery or the biological behaviour of malignant tumours, a variable that is not measured adequately by histopathological staging.

Our retrospective review was of a small number of patients and may be subject to a type II error,[3] obscuring a significant difference between those who had received transfusions and those who had not. Further studies are required to verify the existence of an association between cancer recurrence and transfusions and to identify the determinants of such an association.

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Intranasal calcitonin and plasma calcium concentrations

SIR,—We were as puzzled as Dr J C Stevenson (6 July, p 54) when reading the paper by Dr A E Pontiroli and colleagues (11 May, p 1390) that healthy volunteers could have plasma ionised calcium concentrations anywhere in the range of 2·0-2·5 mmol/l (8-10 mg/100 ml). We were less surprised about their ability to find a slight yet significant effect from intravenous human calcitonin on serum calcium concentrations.

Blanc *et al* found, in 15 volunteers, a small but significant decrease in serum calcium concentrations (0·05 (SD 0·02) mmol/l (0·2 (0·08) mg/100 ml)) six hours after intramuscular injection of 100 U of salmon calcitonin,[1] and Gennari *et al* obtained, in 10 volunteers, a dose dependent decrease of serum calcium concentrations after intravenous administration of the three most widely used types of calcitonin (porcine, salmon, and human). For human calcitonin this was significant between 10 and 120 minutes—that is, the duration of the study—with 0·5 mg and between five and 120 minutes with 1·0 mg intravenously.[2]

The magnitude of the decrease of serum calcium concentration in controls is such that it has always been a controversial point, and many authors have not found any significant decrease at all (admittedly, usually with smaller series). It therefore seemed inappropriate to test the effectiveness of an intranasal spray in volunteers using this variable. It appeared more logical to test the hourly urinary excretion of electrolytes since calcitonin is a potent natriuretic hormone,[3] and thereby a calciuretic hormone as well. We therefore studied an intranasal spray of salmon calcitonin in this way and found that it induced significant excretion of sodium, chloride, calcium, and potassium when 200 U was administered intranasally.[4] This dose was less potent, however, than 100 U of salmon calcitonin given intramuscularly, but it did not

produce any of the unpleasant side effects, which were maximum when calcitonin was given intramuscularly to young volunteers kept fasting in a confined environment for 10 hours. If the side effects are as great with an intranasal spray as with an intravenous injection then the former mode of administration loses one of its advantages over the latter.

As for the clinical effectiveness of a new mode of administration of calcitonin, this should first be assessed in Paget's disease, which remains the ideal model for evaluating such treatment. Evidence that bone pain is relieved in postmenopausal osteoporosis, as assessed by Dr Pontiroli (6 July, p 54), is not convincing. An intranasal spray of calcitonin should appreciably diminish the indices of bone turnover in Paget's disease during a period of at least 12 months and, furthermore, should be able to produce a reconstructive action on the osteolytic lesions as ascertained radiologically.[5] The former result was obtained,[4] and the latter has since been achieved in two cases (unpublished observations).

A previous intranasal spray of human calcitonin did not achieve a sustained suppression of the indices of bone turnover.[6] Whether this can be achieved with the present spray has not yet been shown. Furthermore, it has not been specifically stated whether the present spray differs from the previous one. This is probably so, since the calcitonin peak from the previous spray reached only one third of that obtained after a subcutaneous injection of the same 0·5 mg dose,[6] compared with the surprising equivalent peak from intranasal versus intravenous administration, as shown by Dr Pontiroli.

New modes of administration of calcitonin should be encouraged, especially when they are devoid of the well known side effects of the parenteral mode of administration and provided their effectiveness has been proved. We have also tested a suppository of salmon calcitonin by following the electrolyte excretion in the urine. It proved as effective as the intranasal spray (unpublished results). Its use in Paget's disease is now being tested. We will have to wait until 12 months of administration have been completed before declaring whether it is active or not.

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Nurses' education

SIR,—Professor C M Chapman in his leading article (3 August, p 295) states that "unless radical changes are made the 1990s will be marked by steadily decreasing numbers of qualified nurses—and hence an increasing amount of care of the sick being carried out by the untrained." This is a disturbing prospect and has major implications for the care of very disabled elderly people in hospital who are, at present, largely nursed by untrained staff.

In a recent study in six departments of geriatric medicine in the West Midlands region we looked at a very dependent group of elderly inpatients whom we termed "ultimately immobile." Such people had been in the same geriatric ward for three months or longer and could not walk without help from others. Geriatric wards were then categorised according to the percentage of ultimately immobile people in them. The hours allocated per bed per week to each grade of staff on the different wards were noted. Nurses were described as "registered," "enrolled," or "learner," and figures were also obtained for auxiliary staff. The table shows that the higher the percentage of ultimately immobile people on a ward the fewer the hours worked by trained staff and learners.

Allocated hours of nursing per bed per week by grade of staff and percentage of ultimately immobile people

Percentage of ultimately immobile people	Grade of staff (allocated hours)				
	Registered	Enrolled	Learner	Auxiliary	Total
<10	5·3	7·3	6·5	9·0	28·2
10-24	4·9	8·1	4·5	10·4	27·9
25-49	3·8	7·7	1·2	13·3	25·9
≥50	3·3	7·7	0·6	14·8	26·4

The very dependent elderly will remain at risk of developing even greater dependency unless adequate numbers of highly trained nursing staff are employed. These old people are dependent on nurses for personal hygiene, continence, physical appearance, communication, motivation, entertainment, and quality of life, thus offering rich opportunities for the exercising of nursing skills. By depriving "learner" grade nurses of the experience of working with large numbers of these patients we may further jeopardise recruitment.

When you consider the predicted increase in the numbers of very old people over the next 25 years and the prospect of fewer trained nurses to manage and the already quite inadequate provision of trained nurses to care for the very disabled elderly it is clear that "something has to be done."

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Emergencies at sea

SIR,—Mr J P H Fee and Mr J Moore (13 July, p 156 and 3 August, p 344) barely touch on the fringe of the problem. When we were ordered south to collect Commander Clive Waghorn from Brabant Island at three hours' notice last March nobody bothered to inquire whether we were medically prepared to deal with a broken femur in a patient who had been lying for a week on an antarctic glacier. I hastily looked to see whether we had the statutory Thomas's splint but failed to spot that although we had two middle sized ones, we lacked a large one. Fortunately, the highly competent doctors of the Joint Services Expedition had not just one but two with all the additional attachments and drugs that we also lacked. At the point where the other vessel, which was dealing with the media, apparently reported that the patient was given painkillers and fell into a deep sleep he was actually given a pint of beer and continued to sit up cheefully discussing his interesting experience for several hours, but it might have been otherwise.

It should be emphasised that this subject is now suffering from a serious degree of planning blight. While it is prescribed by law in the Medical Scales Act of 1974 that all ships should carry medical supplies, and those with more than a dozen passengers or 100 people in total a doctor with an enlarged scale of equipment, I fear that the job, in which one is expected to be seen but not heard, hardly attracts the most energetic type of doctor conversant with the most modern anaesthetic techniques; and if he was the current scales, which may be adequately described by saying that the most modern antibiotic is ampicillin and they still include aromatic spirits of ammonia, are hardly calculated to help him. This seems a pity as it would be useful to have a reliable guide on what is needed when the wisest person can hardly be expected to foresee everything. At present one hesitates to order expensive drugs that soon go out of date when for several years we have regularly been assured that new scales are likely to be promulgated at any moment.

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Risk profile for soldiers aged under 40 with coronary heart disease

SIR,—Lt Col Lynch and his colleagues (22 June, p 1868) have shown that mortality from coronary heart disease among soldiers is twice that among comparable civilians and opined that the reason is due to heavier smoking of cigarettes. In a subsequent letter (20 July, p 215) Lt Col Lynch states that he had tried to curtail smoking in the ward "but in the end patients do have rights, and there are moral as well as practical difficulties. . . ." Do not the non-smokers in his wards also have rights? Should they not be protected from the passive inhalation of cigarette smoke? Or does his military hospital have two classes of wards, unlike the tube trains of London Transport, which are all non-smoking?

Further in the correspondence a letter from Dr D L J Bilbey seems to imply, by innuendo, that soldier smokers smoke heavily because of their stressful lives but do not acquire coronary heart disease from indulging in that dirty habit. Dr Bilbey writes that "stress is the most important element in health impairment in modern living" and that "from the day he is enlisted the service-