

I am sure that medical practitioners in Britain, along with their colleagues in New Zealand, are keen to see any fraudulent claiming appropriately dealt with as fraudulent actions by a few in any profession reflect poorly on the rest of the profession.

CHRIS J GEDYE
General manager, contracts

Northern Region Health Authority,
Private Bag 92522,
Auckland,
New Zealand

1 Essex C. Uproar over confidentiality in New Zealand. *BMJ* 1994;309:760. (24 September.)

Catholic beliefs about contraception

EDITOR.—Gerard J Murphy presents Catholic belief about contraception.¹ However, the argument against contraception—that sex should be for pleasure and procreation, not for pleasure alone—applies equally against sex during the “safe period” and sex with a pregnant or lactating partner.

J NICKSON
Orthopaedic physician

Peasemore,
Newbury,
Berkshire RG16 0LJ

1 Murphy GJ. Catholic beliefs about contraception. *BMJ* 1994; 309:1231. (5 November.)

Misoprostol and birth defects

EDITOR.—Two mistakes occurred in Jan Rocha's news article on Brazilian doctors' investigation of a possible link between misoprostol and birth defects.¹ Firstly, misoprostol is sold as 200 µg pills, not 200 mg pills as stated. Secondly, it is not an efficient abortifacient.

To our knowledge, two studies on the abortifacient potency of oral misoprostol have been reported in the English literature. In the first study 300 women (at 9-12 weeks' gestation) were given two doses of misoprostol (2×400 µg or 2×200 µg) or placebo in the evening before a planned legal surgical termination.² Partial or complete abortion occurred in only 11% of the women who received the higher dose and 9% of those who received the lower dose. Similarly, of 40 women given 400 µg misoprostol seven days before surgical termination in the other study, only two had a complete abortion; among the 38 others the pregnancy continued in 32 while six had an incomplete or missed abortion as assessed by ultrasound scanning just before termination.³

In most women misoprostol induces an increase in uterine pressure,³ and this is probably the reason why 35-50% of women given misoprostol experience some degree of vaginal blood loss.^{2,3} Conceivably, the rise in intrauterine pressure or the uterine bleeding, or both, could lead to teratogenic effects. Increased rates of fetal malformations have been observed in rats given another prostaglandin analogue, sulprostone, in intravenous doses of ≥50 µg/kg/day (unpublished results of Schering AG quoted by World Health Organisation⁴).

P F A VAN LOOK
Associate director
H VON HERTZEN
Medical officer

Special Programme of Research, Development,
and Research Training in Human Reproduction,
World Health Organisation,
CH-1211 Geneva 27,
Switzerland

1 Rocha J. Brazil investigates drug's possible link with birth defects *BMJ* 1994;309:757-8. (24 September.)

- 2 Rabe T, Basse H, Thuro H, Kiesel L, Runnebaum B. Wirkung des PGE₁-Methylanalogons Misoprostol auf den schwangeren Uterus in ersten Trimester. *Gebirtschilfe Frauenheilkd* 1987;47: 324-31.
- 3 Norman JE, Thong KJ, Baird DT. Uterine contractility and induction of abortion in early pregnancy by misoprostol and mifepristone. *Lancet* 1991;338:1233-6.
- 4 World Health Organisation. Menstrual regulation by intramuscular injections of 16-phenoxy-tetranor PGE₂ methyl sulfonylamide (sulprostone). A multicentre study. *Br J Obstet Gynaecol* 1989;207:12.

Training in laparoscopic surgery

EDITOR.—We agree with Imran Mushtaq and C Harris's call for structured training in laparoscopic surgery.¹ Regrettably, they seem to be unaware of the pioneering activity of their own royal college in respect of laparoscopic training. The Royal College of Physicians and Surgeons of Glasgow was the first college to offer courses in basic laparoscopic skills and laparoscopic cholecystectomy, the first of which took place in April 1993. Since then a further six courses have been held—some were advertised in the *BMJ*—and 60 surgeons in training and two consultants from outside Britain have attended. The surgeons in training have been predominantly from the west of Scotland, but an associate professor of surgery from the United States attended.

In December 1993 the college opened a clinical skills laboratory, which is specially equipped for laparoscopic training and to allow “dry” training of other manipulative procedures. The college is also involved in the Scottish Training Board for Minimal Access Therapy and with the Edinburgh colleges and Professor A Cuschieri in Dundee in establishing a minimal access training unit for Scotland. We endorse the suggestion that surgical trainees should be encouraged to attend such courses early in their careers, but at present nothing more than encouragement can be offered.

M H LUCAS
Registrar

Royal College of Physicians and Surgeons of Glasgow,
Glasgow G2 5RJ

G T SUNDERLAND
Consultant surgeon

Southern General Hospital,
Glasgow G51 4TF

1 Mushtaq I, Harris C. Laparoscopic cholecystectomy in surgical training. *BMJ* 1994;309:1232. (5 November.)

Vascular surgical services

EDITOR.—J A Michaels and colleagues put forward good reasons for a move towards the organisation of regional vascular surgical services.¹ Although the Oxford Regional Vascular Audit Group may have suggested that a more active vascular service practice results in a lower rate of amputations with huge potential savings in morbidity and costs,¹ other studies, notably that of Evans *et al*, have shown the potentially adverse affect on the level of amputation of failed distal vascular reconstruction and its associated poorer rehabilitation outcome.² There is no clear scientific evidence that active vascular surgical services save more knee joints or reduce morbidity and mortality.

In an audit of amputation levels in patients referred for prosthetic rehabilitation Fyfe found that 39 different surgeons performed 263 amputations. Twenty four of them performed fewer than five amputations and a further five surgeons fewer than 10. Reducing the number of individual surgeons carrying out amputations by concentrating these procedures within specialist vascular centres must improve the overall quality of amputation surgery, quality being essential for a satis-

factory outcome of prosthetic rehabilitation. Close cooperation between the surgical team and the rehabilitation team is essential, and the move towards regional vascular surgical services will certainly help integration of the surgical service with the amputee rehabilitation team, thus improving the quality of service. The move is therefore fully supported by the International Society for Prosthetics and Orthotics (United Kingdom) National Member Society, a multi-disciplinary society with a major interest in rehabilitation after amputation.

R S HANSPAL
Consultant in rehabilitation medicine

Royal National Orthopaedic Hospital,
Stanmore,
Middlesex HA7 4LP

A S JAIN
Consultant orthopaedic surgeon

Royal Infirmary,
Dundee DD1 9ND

- 1 Michaels JA, Galland RB, Morris DJ. Organisation of vascular surgical services: evolution or revolution? [Commentary by R Greenhalgh.] *BMJ* 1994;309:387-8. (6 August.)
- 2 Evans WE, Hayes JP, Vermilion BD. Effect of a failed distal reconstruction on the level of amputation. *Am J Surg* 1990;160: 217-20.
- 3 Fyfe NCM. Audit of amputation levels in patients referred for prosthetic rehabilitation. *Prosthet Orthot Int* 1990;14:67-70.

Hepatitis C virus antibodies and Graves' disease

EDITOR.—J C Duclos-Vallée and colleagues have reported a high prevalence of antibodies to hepatitis C virus in patients affected by Hashimoto's thyroiditis,¹ and Tran *et al* have described two cases of the same association.² In response to these reports we studied the prevalence of hepatitis C virus antibodies and viraemia in the serum of 39 patients (3 male) with a mean age of 46 years who had various autoimmune thyroid diseases: 18 (3 male) had Graves' disease, 16 had asymptomatic thyroiditis, and five had Hashimoto's thyroiditis.

Samples from 14 subjects gave positive results for hepatitis C virus antibodies on enzyme linked immunosorbent assay (ELISA), and four of these were also positive on a confirmatory test of second generation ELISA. Hepatitis C virus was detected in the serum of three of these four subjects, all of whom had Graves' disease. Hepatitis C virus antibodies and hepatitis C virus RNA were not found in the patients with Hashimoto's thyroiditis or with asymptomatic thyroiditis. Simple linear regression analysis failed to show any correlation between concentrations of thyroid hormones and hepatitis C virus antibodies. None of the samples that were positive for hepatitis C virus contained autoantibodies (antinuclear, antimitochondrial, anticardiolipin, and anti-liver-kidney-microsome), excluding an autoimmune hepatitis or any other associated autoimmune disease. We found hepatitis C virus RNA in a fifth of patients with Graves' disease but not in patients with Hashimoto's thyroiditis, possibly because of the small number of samples tested (O Len *et al*, 4th world congress international gastrosurgical club, Madrid, 1993). These results are particularly interesting given the epidemiological reports of the national statistics information service that show the rarity of hepatitis C in the Italian population.

Several studies have suggested that alteration of the immunoregulatory system by factors such as stress or viruses may lead to Graves' disease by the breakdown of tolerance for autoantibodies to thyroid stimulating hormone receptor.³ Recently, we have also found the presence of antibodies to 70 kDa heat shock protein in the serum of patients with autoimmune thyroid disease, and this result supports the link between those immunogenic molecules and thyroid autoimmune processes.⁴ To clarify the nature of this association we need

a direct approach—for example, isolation or molecular identification of a potentially infecting organism from thyroid gland and injection into an experimental animal to test for possible induction of autoimmune thyroid diseases.

ORIANA LERI
Researcher
MARIA TERESA SINOPOLI
Doctor
MARIA ANNA DI PRIMA
Researcher

Department of Infectious and Tropical Diseases,
University "La Sapienza,"
Rome,
Italy

ANNA PAGGI
Associate professor

Department of Internal Medicine,
University "La Sapienza"

- 1 Duclos Vallée JC, Johanel C, Trinchet JC, Deny P, Laurent MF, Duron F, *et al.* High prevalence of serum antibodies to hepatitis C virus in patients with Hashimoto's thyroiditis. *BMJ* 1994;309:846-7. (1 October.)
- 2 Tran A, Quaranta JF, Beusnel C, Thiers V, De Souza M, François E, *et al.* Hepatitis C virus and Hashimoto's thyroiditis. *Eur J Med* 1992;1:116-8.
- 3 Tomer Y, Davies TF. Infection, thyroid disease and autoimmunity. *Endocr Rev* 1993;14:107-20.
- 4 Paggi A, Di Prima MA, Paparo BS, Pellegrino C, Faralli AR, Sinopoli MT, *et al.* Anti 70 kDa heat shock protein antibodies in sera of patients affected by autoimmune and non autoimmune thyroid disease. *Endocr Res* (in press).

Enalapril and β blockers in chronic renal failure

EDITOR,—T Hannedouche and colleagues report a randomised controlled trial of enalapril and β blockers in patients with non-diabetic chronic renal failure.¹ The importance of hypertension and progression of renal insufficiency is well established.^{2,3} The authors' conclusion that enalapril was superior to β blockers in preventing end stage renal failure in patients with chronic renal insufficiency was partly based on the statement that "no differences in blood pressure were seen at any point of the follow up between the two groups." Table III of their paper, however, shows blood pressure only at one year intervals for a study consisting of three year follow up.

Table IV shows that the patients in the conventional group had a significantly lower incidence of adequate control of blood pressure when taking only one drug—namely, the β blocker. As far as we can tell, additional antihypertensive drugs were added at three month intervals. The conventional group may thus have had poorer control of blood pressure for the first six to nine months of follow up. We wonder if the authors can provide comparisons of blood pressure, especially during the first year of follow up, at three month intervals. Without this information one cannot exclude better control of blood pressure in the enalapril group as the explanation for the drug's beneficial effect. This is especially true as the length of follow up is only three years and even a three to six month period of better control may alter the rate of progression of renal disease.

DERYA BORA HAZAR
Renal fellow
LITSO
Renal fellow

Renal Unit, Massachusetts General Hospital,
Jackson 825, Boston,
MA 02114,
USA

- 1 Hannedouche T, Landais P, Goldfarb B, El Esper N, Fournier A, Godin M, *et al.* Randomised controlled trial of enalapril and β blockers in non-diabetic chronic renal failure. *BMJ* 1994;309:833-7. (1 October.)
- 2 Brazy PC, Stead WW, Fitzwilliam JF. Progressive renal disease: role of race and antihypertensive medications. *Kidney Int* 1990;37:1113-9.
- 3 Hannedouche T, Albouze G, Chauveau P, Lacour B, Junger P. Effects of blood pressure and antihypertensive treatment on progression of advanced chronic renal failure. *Am J Kidney Dis* 1993;21(suppl 2):131-7.

Computed tomography for single seizures

EDITOR,—Ronald A Schoenenberger and Sabine M Heim suggest that cerebral imaging after a single seizure may be unnecessary if a score of ≥ 3 is elicited with the CAGE questionnaire (a screening questionnaire on alcohol misuse).¹ Their study raises several related issues that merit further comment.

Focal cerebral lesions thought to be responsible for the presenting seizures were found in 34% of cases. In these cases there was presumably a focal onset before generalisation, which was not evident on ictal clinical assessment. It follows, therefore, that the clinically generalised seizure was in fact a partial seizure with secondary generalisation in an appreciable minority of cases. This fact alone should lower thresholds for imaging in this clinical scenario.

While I accept the validity of the CAGE questionnaire, using it after obtaining a detailed alcohol and drug history, as should be the case, may elicit unreliable answers, especially in a period of postictal confusion. False positive and false negative responses must occur. Moreover, if a seizure is precipitated by alcohol withdrawal (and this is not synonymous with a score of ≥ 3 on testing the CAGE questionnaire) there are immediate clinical implications, not the least of which is the possible need for detoxification.

The possibility of behavioural disturbance during this period is high. Given the frequent interrelation among cerebral trauma, disordered haemostasis, and alcohol misuse, the ratio of risk to benefit in this subgroup of patients with a single seizure seems to be strongly in favour of cerebral imaging irrespective of scores obtained with the CAGE questionnaire.

J R C BOWEN
Neurology registrar

Princess Alexandra's Hospital,
Wroughton,
Wiltshire SN4 0QJ

- 1 Schoenenberger RA, Heim SM. Indication for computed tomography of the brain in patients with first uncomplicated generalised seizure. *BMJ* 1994;309:986-9. (15 October.)

Seasonal variations in fatal pulmonary embolism

Several mechanisms contribute

EDITOR,—Peter Wilmschurst draws attention to the increased incidence of coronary heart disease and stroke associated with cold weather.¹ This conclusion is drawn largely from epidemiological data from studies that were not based on postmortem examinations. We are surprised that he does not mention another major cause of cardiovascular mortality, pulmonary embolism.

Fatal pulmonary embolism causes over 20 000 deaths annually in Britain and accounts for a tenth of all deaths in hospital.² It also has a seasonal variation, with both postoperative and "spontaneous" emboli being significantly more common in winter.^{3,4} The cause of many deaths due to pulmonary embolism may be registered as myocardial infarction in the absence of routine postmortem examination, and this may contribute to the seasonal increase in deaths registered as due to ischaemic heart disease.

The seasonal increase in fatal pulmonary embolism may partly be explained by the changes in coagulation described in the editorial, but other factors, such as peripheral vasoconstriction and reduced activity resulting in a fall in blood flow in the lower limbs, may also contribute.⁵ We agree with Wilmschurst that cold weather causes an increase in preventable cardiovascular deaths. The

mechanisms of this increased death rate may include an increase in numbers of cerebrovascular, coronary, and thromboembolic episodes. In the absence of a large study based on postmortem findings it is difficult to determine the contribution of each mechanism and the preventive measures required.

E A COOKE
Research fellow
M A McNALLY
Senior registrar
R A B MOLLAN
Professor of orthopaedic surgery

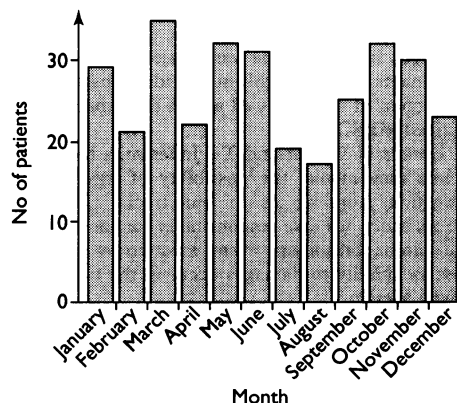
Department of Orthopaedic Surgery,
Queen's University of Belfast,
Musgrave Park Hospital,
Belfast BT9 7JB

- 1 Wilmschurst P. Temperature and cardiovascular mortality. *BMJ* 1994;309:1029-30. (22 October.)
- 2 Sandler DA, Martin JF. Autopsy proven pulmonary embolism in hospital patients: are we detecting enough deep vein thrombosis? *J R Soc Med* 1989;82:203-5.
- 3 Wroblewski BM, Siney PD, White R. Fatal pulmonary embolism after total hip arthroplasty. Seasonal variation. *Clin Orth* 1992;276:222-4.
- 4 Gallerani M, Manfredi R, Ricci L, Grandi E, Cappato R, Calo G, *et al.* Sudden death from pulmonary thromboembolism: chronobiological aspects. *Eur Heart J* 1992;13:661-5.
- 5 McNally M, Mollan RAB. Total hip replacement, lower limb blood flow and venous thrombogenesis. *J Bone Joint Surg [Br]* 1993;75:640-4.

Malignant phase hypertension does not vary by season

EDITOR,—In his editorial on temperature and cardiovascular mortality Peter Wilmschurst comments that the difference in temperature between summer and winter in Britain should result in a difference in blood pressure of 5 mmHg.¹ Malignant phase hypertension represents a syndrome of high blood pressure that is associated with a high mortality if left untreated. We recently reported that we had not noted a decline in the incidence of this condition between 1970 and 1993.²

To investigate whether the presentation of malignant phase hypertension varied by season we reviewed the month of presentation of 315 patients (211 men, 104 women; mean age 49.4 (SD 12.7) years) with the condition who were referred to our hospital between 1965 and 1994. There was no clear relation between the number presenting and season, although the largest number of patients first presented in March (n=35) and the lowest number of patients first presented in August (n=17) (figure). When patients who presented in March were compared with those who presented in August there were no significant differences in mean age (49.6 (13.3) v 46.2 (8.3) years; unpaired *t* test, P=0.27), mean duration of known hypertension before presentation (17.5 (43.8) v 6.4 (14.7) months; P=0.18), and mean diastolic blood pressure (144.3 (19.8) v 140.0 (30.5) mmHg; P=0.61). There was, however, a trend towards a high mean systolic blood pressure (234.2 (28.0) v



Number of patients presenting with malignant phase hypertension by month (n=315)