outcome is difficult to judge, but certainly many of the final necropsy diagnoses would have been amenable to active medical treatment. Interestingly, the incidence of clinical misdiagnosis was similar in both teaching and non-teaching hospitals. Three additional cases in my records also illustrate that jaundice in a patient with a previously established diagnosis of malignancy should not be attributed to carcinomatosis in the absence of histological evidence of spread, the final necropsy diagnoses in these cases being chest infection, cirrhosis, and amyloidosis. It is particularly important that a false positive isotope liver scan was again the main cause of clinical difficulty.

During the same period my necropsies have shown only one histopathological misdiagnosis of malignancy, although four cases of cytopathological error are recorded, an error surprisingly not experienced by Dr Rees and colleagues in their 1635 admissions.

Dr Rees and coworkers support my long held view that a clinical diagnosis of terminal cancer must always be supported by a definitive histopathological diagnosis. In addition, it would seem desirable for cytopathological diagnoses to receive tissue confirmation whenever possible.

For reasons that remain obscure, the unqualified and grossly inadequate term "carcinomatosis" remains acceptable to both registrars and referees on death and cremation certificates. Fortunately, however, some coroners place histologically unproved carcinomatosis in the "cause of death which appears to be unknown" category and request the performance of a necropsy in such cases. My statistics illustrate that such a policy is well founded and should receive wider, if not national, acceptance by all those concerned with certification of death.

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Pinch skin grafting or porcine dermis in venous ulcers

SIR,—We would like to address the first two paragraphs of Dr L O Simpson's letter (4 July, p 53).

Our preliminary findings after measuring transcutaneous oxygen tension at 43°C (in the inner aspect of the lower third of the leg) in patients with venous, mixed arteriovenous, and arterial ulcers enabled us to discriminate between patients and controls as well as between ulcers of venous and other aetiologies.¹

In the same preliminary communication we also reported our inability to agree with the findings of Dodd *et al*, who measured oxygen tension at 37°C on the dorsum of the foot and found very low absolute values.² The point that we would like to emphasise, as Dr Simpson draws support from Dodd *et al*, is that transcutaneous oxygen tension measured at 37°C yields very low absolute values (2-10 mm Hg), and changes within such small absolute values must be interpreted cautiously.

Percentage change in blood flow on dorsum. Information in parentheses indicates change on dependence*

	Mean (SD)	Range
Patients with venous disease and ulcers (n=19)	43 (17) (decrease)	11.0-66.6
Controls (n=9)	55.2 (27.2) (decrease)	26.6-100
Patients with venous disease and ulcers (n=3)	386.2 (increase)	87.5-700

*% Change=(supine-dependent)/supine.

We have obtained many results using the protocol described in our preliminary communication, and at present our findings are consistent with the concept of a barrier to oxygen transport in the legs of patients with venous disease. Clyne *et al*, who reported findings of oxygen tension similar to ours, support the concept of the fibrin barrier proposed by Professor Browse.³ Other workers, notably Bollinger *et al*⁴ and Fagrell,⁵ have used sodium fluorescein to image the veins and have reported observing "haloes" of micro-oedema around capillaries in the skin of patients with chronic venous incompetence. These workers suggest that such "haloes" may act as barriers to the transport of oxygen to tissues.

Dr Simpson has also extrapolated from Dodd *et al*'s findings to say that "it is unlikely that vascular changes occurred when the body changed from the horizontal to the vertical plane." We have investigated the change in blood flow in the dorsum of the foot after a passive lowering of the foot from the supine position through 50 cm. The table shows the changes in cutaneous blood flow measured on the dorsum with a laser Doppler flowmeter (Periflux PF1C, Perimed, Sweden). The decrease in blood flow agrees with the findings of Hassan and Tooke.⁶ The increase measured in the three patients was absent when experiments were repeated with patients wearing graduated compression bandaging.

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- 1 Mani R, Gorman FW, White JE. Transcutaneous measurements of oxygen tension at edges of leg ulcers: preliminary communication. *J R Soc Med* 1986;79:650-4.
- 2 Dodd HJ, Gaylarde PM, Sarkany I. Skin oxygen tension in venous insufficiency of the lower leg. *J R Soc Med* 1985;78:373-6.
- 3 Clyne CAC, Ramsden WH, Chant ADB, Webster JH. Oxygen tension of the skin of the gaiter area of limbs with venous disease. *Br J Surg* 1985;72:644-7.
- 4 Bollinger A, Junger M, Jager K. Fluorescence videomicroscopy techniques for the evaluation of human skin microcirculation. *Prog Appl Microcirc* 1986;11:77-97.
- 5 Fagrell B. Local microcirculation in chronic venous incompetence and leg ulcers. *Vascular Surgery* 1979;13:4.
- 6 Hassan AAK, Tooke JE. Effect of local nervous blockade on postural vasoconstriction in man. *Proceedings of the Physiological Society* 1986;381:63.

Cervical carcinoma: prognosis in younger patients

SIR,—The review by Dr J M Russell and colleagues (1 August, p 300) of 2870 patients with cervical carcinoma showed results that were compatible with the Office of Population Censuses and Surveys' returns for similar years.¹ The age related incidence of cervical cancer is, however, now different. Individual gynaecologists have for some years been aware of a dramatic increase in the disease in very young women. This is now apparent in the Office of Population Censuses and Surveys' returns and since 1985 figures for women aged 15-24 have been cited. Compared with 1976-80 the number of reported cases of carcinoma of the cervix in women aged 25-34 rose from 348 to 492, an increase of 41%. This increase has continued after the period of analysis covered by the paper by Dr Russell and coworkers.²

In young women the degree of tumour differentiation and the rate of tumour progression are likely to dictate outcome. Hall and Monaghan reported on a small series of women under 35 years with cervical carcinoma; all five with microinvasion were alive, but of the remaining 37 patients with squamous carcinoma, 34 had poorly differentiated or anaplastic tumours and 17 were dead.³ Although it does not give survivals at five years, this report is alarming. The study by Dr Russell and colleagues,

valuable as it is, is a retrospective analysis of a retrospective situation. A similar study in 1997 may well tell a different story.

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- 1 Office of Population Censuses and Surveys. *OPCS monitor*. London: Office of Population Censuses and Surveys, 1984. (MB1 84/1.)
- 2 Office of Population Censuses and Surveys. *OPCS monitor*. London: Office of Population Censuses and Surveys, 1986. (MB1 86/1.)
- 3 Hall SW, Monaghan JH. Invasive carcinoma of the cervix in younger women. *Lancet* 1983;iii:731.

SIR,—Dr M Ashby (27 June, p 1688) and Dr J M Russell and colleagues (1 August, p 300) suggest that the prognosis for young women with cervical carcinoma is as good as, if not better than, that in older women, despite previous reports to the contrary.¹

I reviewed the records of all patients with invasive squamous cancer of the cervix presenting to the radiation oncology unit at the Western General Hospital in Edinburgh in the years 1974 and 1983. Though the overall numbers had altered little (75 patients in 1974, 83 in 1983), the proportion of women under 35 had increased from 4% in 1974 to 18% in 1983. Only three cases (4% in 1974 and five (6%) in 1983 were detected by routine cervical cytology; the rest of the women had symptoms at the time of diagnosis.

Of the young women who presented in 1983, most presented with International Federation of Gynaecology and Obstetrics stage Ib (67%) or II (27%) disease, and 54% of all patients had stage Ib and II disease. Of the women under 35, half were shown to have lymph node disease by lymphangiography or node biopsy. Treatment was by external beam radiotherapy and intracavitary caesium or by radical hysterectomy and external beam radiotherapy (eight patients).

After one year 27% of those under 35 had died of their disease (all had had lymph node disease). By contrast, only 11% of women over 35 with stage Ib and II disease had died at one year, and three of these four women were in the 36 to 40 age group. Though the numbers are small and figures for five year survival cannot be given, these findings do not support the suggestion that stage for stage survival in women under 35 is as good as that in older women.

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- 1 Stanhope CR, Smith JP, Wharton JT, Rutledge FN, Fletcher GH, Gallagher HS. Carcinoma of the cervix: the effect of age on survival. *Gynecol Oncol* 1980;10:188-93.

Ruptured abdominal aortic aneurysm presenting as ureteric colic

SIR,—We believe that the presentation of a ruptured abdominal aneurysm as ureteric colic, as discussed by Mr C G Moran and colleagues (16 May, p 1279) and Dr J B Roussak and Mr E R C T Owen (25 July, p 267), is so common that all the staff in the urology department are routinely told consciously to exclude a leaking aneurysm in all cases of ureteric colic in patients over 50 years old. To our knowledge there have been four such cases in the past 12 months in Bristol.

We would also like to point out the hazards of relying on ultrasound for the diagnosis of ruptured abdominal aortic aneurysm. Recently, a 60 year old man was referred to the department of urology from the accident and emergency department

with a diagnosis of left ureteric colic. Six hours previously he had collapsed with severe pain suggestive of ureteric colic. When seen he was in pain and hypotensive (blood pressure 90/60 mm Hg), his pulse was 80, and there was tenderness in the left loin, but no abdominal mass was palpable. Urine analysis yielded normal results. On referral he was immediately sent for abdominal ultrasound, which showed a 3 cm abdominal aortic aneurysm but no evidence of a leak. He was thus considered not to have a leaking aneurysm. Intravenous pyelography yielded normal results. Other diagnoses were considered, but amylase activity was normal, as were an electrocardiogram and a chest radiograph. Three hours after referral his condition had not improved despite resuscitative measures, and examination of his abdomen showed a tender mass in the left abdomen. A ruptured abdominal aortic aneurysm was diagnosed, and he was referred for a laparotomy, at which a small, leaking, infrarenal aneurysm was found. This was repaired, but he died four days later of an acute myocardial infarction.

As this case shows, all cases of presumed ureteric colic must be assessed carefully as even the alert may be misled.

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Gender reassignment today

SIR,—Dr Philip Smith's leading article (22 August, p 454) cannot go unanswered. Having been concerned with John Randall in the early gender reassignment surgery performed before 1974, I feel that I must comment.

Sadly, the academic department of psychiatry at Charing Cross Hospital has never undertaken a randomised trial of whether gender reassignment surgery has any value at all. Conversation with many patients and, more important, nursing staff would have shown that 30% of patients dissatisfied with their gender reassignment surgery is an appalling figure. It is not uncommon for patients to complain to the nursing staff that they regret having had their surgery, and Dr Smith correctly points out that suicide after gender reassignment surgery certainly occurs.

Many of these patients become extremely demanding. After genital surgery many wanted breast augmentation, some wanted their distal limbs shortened, others wanted their thyroid cartilage shaved down; the whole situation became utterly impossible, and I therefore stopped doing any more of this surgery.

However, whatever the morals of continuing with this sort of surgery when there is such a dissatisfaction rate, Charing Cross Hospital nevertheless decided to continue with it after the retirement of my colleague, who did most of this surgery. It may be a surprise to many people that gender reassignment surgery is available as a National Health Service commitment. Meanwhile, the urology department at Charing Cross Hospital has had its beds depleted and some of its theatre sessions removed, and the management seems undismayed at a spiralling waiting list for straightforward urological admissions. This week I have a waiting list of about 250 people, and patients with tumours cannot be admitted for several weeks, but the hospital blithely goes on providing gender reassignment services. One patient undergoing surgery for gender reassignment occupies a bed for about 10 days. During that time 10 check cystoscopies or bladder tumour resections could be performed. It is therefore hardly surprising that

since mid-February of this year I have had to cancel 67 urological admissions because there was no theatre space or no beds. Many people may feel that the hospital has its priorities wrong.

Many of these patients say that they have never engaged in homosexual activity, but nobody has quite explained how a small percentage of the transsexual patients at Charing Cross Hospital carried the hepatitis B virus when causes other than homosexual activity had been excluded. Certainly the incidence was higher than the incidence of hepatitis B among patients undergoing dialysis at the same hospital. Some of the overseas candidates for gender reassignment surgery were later to be found in the transvestite area of Athens after their operations.

In the days when I undertook this surgery I ended up accepting only patients who were accepted as women by the female nurses. It was almost as if it needed a woman to recognise a woman, but these were a very small proportion of all the patients requesting gender reassignment surgery. It is more than time that audit was performed of this service.

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A shocking American report with lessons for us all

SIR,—Professor T J Hamblin suggests that "trials in healthy subjects must always be ethically dubious" (11 July, p 73). He gives no support for this extraordinary conclusion.

Studies in healthy volunteers have a long and honourable history in medicine in the elucidation of normal physiology and metabolism as well as in studies of the ways in which the body handles chemicals. These studies give us the information to decide whether human beings handle a drug differently from animals and so to decide whether toxicity studies in animals give us any indication of the likely effects of the chemical in man.

I will confine myself to pharmacokinetic studies, which can be carried out with exceedingly small doses and which seem to me to be one of the most useful types of healthy volunteer studies. Properly carried out, studies of this kind are unlikely to harm healthy volunteers. The benefits to the community are clear; just as we ask firemen, lorry drivers, and many others to take risks for the sake of the rest of us so I think it is proper to do so for minimal risks where the studies are properly carried out in terms of planning, information to the volunteers, and proper ethical committee supervision.

Professor Hamblin does not seem to have thought about the problem from the point of view of the volunteer. Having acted as both volunteer and experimenter in many studies there is still an element of anxiety to be faced when one is at the sharp end of the needle (there is anxiety in planning an experiment on a new substance as well). The important thing is that the volunteers should be part of a coherent group who can talk to each other and have good contact with the medical and scientific people who are conducting the experiment. In this way anxieties can be expressed and allayed, a sense of trust can be developed, and there is less danger that any of the volunteers will have concealed a contraindication to participation in the study.

For this reason it is important that volunteers should have a corporate existence, as students, employees, or members of some society. For instance, a sports or recreational club would be a very suitable group setting in which to conduct

studies. Individuals who are not well known to the organisers and who do not have some formal contact with the organisers seem in principle to be defenceless and exploitable. I therefore take the opposite view from Professor Hamblin. Properly organised and supervised groups of students or employees, with their tutors or supervisors to see that they are not taken from their studies or work, form a group with whom studies can be ethically conducted. Students from a different institution with whom one has no continuing contact are much less suitable. Volunteers "off the street," who cannot be followed up, seem to me to be unjustifiable.

In considering the ethics of an action one has to consider the ethics of not performing that action. From that point of view it is clear that to fail to perform proper studies in healthy volunteers under proper conditions of supervision and care can be the really unethical action.

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Hypotensive and sedative effects of insulin in autonomic failure

SIR,—Dr Christopher J Mathias and colleagues found that intravenously administered insulin had a hypotensive effect in patients with chronic autonomic failure (18 July, p 161). Blood pressure fell no further after the slow intravenous administration of glucose 25% given to reverse the insulin induced hypoglycaemia. In contrast, rapid intravenous injection of glucose 50% without previous insulin administration led to an almost immediate and serious fall of blood pressure. They concluded that glucose 25%, instead of glucose 50%, should be given to prevent a further fall of blood pressure after insulin induced hypotension. Their study design, however, does not warrant such a conclusion.

Intravenous administration of hypertonic solutions is known to cause an immediate, short lasting vasodilatation. Since glucose 25% was administered at the moment of peripheral vasodilatation induced by the previous insulin administration the absence of a further fall in blood pressure was to be expected. Therefore glucose 50% might also have no hypotensive effect when administered under the same conditions.

The authors wondered whether comparable effects could be also observed in the elderly. We studied the effects of intravenous administration of glucose 40% on blood pressure in seven normotensive and seven hypertensive elderly subjects (mean age 76 (SD 2) years and 75 (2) years respectively).¹ This study was performed after we had found that oral glucose loading caused an age and blood pressure related reduction in supine blood pressure, whereas oral fructose loading had no effect on blood pressure.² Two minutes after injection of 100 ml glucose 40% systolic blood pressure decreased from 172 (SD 5) to 156 (5) mm Hg (9%, $p < 0.05$) in the hypertensive group and from 140 (6) to 127 (8) mm Hg (10%, $p < 0.01$) in the normotensive group. Diastolic blood pressure fell only in the normotensive group, from 80 (2) to 71 (2) mm Hg (11%, $p < 0.05$). In both groups heart rate increased by 12-15%. Within 10 minutes after the start of glucose injection blood pressure had returned to basal values and remained unchanged for the following two hours of observation. All subjects had a transient flush and complained of feeling hot for a few minutes. The