

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 straight-forward 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).<sup>1</sup> 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.<sup>2</sup> 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

peak plasma insulin value was reached 15 minutes after glucose injection.

These findings lead us to conclude that intravenous administration of hypertonic solutions such as glucose 40%, but probably also radiographic contrast media, may cause a fall of blood pressure in the elderly, probably through direct vasodilatation. Secondly, the endogenous insulin response to glucose 40% given intravenously elicited no effect on blood pressure in the elderly.

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### Health and nutrition of Ethiopian refugees in emergency camps

SIR,—Dr Paul Shears and colleagues draw attention to the high mortality among Ethiopian refugees arriving in the Sudan in 1985 (1 August, p 314). The mortality remained high despite the relief programme in the area and was observed in a number of camps with differing standards of relief services.

The main determinant of mortality was the extremely poor nutritional state of the population on arrival. Severely malnourished people of all ages may be kept alive for some time by the efforts of relief agencies, but they often fail to improve nutritionally because of impaired gastrointestinal and metabolic function and finally succumb to infection weeks later. Reactivation of infections with refeeding was not specifically recognised but might have contributed to the delayed mortality in that confused environment.<sup>1,2</sup>

The authors do not regard water supplies as a major problem. As one who was working in the area at that time, I know that in many of the camps the water supply was the weak link in the provision of early services in the emergency. Both the quality and, more importantly, the quantity of water were inadequate.

There was another factor which probably added to the high mortality. Non-governmental agencies appeared at times to be more concerned with interagency rivalry and the pursuit of rigid ideology than the welfare of the refugees. On one occasion three agencies were asked to provide medical services for a large group of new arrivals in very poor condition. None of these agencies wanted to be involved in "curative medicine." As a result, during the first critical weeks, when many of the population were acutely ill, the curative services provided were quite inadequate and many died of treatable conditions. Agencies concerned in disaster relief programmes must make the welfare of the victims their prime concern rather than their own prestige or ideology.

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### Regular Review: Somatostatin

SIR,—We would like to comment on the statement made by Professors S R Bloom and J M Polak (1 August, p 288) about the efficacy of somatostatin in controlling variceal haemorrhage. They state that "the initial reports were good but have not been confirmed, and the long acting analogue is of doubtful usefulness in treating either bleeding peptic ulcer or bleeding varices." Though studies of the efficacy of somatostatin in controlling haemorrhage from peptic ulceration have produced conflicting results, this is not the case with bleeding oesophageal varices. Thus control of bleeding was achieved in 47 of the 62 episodes of variceal haemorrhage treated with somatostatin in the three published randomised controlled clinical trials, a success rate of 74%.<sup>1,3</sup> Such an outcome compares favourably with that achieved with vasopressin, which in the 13 randomised control trials reported to date has controlled bleeding in 122 out of 238 (51%) episodes of bleeding.<sup>4</sup> Moreover, no major complications have been associated with the use of somatostatin to control variceal haemorrhage, in contrast to vasopressin, which, at the dosages used to control variceal haemorrhage, may produce serious, and sometimes fatal, side effects in about 15-25% of patients. Therefore at present the evidence suggests that somatostatin is safer and more effective than vasopressin for the control of acute variceal haemorrhage.

There is little doubt that injection sclerotherapy is currently the treatment of choice for the control of acute variceal haemorrhage, bleeding being controlled in about 85-95% of patients presenting for treatment. The facilities for injection sclerotherapy, however, are not always available at the admitting hospital, and there may be no one present with the skill to inject a copiously bleeding varix. Consequently, there is a need for a stop gap treatment that is safe and effective and can be instituted rapidly without the need for special skills. As balloon tamponade of the oesophagus may be associated with a prohibitively high complication rate and requires skilled use, we believe that such circumstances necessitate a safe pharmacological agent to control bleeding. Evidence suggests that somatostatin is effective for this purpose. Clearly, however, further prospective randomised trials are required to confirm the role of somatostatin, and possibly its analogues, in controlling acute variceal haemorrhage.

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### Abuse of fresh frozen plasma

SIR,—I agree wholeheartedly with Dr Jennifer Jones about the abuse of fresh frozen plasma (1 August, p 287), but she does not discuss its use in the special care baby unit, where it has been recommended for premature infants who are at

risk from intraventricular haemorrhage and who commonly have a haemostatic defect which may contribute to their death.<sup>1,6</sup>

Over two years we identified 21 premature infants (gestational age 29 weeks, range 25-32 weeks) with abnormal clotting on the first day of life (international normalised ratio greater than 2.0, kaolin-cephalin clotting time ratio greater than 2.0). Fifteen babies with abnormal clotting received fresh frozen plasma in a dose of 10 ml/kg and had a repeat clotting sample tested within 24 hours. In all the clotting ratios were normal. The mean reduction in international normalised ratio was 0.7 (range 0.2-1.5) and mean reduction in kaolin-cephalin clotting time ratio was 1.6 (range 0.6-4.5).

During the period of study seven babies were found at necropsy to have substantial intraventricular haemorrhage. Of these, two babies with abnormal clotting ratios (international normalised ratio 1.9 and 3.2, clotting time ratio 6.0 and 6.0) had received fresh frozen plasma while five babies with normal clotting ratios had not received fresh frozen plasma.

Thus, although we are confident that we can correct the haemostatic defect with fresh frozen plasma, we have no evidence that this can save lives.

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### Rapid resolution of signs of primary intracerebral haemorrhage in computed tomograms of the brain

SIR,—I cannot agree with the uncritical dismissal by Dr M S Dennis and colleagues of magnetic resonance imaging in the investigation of stroke (8 August, p 379). They are also mistaken in their belief that it is the T<sub>2</sub> relaxation time which distinguishes subacute haemorrhage from infarction and cite early work which did not compare haemorrhage and infarction but dealt with a small heterogeneous collection of intracranial haemorrhages imaged at different times on a low resolution prototype 0.147 tesla resistive system.

Numerous clinical studies have documented the superiority of magnetic resonance imaging over computed tomography in detecting cerebral infarcts.<sup>1,3</sup> These changes in ischaemic brain are shown earlier on magnetic resonance imaging than computed tomography,<sup>4</sup> because small increases in tissue water insufficient to change x ray attenuation coefficients are shown by a prolongation of the magnetic relaxation time. This gives a typical hyperintense signal on a T<sub>2</sub> weighted image and an isointense or hypointense signal on a T<sub>1</sub> weighted image.

Although more noticeable on high field than on