four patients with liver cirrhosis, in which a renal impairment is often present. After administration of osmotic agents (mannitol, dextran)⁷ or radiological contrast media⁸ the increase of urinary enzyme and protein excretion is more evident in patients with chronic renal diseases than in subjects with normal renal function.

We conclude that the urinary excretion of α -glucosidase and probably of other renal glucosidases is not influenced in normal subjects by the induction of a diuresis and may be considered a reliable and sensitive index of tubular damage after drug administration. In patients with underlying liver or renal diseases, however, the possible administration of diuretic agents must be taken into account before drawing any conclusion. One must be cautious in normal subjects too when determining enzyme or protein indexes of tubular proteinuria such as lysozyme and β_2 -microglobulin. Conversely, the determination of tubular enzyme excretion after induction of a diuresis (chiefly after an osmotic load) might be used as a sensitive test of underlying renal diseases, as suggested also by Burchardt *et al.*⁷

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⁴ Ceriotti, G, and Guarnieri, G F, *Proceedings of the Sixth International Symposium on Clinical Enzymology*. Milan, Kurtis, 1974.

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Vaginal microbial flora in normal young women

SIR,—I was interested to read the careful study of vaginal microbial flora in normal young women in Edinburgh (2 June, p 450) but feel that it may not fully reflect the situation in all parts of Britain.

In particular, I feel that *Trichomonas vaginalis* is, at least in Cleveland, a more frequent pathogen than the Edinburgh study suggests. Analysis of the findings in 1000 cervical smears received consecutively by this laboratory in January and February this year from family planning clinics shows that *Trichomonas vaginalis* was positively identified (by at least two observers) in 70 (7%). In addition, cytological features suggesting trichomonas infestation were present in a further 61 in which the parasite could not be identified with certainty. Inflammatory changes were present in all but three of those 131 smears and vaginal discharge was recorded on the accompanying request form in 107 (82%). By contrast, *Candida* organisms were identified in only 24 of the 1000 smears, though cytological features suggestive of candidiasis were seen in a further 12. Comparison with a similar study made in 1969 showed that the findings are relatively constant in this area.

While I admit that a cervical smear is an inferior technique to culture in demonstrating vaginal candidiasis, there is no doubt that examination of a smear is an effective way to demonstrate trichomonas infestation and that

this pathogen is a major cause of vaginal discharge. Though there clearly may be differences in selecting the patients studied here and in Edinburgh, it is difficult to account for the different frequency of *Trichomonas vaginalis* in cervical smears in Cleveland (at least 7.0%) and Edinburgh (1.2%) except by postulating a difference in prevalence. It would be of interest to know the position in other parts of Britain.

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Uterine rupture after intra-amniotic injection of prostaglandin E₂

SIR,—We wish to report a case of uterine rupture following intra-amniotic injection of prostaglandin E₂ and hypertonic saline in order to induce abortion.

The patient, aged 39 years, had had three previous vaginal deliveries and requested abortion at the 20th week of pregnancy. This was induced by an eventful transabdominal amniotic injection of 5 mg prostaglandin E₂ and 100 ml of 30% hypertonic saline following the removal of 150 ml of clear liquor. Contractions commenced after four hours but after 11 hours the patient developed continuous lower abdominal pain and a pulse rate of 120 beats per minute. Abdominal examination revealed a tender suprapubic mass, equivalent to a 16-week gestation and a separate firm mass, 8 cm in diameter, in the right hypochondrium. A diagnosis of ruptured uterus was made and at laparotomy there was a rupture at the junction of the upper and lower segments involving the anterior wall and both lateral walls of the uterus. The intact gestation sac was bulging through the deficit. Total abdominal hysterectomy was performed and the postoperative course was uneventful. The cervix was normal.

This is the first reported case of uterine rupture following mid-trimester termination of pregnancy with prostaglandin E₂ and hypertonic saline, although one case has been reported following intra-amniotic injection of prostaglandin F₂ and hypertonic saline.¹ Cervicovaginal fistula, however, has been reported following 1% of terminations induced using intra-amniotic prostaglandin.² We report this case in order to draw attention to an unusual complication which must be taken into account when choosing a method of terminating a pregnancy in the mid-trimester.

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¹ Borten, M, and Friedman, E, *Prostaglandins*, 1978, 15, 187.

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An open-access morbid pathology facility for GPs?

SIR,—Family doctors have often received a rap over the knuckles for inaccurate certification of death. We are as interested as are any of our colleagues in knowing why patients die, but we are often prevented from finding out.

An elderly patient dies at home after an illness in which investigation by open-access pathology requests, consultant domiciliary consultation, or a period of inpatients or out-patient surveillance has produced a variety of possible pathological diagnoses. Age, frailty, and humane considerations have precluded

further probing. The obvious need, then, is for a postmortem examination. The only way that this can be procured is by reference to the coroner and then only at his discretion. This cumbersome procedure is quite inappropriate where there is no question of foul play, where the final mode of death (but not the antecedent condition) is obvious, and where a visit from a police officer, however kindly, is an ordeal for the relatives. How many doctors can honestly say that they have not certified deaths as being due to, for example, bronchopneumonia, while knowing that a deeper cause for that has not been uncovered?

There is a clear need for an open-access morbid pathology facility for general practitioners. We should all be humbled, but enlightened, by this; and our patients would stand to gain.

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Enterotoxigenic *Escherichia coli* and travellers' diarrhoea

SIR,—Mr R J Gross and others (2 June, p 1463) reported that they isolated enterotoxigenic *Escherichia coli* (ETEC) from the faeces of 6/55 (11%) patients who developed diarrhoea during or shortly after travel abroad, and also from 1/50 (2%) patients with diarrhoea but no history of recent travel outside the UK. We have been conducting similar studies in Manchester and wish to report our confirmatory results.

We tested the toxigenicity of five colonies of *Escherichia coli* isolated from the faeces of each of 13 cases of diarrhoea in travellers returning to the Manchester area from abroad, and also in a control group of 13 patients who developed diarrhoea at about the same time but gave no history of recent travel. A group of 13 babies with diarrhoea admitted to Wythenshawe Hospital, South Manchester, were also included in this survey. In an earlier study we examined 210 strains of "specific" *E coli* isolated from cases of infantile diarrhoea by various hospital laboratories in the north-west. Heat-labile enterotoxin was detected by the Chinese hamster ovary cell assay¹ and heat-stable enterotoxin by the infant mouse gut test.² All toxigenic strains isolated were tested serologically using *E coli* O-agglutinating antisera (Wellcome) and then sent to Dr B Rowe of the Central Public Health Laboratory, Colindale, London, for further serotyping.

Our results show that 6/13 (46%) of travellers with diarrhoea were infected with ETEC, each of a different serotype. None of the control group yielded ETEC. All 13 infants from Wythenshawe Hospital were clear of ETEC. Furthermore, all the strains (210) of specific *E coli* from cases of infantile diarrhoea in the north-west were non-toxicogenic.

While confirming the conclusions drawn by Mr Gross and his colleagues, our results show a significantly higher isolation rate of ETEC from travellers with diarrhoea than their results. We note, however, that, whereas they examined only one or sometimes two "cultures" (*sic*) from each patient, we have been routinely screening five colonies of *E coli* from each patient. We feel that this may account for our higher isolation rate. We also find that in the north-west of England ETEC do not appear to be a significant cause of sporadic diarrhoea in infants or adults; this is in agreement with the results of Gross *et al* and other workers in the United States³ and Sweden.⁴

Finally, it is necessary to report that not all the toxigenic strains of *E coli* we isolated from

cases of travellers' diarrhoea belonged to serogroups previously associated with infantile gastroenteritis. Indeed, one of our toxigenic strains could not be typed at all. Therefore in screening for ETEC in travellers with diarrhoea not associated with *Salmonella* and *Shigella* we feel that it is important to underline the need to test several colonies of *E. coli* isolated from the primary culture, regardless of serotype.

Full details of this work will be published separately.

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¹ Guerrant, R L, *et al*, *New England Journal of Medicine*, 1975, **293**, 567.

² Dean, A G, *et al*, *Journal of Infectious Diseases*, 1972, **125**, 407.

³ Echeverria, P, Blacklow, N R, and Smith, D H, *Lancet*, 1975, **2**, 1113.

⁴ Bach, E, Blomberg, S, and Wadstrom, T, *Infection*, 1977, **5**, 2.

Pituitary suppression in chronic airways disease?

SIR,—We were interested to read the letter "Pituitary suppression in chronic airways disease?" by Dr Pd'A Semple and others (19 May, p 1356). We have been assessing pituitary function in our patients with radiological changes in the pituitary fossa,¹ including also a further group of male hypercapnic patients.

Preliminary results show that in two-thirds of the patients a subnormal serum testosterone level was associated with low or normal levels of serum luteinising hormone (LH) and follicle-stimulating hormone (FSH). Moreover, in these patients the LH response to an intravenous injection of 100 µg of gonadotrophin-releasing hormone was impaired, supporting the suggestion of Dr Semple and his colleagues that abnormal hypothalamic-pituitary function is present in these patients. Basal thyroid-stimulating hormone (TSH) levels and TSH responses to thyrotrophin-releasing hormone were normal.

Thus evidence is mounting of endocrine dysfunction mainly involving hypothalamic-pituitary-gonadal function in these patients, for which there may be a therapeutic dividend.

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¹ Newton, D A G, Bone, I, and Bonsor, G, *Thorax*, 1978, **33**, 684.

A luxury drug?

SIR,—Some issues of the *BMJ* have carried treble-page colour spreads advertising Timoptol. Never in my 40 years of ophthalmology have we been exposed to such a barrage of salesmanship. Yet from none of the representatives and copious brochures, the various glaucoma symposia subsidised by the manufacturers, or the reports from radio and television and the national and medical press has there been any mention of the one major non-asset, its enormous price.

The manufacturers deserve particular re-

proof for directing their publicity unabashedly at the layman, so that we oculists are now being constantly assailed by patients demanding the new wonder treatment, which they or their friends have all seen, heard, or read about (a little blame, too, to the media for conniving at the propaganda).

We appreciate that research is always costly, but beta-blockers are not so expensive to prepare, particularly in such tiny quantities; yet the cost of Timoptol, even at its cut-rate for NHS hospitals, is about 25 times that of the pilocarpine we use (£5 for a 5 ml bottle compared with about 20p). It was reckoned by the pharmacist of one major eye hospital that, if all our glaucoma patients were changed over from pilocarpine to Timoptol, this would swallow up well over half of our entire annual drug budget. The loss to the taxpayers would be vast, given that there are around a quarter of a million people with glaucoma in the UK.

Timoptol has indeed advantages over pilocarpine in certain cases; it is sad that, if we are to remain solvent, so few will be able to afford this luxury. If only the manufacturers could have spent less flamboyantly on all that advertising, and charged us a little less for those few drops.

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Heatstroke in a "run for fun"

SIR,—In his letter (20 January, p 197) Dr Tom Bassler describes four cases of death in marathon runners, each of which he ascribes to heatstroke. We would like to point out that in none of these cases is there sufficient evidence to implicate heatstroke as the primary diagnosis, although as three of these athletes died during prolonged exercise the possibility that an elevated body temperature, in contradistinction to heatstroke, may have played some role cannot be excluded.

The first case, reported in detail by Green *et al*,¹ was that of a 44-year-old runner who collapsed, pulseless and apnoeic, after running 24 miles of the 1973 Boston marathon. Cardiopulmonary resuscitation was instituted. On admission to hospital the patient was in ventricular fibrillation and his rectal temperature was 38.4°C, features which are both inconsistent with a diagnosis of heatstroke. In five large series²⁻⁶ of exertion-related heatstroke, involving 297 patients, there was not one reported case of ventricular fibrillation or of cardiac arrest. To support a diagnosis of heatstroke in the patient of Green *et al* there would have to be an explanation of why the rectal temperature on hospital admission was only 38.4°C. In a group of 30 heatstroke victims, a mean rectal temperature of 41.2°C was recorded even half an hour to two hours after the initial collapse.⁵ Thus the combination of ventricular fibrillation and a low rectal temperature makes a diagnosis of heatstroke untenable unless further information is forthcoming.

Because sudden death due either to ventricular fibrillation or to cardiac arrest is not a feature of heatstroke, it also follows that heatstroke was not the cause of death in two of the other three cases of death among our South African marathon runners—a 19-year-old athlete who died suddenly during a marathon race and a 47-year-old who collapsed and died in sight of the finish of an eight-mile mountain race. The fourth case, that of a 35-year-old highly trained athlete, has been fully reported,⁷ yet Bassler fails to report all the clinical features. For the benefit of your readers, we would like to restate what we consider to be significant features of this case.

A 35-year-old athlete developed chest pain or pain between the shoulder blades or both on six of eleven runs in January 1974. The pain was severe

enough to force him to stop running on a number of occasions. He did not run on the day of his death, choosing rather to go surfing. However, while surfing he became "too breathless" to continue. He left the water and drove home, but within the hour he developed severe precordial chest pain. He was driven to his physician, who referred him to hospital. During the car ride he complained that his chest pain was now worse and that his left hand felt paralysed. He died shortly after admission to hospital. The electrocardiogram showed ST depression in leads 2, 3, and AVF. In the absence of a necropsy, ischaemic heart disease as the cause of death seems likely but cannot be proved. However, on the basis of the clinical history, heatstroke can absolutely be excluded as a diagnostic possibility.

We agree with Dr Bassler that heatstroke is a menace in long-distance running and we did in fact first draw attention to this as early as 1973.⁸ By incorrectly attributing all cases of exertional collapse in marathon runners to heatstroke Dr Bassler is not, as he claims, increasing the safety of this sport, because he ignores the dangers imposed by other conditions such as coronary heart disease and hypertrophic cardiomyopathy, both of which occur in marathon runners.^{7, 9, 10}

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¹ Green, L H, Cohen, S I, and Kurland, G, *Annals of Internal Medicine*, 1976, **84**, 704.

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⁵ Shibolet, S, *et al*, *Quarterly Journal of Medicine*, 1967, **36**, 525.

⁶ Costrini, A M, *et al*, *American Journal of Medicine*, 1979, **66**, 296.

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NHS security beds

SIR,—Your leading article on Butler-type regional security units (16 June, p 1585) has given encouragement to those of us who publically opposed the setting up of these units, and who favoured instead the concept of the "simple staff-intensive units."

Mr S Quinn, nursing officer of the Lyndhurst Unit at Knowle Hospital, Fareham (the first and, so far as I know, the only open-door, simple staff-intensive unit in existence), discussing the efficacy of the unit, has said, "...inquiries in February indicated that virtually no patients with mental illness were going to prison in Wessex who should certainly be in a hospital. There are none at present, to our knowledge, being held up in special hospitals for want of a bed in Wessex. Regional health authorities are no longer receiving complaints that beds cannot be found for those difficult mentally ill patients, though there is still a problem with the subnormal patients."

If this is the case, what a tragedy that such specialist open-door forensic units were not set up many years ago—a tragedy both in terms of the suffering of the patients waiting for transfer in grossly overcrowded Broadmoor and also in terms of the harm done to relationships between those working in the special