were undergoing endoscopy for clinical reasons. These patients were of similar age distribution to the study group (their mean age was 61). No patient had active ulceration at the time of endoscopy. The question is, therefore, whether or not it is ethical to do gastric biopsies on patients with previous duodenal ulceration during routine endoscopies to look for premalignant lesions or early gastric cancer.

At the outset it was unknown whether mucosal abnormalities in patients who had had operations were due to the surgery, in which case they would be commoner in the study group, or to the underlying ulcer diathesis, in which case they would be equally common in each group. Although our hypothesis was that the abnormalities were the result of the surgery, there were theoretical reasons for suspecting the underlying ulcer diathesis. Patients with duodenal ulcers have a high incidence of antral gastritis,¹ which may be a first stage of more serious mucosal changes.^{2,3} Ellis *et al* found that over 8% of patients with gastric cancer had previously proved or probable duodenal ulceration treated by medical means only.⁴ It is our opinion that if it was ethical to do gastric biopsies on patients who had operations for duodenal ulcers it was also ethical to take them on patients with duodenal ulcers but who had not had operations, in the absence of any data to show that the latter were not at risk from developing gastric cancer. If it were ethical to do biopsies only on patients proved to be at high risk it would then be impossible to identify high risk groups in the first instance. We cannot accept that our study becomes unethical in retrospect because one of the groups studied had less mucosal abnormality than the other.

The risk of doing biopsies during gastroscopy appears to be very small. Colin-Jones *et al* discussed complications in a review of endoscopic practice in the UK and did not mention the problem.⁵ A survey carried out by the American Society of Gastrointestinal Endoscopy⁶ reported one death from haemorrhage after biopsy in 211 410 endoscopies.⁶ The incidence of death from gastric cancer in Northern Ireland in the 55-64 age group was 42 per 100 000 in 1979.⁷ These figures cannot be directly compared, but they suggest that the benefit of doing biopsies during routine endoscopy to look for early gastric cancer far outweighs the risk of the biopsy procedure.

The number of biopsies done in our study was generally less than in comparable studies referred to in our paper. Schrupf *et al* usually took 20; they emphasised the importance of multiple biopsies as serious mucosal lesions may be patchy and not appreciated macroscopically at endoscopy.⁸ Other authors have studied gastric biopsy specimens from normal individuals⁹ and from patients with duodenal ulcers who had not had operations.¹ We had no complications after endoscopy in any of our patients, and we intend to follow up patients with appreciable mucosal change from either group.

The fact that a control group would be subject to biopsy was clearly stated in the protocol submitted to our ethical committee. The chairman of our ethical committee has seen Mr Hugh's letter and has written confirming that "The committee considered the protocol to describe a research project that was ethical."

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¹ Johnston DH. Blind gastric and duodenal mucosal biopsies in patients with duodenal ulcer and those with an ulcer like syndrome. *South Med J* 1964;57:79-84.

² Correa P. Precursors of gastric and esophageal cancer. *Cancer* 1982;50:2554-65.

³ Morson BC, Dawson IMP. *Gastrointestinal pathology*. Oxford: Blackwell, 1979:108.

⁴ Ellis DJ, Kingston RD, Brookes VS, Waterhouse JAH. Gastric carcinoma and previous peptic ulceration. *Br J Surg* 1979;66:117-9.

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⁷ Registrar General for Northern Ireland. *Annual report 1979*. Belfast: HMSO, 1980.

⁸ Schrupf E, Stadas J, Myren J, Serck Hanssen A, Aune S, Osnes M. Mucosal changes in the gastric stump 20-25 years after partial gastrectomy. *Lancet* 1977;ii:467-9.

⁹ Siurala M, Isokoski M, Varis K, Kekki M. Prevalence of gastritis in a rural population. Biopsic study of subjects selected at random. *Scand J Gastroenterol* 1968;3:211-23.

Boxers' brains

SIR,—As Scrutator observes (17 March, p 872), the media and the BMA have placed great emphasis on the refusal of the British Board of Boxing Control to cooperate with the BMA's working party on boxing (17 March, p 876). As the chief medical officer to the board there are several points I want to make about the report.

We informed the BMA before it started that without our cooperation the report would be useless in regard to modern professional boxing. We suggested an independent inquiry, but we were ignored. We suggested rescinding the original ARM decision and starting again, and again we were ignored.

The report is by necessity partly a study of amateur boxing today, partly a study of boxing in Europe, America, and elsewhere, and partly a study of professional boxing in the past when the medical care was by our present standards not as efficient.

At least one, and possibly two, members of the BMA working party had already published studies on boxers and may well, therefore, not have had an open mind.

In the past we always cooperated completely in any survey in professional boxing as Professor J A N Corsellis, a member of the working party, and Dr A Roberts, author of the Royal College of Physicians' report on boxing, will confirm.

The BMA released the report to lay and professional media on 5 March, but we did not receive our copy until seven days later. I think that out of common courtesy it should have released the report to professional colleagues.

Finally, I must take issue with the work done on eye injuries. This could not by any stretch of the imagination be considered a scientific study, and any deductions are irrelevant. To rely on a specialist's recollection whether a patient with a detached retina was or was not a boxer and then to draw conclusions is totally unscientific. I would like to see these cases reported to an independent ophthalmologist and the board would guarantee to match up the professional boxer—then and only then could any conclusions be made.

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SIR,—All boxers, amateur and professional, know that there is a risk of injury in the sport, but all go into the ring voluntarily. The BMA working party fails to recognise the beneficial effects of boxing—that is, the high standard of physical fitness attained and required, the personal discipline, the art of self defence attained, the brotherhood and concern shown by boxers for each other, and the expression of

aggression under strict control by many healthy young men.

The numbers of deaths and serious injuries in the sport in this country and even worldwide are minute, particularly when compared with other sports—such as mountaineering, skiing, rugby, horse riding and racing, swimming and boating (especially round our shores), hang gliding, motor racing, and motorcycling. Perhaps the BMA should campaign for abolition of all these activities.

Many people condemn boxing because they say it is the only sport in which one competitor deliberately tries to disable another. But I suggest that all a boxer intends when he enters the ring is to win his contest and to protect himself from injury. For this he requires and frequently displays great strength, speed, stamina, skill, determination, discipline, self control, and courage.

As a spectator I admire all boxers, and as a doctor I do my best to protect and treat them should accidents occur—in exactly the same way as I do for footballers.

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The heroin problem

SIR,—Dr P H Connell and Dr M Mitcheson describe how London drug clinics deal with their patients (10 March, p 767). This article was accepted two months later than the average in the same issue—thus revealing an admirable sense of priority and an acknowledgment of the importance of heroin addiction.

But if we had an epidemic of, say, tuberculosis increasing by 30-40% annually and the medical establishment was to issue a description of chest clinic procedure without pointing out that they were seeing only 5% or less of cases; that many of these were being reinfected even while attending the clinic; that huge numbers of cases were refusing to go to the clinics; that no measures were being taken to attract and treat these cases; and no encouragement was being given to the rest of the profession to help or become involved—not even a small fee for notifying cases—then I wonder whether the *BMJ* would publish it so readily—at least not without a swingeing accompanying leading article.

Yet this is the problem in heroin addiction today.

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Genital wart virus infections: nuisance or potentially lethal?

SIR,—Your leading article (10 March, p 735) amply reviews the background to the increasing worry about the possible oncogenic nature of genital wart virus. The genitourinary physician is as likely as the gynaecologist to be faced with cytological smears showing warty changes. Genital warts occur in a high percentage of patients treated at sexually transmitted diseases clinics—17 930 men and 10 246 women were treated in 1980, which represents a 15% increase over 1979.¹

One vital point is omitted in the reasons given for destroying cervical lesions showing warty changes. The wart virus is sexually

transmissible and failure to eradicate it from the cervix will expose the male partner to risk. It may be that in time increases in penile cancer will also become evident—with the wart virus as the prime suspect.

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¹ Chief Medical Officer. Sexually transmitted diseases: extract from the annual report of the Chief Medical Officer of the Department of Health and Social Security for the year 1981. *Br J Vener Dis* 1983;59: 206-10.

SIR,—Most genital and extragenital warts undergo spontaneous resolution (10 March, p 735). Cervical human papillomavirus infection is usually discovered only in patients with cytological abnormality referred for colposcopic assessment. As most of these patients are subsequently treated for an associated dysplastic lesion, the natural progression of human papillomavirus infection has not been studied. A recent study in the Birmingham and Midland Hospital for Women showed that of 48 women referred for evaluation of abnormal cytology with cervical human papillomavirus infection without associated cervical intraepithelial neoplasia 27 (56%) showed no cytological or colposcopic abnormalities after a median follow up of 10 months. This suggests that cervical human papillomavirus infection is often self limiting and with resolution of the viral infection cytological, colposcopic, and histological abnormalities may regress.

Alternatively, incorporation of the viral genome into metaplastic cells may produce an irreversible progression of dysplastic change making it imperative to treat these lesions whenever found. Dr Albert Singer and others cite the excellent results achieved with local destructive techniques in the treatment of cervical intraepithelial neoplasia. This is based on the premise that all histologically abnormal epithelium can be identified by colposcopic assessment, but this assumption may be invalid in human papillomavirus infection of the cervix. Colposcopically normal mature squamous epithelium may harbour sufficient quantities of the viral genome to maintain a productive infection after destruction of all colposcopically atypical epithelium. In addition the human papillomavirus genome may be sequestered in tissue below the depth of destruction normally achieved by local destructive treatment. A controlled study of the use of local destructive techniques in the management of cervical human papillomavirus infection is needed.

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ABC of sexually transmitted diseases

SIR,—Dr E M C Dunlop (25 February, p 641) worries too much about the aptness of the term "genitourinary medicine" to describe our specialty. I agree with him that it is not perfect but it is immeasurably better than the titles venereology or venerological medicine. To the man in the street venereology or venereal disease means something to do with syphilis or gonorrhoea. As these illnesses now account for less than 16% of the patients seen in the clinics, it seems unkind to add to

patients' fears no matter how illogical this may seem to doctors.

In 1970 in response to a letter about the difficulty in recruitment to venereology, I wrote, "To my mind there is no simple, single measure which could do so much for the status of the specialty and for the well-being of the majority of our patients as a change of name, such as that suggested in your leading article of 21 February, p 447."¹ The success of the term genitourinary medicine may be measured by the fact that today three quarters of clinics have adopted this title.

Finally, I agree with him that one of our major tasks is to control sexually transmitted disease, and I think the figures show that compared with many other countries we do a most effective job. Reviewing the past five working days during which I conducted 10 clinic outpatient sessions in two separate hospitals, only 40% of my work was connected with venereal disease and sexually transmitted diseases. The problems in any clinic will depend to some extent on the population it serves and the interests of the doctors working there, but I do not think my experience is particularly unusual.

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¹ Oates JK. Recruits for venereology. *Br Med J* 1970; ii:296.

"Third drug" trial

SIR,—A major part of the analysis by Dr D McAreevey and others (14 January, p 106) relied on the comparison of reductions in systolic blood pressure for the patients who successfully completed treatment with a third drug. The reduction in blood pressure was defined as the difference between the blood pressure at the end of a run in period (which had to be greater than 140/95 mm Hg) and that at the end of the third drug phase. A target of less than 140/95 mm Hg was set, and dosage schedules were manipulated to try to achieve this.

Although it is not as certain as Dr McAreevey and colleagues suggest, even fixed dose anti-hypertensive treatment may achieve greater reductions in blood pressure for those with initially higher pressures. The authors seem unaware, however, of two other reasons why the reduction achieved is likely to be greatest for those with initially highest pressures: the attempt to achieve target pressures and the effect of regression to the mean. The effect of regression to the mean has been discussed often,¹ notably in relation to blood pressure.² The authors' analysis entailed regressing systolic blood pressure reduction on initial systolic blood pressure, but a positive correlation is to be expected between reduction in blood pressure and initial value even for ineffective treatment, which is why such analyses are strongly discouraged.³ Furthermore, their figure showed only the fitted regression lines and not the widely ranging data values, and the fact that the low average initial systolic blood pressure of those successfully completing the minoxidil regimen was off the edge of their figure was obscured. The average reduction in lying blood pressure for the minoxidil group was similar or even less than that for the other four active regimens studied; this is not evident from their figure. A large proportion of subjects were unable to complete their regimens (through side effects and so on), ranging from 30% to 78% for the different active drug groups. An analysis restricted to those who completed the study should lead to only tentative conclusions.

The authors' assertion that minoxidil was more potent than all other agents is not justified.

The statistical methods used in other parts of the paper were not identified. In particular, it is not clear whether appropriate allowance was made in the quoted significance levels for the multiple comparison of pairs out of the five active drugs. It is well known that the naive multiple testing of pairs of differences between a number of groups gives exaggerated significance levels. Testing each pair of active drugs at a nominal 5% significance level yields a false positive rate of 40%.

A test of efficacy of such drug regimens should be based on all the patients randomly allocated to each regimen, and not just on the patients successfully completing the course. Because so many patients were withdrawn, it seems inappropriate to use the reduction in blood pressure as a criterion, and we would recommend the comparison of the proportion of patients responding—that is, not being withdrawn, and attaining targets of blood pressure reduction—among the five active drug groups. This analysis is not affected by regression to the mean, and the appropriate χ^2 test based on the authors' figures yields $\chi^2 = 3.73$, $p = 0.44$. Thus there is no evidence to reject the hypothesis of equal efficacy of the five active drugs. This analysis does not directly weight the severity of side effects, which of course have to be discussed explicitly.

The strongly asserted conclusions given by Dr McAreevey and colleagues are thus unsupported when the results are examined closely.

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¹ Oldham PD. A note on the analysis of repeated measurements on the same subjects. *J Chronic Dis* 1962;15:969-77.

² Shepard DS, Finison LJ. Blood pressure reductions: correcting for regression to the mean. *Prev Med* 1983;12:304-17.

³ Altman DG, Gore SM, Gardner MJ, Pocock SJ. Statistical guidelines for contributors to medical journals. *Br Med J* 1983;286:1489-93.

*.*The authors reply below.—Ed, *BMJ*.

SIR,—Mr D G Altman and Mr S G Thompson criticise, firstly, the use of regression analysis to compare different drug regimens and the figure illustrating this.

Having fitted, separately for each regimen, a regression of reduction in blood pressure on initial blood pressure, we compared expected reductions for a given initial pressure. For instance, for an initial lying systolic blood pressure of 180 mm Hg minoxidil was significantly more hypotensive than any of the other regimens. For an initial pressure of 160 mm Hg minoxidil was significantly more hypotensive than prazosin, hydralazine, or placebo. Initial pressure is a classic concomitant variable¹; the fact that it is correlated with reduction in pressure, whether the regimen is effective or not, is the very reason for including initial pressure in the analysis. The precise explanation of the correlation between reduction and initial pressure is irrelevant to the statistical comparison of regimens, provided that initial pressure is not itself affected by that regimen. The inference by Mr Altman and Mr Thompson that we are unaware of reasons for the correlation is incorrect. In our trial, initial pressure was measured before a patient started taking the third drug. Mr Altman and Mr Thompson appear to favour a comparison of average reductions ignoring initial values. This is obviously more sensitive than merely comparing average final pressures, and the reason for the