of Otago Act of 1961 gave autonomy back to the University of Otago, which it had lost to the University of New Zealand in 1869. The MB ChB(Otago) dates from 1962. Professor Morrell describes how "the university celebrated its recovered autonomy by a degree-giving ceremony on 27 July 1962," not, as stated by Dr Hocken, in 1972.²

In the last paragraph of the first column on p 325 Dr Hocken says that "the first 120 students from the self-sufficient school at Auckland graduated in 1974." It was on 23 November 1973 that 40 students graduated from an initial intake of 60 students.³

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¹ *New Zealand Medical Journal*, 1968, **68**, 186.

² Morrell, W P, *The University of Otago—A Centennial History*, pp 194 and 223. University of Otago Press, 1969.

³ *New Zealand Medical Journal*, 1973, **78**, 543.

Oral hyoscine butylbromide for irritable bowel syndrome?

SIR,—Drs J A Ritchie and S C Truelove (10 February, p 376) report an elegantly designed trial of lorazepam, hyoscine butylbromide, and ispaghula husk in the irritable bowel syndrome. This syndrome is difficult to study, but we were surprised that hyoscine butylbromide was one of the drugs chosen, because there is good evidence^{1,2} that this drug is very poorly absorbed and therefore inactive by mouth, although it relieves gastrointestinal spasm when given parenterally. The authors' conclusions therefore seem questionable. We would suggest that any improvement their patients may have derived from the treatment must have been due to the ispaghula and possibly lorazepam, but not to the hyoscine butylbromide.

It is reassuring that the results of therapy with the "real" and "dummy" anticholinergic tablets (their table I) did not differ significantly, as both groups of patients in effect received a placebo. The results of treatment with different combinations (table II) do not support the authors' interpretations. Although the patients given ispaghula with hyoscine butylbromide and those who had all the three treatments did much better than the placebo group, neither did significantly better than the group given only ispaghula.

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¹ Herxheimer, A, and Haefeli, L, *Lancet*, 1966, **2**, 418.

² Beerman, B, et al, *European Journal of Clinical Pharmacology*, 1972, **5**, 87.

SIR,—Drs J A Ritchie and S C Truelove are to be congratulated on their use of a factorial design in their trial on the treatment of irritable bowel syndrome (10 February, p 376). They conclude that each of the three agents studied is more effective than its corresponding placebo, that a combination of two agents is better than a single agent, and also that the use of all three agents together is better than any two. They based these conclusions on their findings that the triple placebo gave no

successes in 12 patients, the single agents gave either 4 or 5 successes in 12 patients, the two-agent combinations gave 5 or 6 successes in 12, and all three agents combined gave 7 successes in 12 patients.

Three points ought to be made about how the authors have interpreted these results. Firstly, although it can be concluded that most of the active treatments did significantly better than the placebo, none of the differences among the active treatments, singly or in combination, are anywhere near to being statistically significant. It is therefore invalid to claim superiority for two agents over one, or three over two. Secondly, the small sizes of the treatment groups do not allow us to be at all precise about the "true" level of efficacy of any of the treatments studied. For example, although the apparently best treatment—all three agents used in combination—gave 7 successes in 12 patients, a response rate of 58%, this only allows us to be 95% confident that the "true" response rate is somewhere between 31% and 81%. It would also be unwise to conclude that the placebo response rate really is zero, 0 successes in 12 patients merely allowing us to be 95% sure that the "true" placebo response rate is 25% or less.

Finally, although this study does not provide useful data from which we can judge the merits of the various treatment options, it would seem rational none the less to use the form of treatment which at least appears to be the most effective—namely, all three agents in combination. However, as, a priori, fewer agents are always preferable to more, the costs and risks of using three agents must be set against the weakness of the evidence in favour of this option. What these costs and risks are, a statistician, must leave for others to judge.

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SIR,—The choice by Drs J A Ritchie and S C Truelove (10 February, p 376) of oral hyoscine butylbromide as an antispasmodic because of its effectiveness in a similar dose intravenously was unfortunate. Early work with this drug indicated very slight absorption from the gastrointestinal tract.¹ Further studies using the labelled compound have confirmed that it is taken up very poorly throughout the gut.² Even when given parenterally, it causes effects of very short duration³ and this makes it unsuitable for long-term use. The controversial reports about the spasmolytic effects of oral hyoscine butylbromide² illustrate the difficulties in evaluating clinical trials with these types of drugs, and it would seem of great importance to study first the gastrointestinal absorption for each substance recommended for oral use.

D GIBBONS

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¹ Herxheimer, A, and Hafeeli, L, *Lancet*, 1966, **2**, 418.
² Helström, K, Rosén, A, and Söderlund, K, *Scandinavian Journal of Gastroenterology*, 1970, **5**, 585.

³ Möller, J, and Rosén, A, *Acta Medica Scandinavica*, 1968, **184**, 201.

Benzodiazepine pharmacokinetics

SIR,—Though I appreciate that one of the reasons for using lorazepam as a tranquilliser was the availability of matched placebos in the

excellent trial by Drs J A Ritchie and S C Truelove (10 February, p 376), I would disagree with the statement "Lorazepam has a longer duration of action than other benzodiazepines. . ."

Lorazepam possesses an elimination half life of about 12 hours and has no pharmacologically active metabolites.¹ Twice-daily dosing would therefore maintain fairly stable steady state plasma concentrations. Diazepam and its major active metabolite desmethyldiazepam have elimination half lives of over 24 hours,² and clinical effectiveness would therefore be expected after once-daily dosing with diazepam. Potassium clorazepate is marketed as a once-a-day tranquilliser. It is hydrolysed in the stomach to desmethyldiazepam, which is then absorbed.³

There are now more than a dozen different benzodiazepine derivatives available on the market. Choosing from a very similar group of compounds should perhaps be influenced largely by cost.⁴

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¹ Elliott, H W, *British Journal of Anaesthesia*, 1976, **48**, 1017.

² Garattini, S, Mussini, E, and Randall, L O, *The Benzodiazepines*. New York, Raven Press, 1973.

³ Shader, R I, and Greenblatt, D J, *American Journal of Psychiatry*, 1977, **134**, 652.

⁴ Smith, A, and Rawlins, M D, *British Medical Journal*, 1977, **2**, 447.

Open-access endoscopy service for general practitioners

SIR,—We were interested in the recent paper by Dr G Holdstock and others (17 February, p 457) regarding experiences with an open-access endoscopy service for GPs. The authors suggest that the open-access approach has the advantage of avoiding the need for clinical referral entirely, and that it is a logical progression from our instant endoscopy clinic.¹ We feel, however, that a clinical assessment before endoscopy has a distinct advantage, because it may lead to the diagnosis of other, non-gastrointestinal disease, which would otherwise be missed.

During the first year of our "one-visit clinic," in approximately 240 patients seen we diagnosed rectal carcinoma (1 case), cholelithiasis (2), hepatic disease (2), diverticular disease (2), hypolactasia (1), and pancreatitis (1), all in patients with dyspeptic symptoms but no gastroduodenal pathology. These diagnoses were made as a direct result of the clinical assessment made in the endoscopy clinic and investigations instituted there.

Although this is more time consuming, we have found that the full assessment and endoscopy can be easily completed in 40 minutes, and feel that the increased diagnostic yield makes this worthwhile.

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¹ Beavis, A K, La Brooy, S, Misiewicz, J J, *Gut*, 1978, **19**, 447.

SIR,—With reference to the paper on open-access endoscopy service for general practitioners (17 February, p 457), I would like to comment on the surprising finding of not picking up more early "gastric carcinomas"

as the number of endoscopies increased. The experience in Japan is that the proportion of early gastric cancers increases as the rate of endoscopies and other investigations, such as the double-contrast barium meal and gastro-camera, increases; and there is sufficient evidence to support the view that early gastric cancer in this country is the same as in Japan, where the resectability and survival rates are considerably better.¹

The authors have noticed an increase in patients with "inflammatory changes." However, they do not comment on the exact histological picture. A relation between chronic gastritis and gastric carcinoma has been shown to exist by several workers. It has been said by others that carcinoma develops more commonly when cellular metaplasia or hyperplasia are present. Could this increase in the number of patients with inflammatory changes therefore hide an increase in early gastric cancer?

I think that it would be prudent to follow up the patients with inflammatory changes by repeated endoscopies, multiple biopsies, and cytological examination. It would not be surprising if more exhaustive search and closer follow-up revealed several cases of early gastric carcinoma. Earlier diagnosis is the only factor that would make the resectability and survival rates in this country similar to those in Japan. I would also stress that the conventional barium meal is not only inferior to endoscopy in the diagnosis of gastric carcinoma but also unnecessary, since whatever the radiological findings endoscopy will be needed.²

In conclusion, the authors' statement that their direct-referral endoscopy service has given little objective benefit is premature until the possible connection between inflammatory changes in gastric mucosa and early gastric cancer is explored further.

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¹ Evans, D M D, *Gut*, 1978, **19**, 1.

² Moshakis, V, and Hooper, A A, *Clinical Oncology*, 1978, **4**, 359.

Emotion and empiricism

SIR,—I agree with Dr A L Cochrane and his colleagues (17 February, p 486) that "informed consent" is an emotive issue and wish to raise a difficult ethical consideration in this context.

It is simple to give "full" information when inviting a patient to partake in a prospective randomised controlled trial comparing a potentially better treatment with a known effective treatment. It is more problematical, however, when no treatment of proved efficacy exists in the context of the study being undertaken. It is usual in this situation to compare the drug under test with an inert substance. If one invites patients to partake in such studies and informs them that drug A is being compared with drug B then one can determine the effect of both the drug under study and the "placebo effect." This placebo effect consists not only of the inert substance but the effect of the doctor-patient relationship. If, on the other hand, one informs the patients that one of the tablets is inert then one may lose the placebo effect from all patients when they are on "active" drug or inert substance.

I believe that in the interest of patients' wellbeing as well as in the interest of scientific progress the degree of information divulged must vary depending on the clinical context

and should never be such as to harm the patient or the doctor-patient relationship. Furthermore, the intended degree of information to be divulged should form part of any protocol submitted to an ethical committee. This body should judge this aspect of the protocol in its clinical context rather than be guided solely by the rarely (if ever) obtainable "free and informed consent."

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Colonoscopy for unexplained rectal bleeding

SIR,—I read with interest and appreciation the article by Dr E T Swarbrick and others (16 December, p 1685) concerning the value of colonoscopy for unexplained rectal bleeding. All their data are extremely interesting and helpful. I do question, however, the incidence of ulcerative colitis found at colonoscopy. I believe their data indicated that of the 24 patients with inflammatory bowel disease none had rectal involvement and yet 14 patients were said to have ulcerative colitis. My impression was that current dogma indicated that 95% or more of patients with ulcerative colitis had rectal involvement and I find their numbers somewhat at odds with this dogma. I would appreciate any elaboration of these data or explanation that the authors might have.

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* * * We sent a copy of this letter to the authors, and Dr Swarbrick's reply is printed below.—
Ed, *BMJ*.

SIR,—We do not routinely undertake colonoscopy on all patients with inflammatory bowel disease and have no figures on the incidence of rectal sparing; but we agree with Dr Fried's belief that while it may be a feature of Crohn's colitis it is rare in ulcerative colitis. Nevertheless, our results confirm that it does occur.

We would like to emphasise that all our patients had been referred from gastroenterologists, surgeons, or physicians and were therefore a highly selected population. In addition they had already been screened for causes of rectal bleeding by sigmoidoscopy and barium enema, and any inflammatory bowel disease found on colonoscopy would not by definition involve the rectum.

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Bombs and hospitals

SIR,—The leading article "Bombs and hospitals" (24 February, p 506), makes a grave omission in its otherwise common-sense review of how to deal with a major disaster. Any hospital designated in such a disaster will have a recognised accident unit with its consultant. The consultant and the casualty officers (SHOs, registrars, and even senior registrars) are all trained in quick and accurate assessment of all types of injury and deal with them each day. Many designated accident units also have

flying squads, the accident consultant or his deputy attending the scene of the accident and performing triage on site—this again being part of the day-to-day activities.

To suggest that the first "senior surgeon" called should spend valuable time summoning "the required members of staff" and alerting the blood bank, the x-ray department, and the senior nursing officer is ludicrous. What is the switchboard doing?

The danger in disaster planning is departure from routine. Triage is best carried out by people who perform it each day.

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SIR,—Your leading article on bombs and hospitals (24 February, p 506), in listing the patients who will need operation or intensive care, gives pride of place to blast lung.

In a follow-up study of 1532 consecutive patients injured by bombing in Northern Ireland, there were two cases of blast lung.¹ Multiple contaminated wounds, traumatic amputations, extensive burns, and smoke inhalation are more common indications for such care, but are not mentioned.

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¹ Hadden, W A, Rutherford, W H, and Merrett, J D, *British Journal of Surgery*, 1978, **65**, 525.

Dexamethasone in acute stroke

SIR,—We wish to comment on several points raised by the correspondence about our recent article (7 October, p 994).

Many of the letters have illustrated the problems posed by the publication of "condensed reports." Editors naturally wish to ensure that as many papers are published as possible, while authors wish to ensure that their papers are as complete as possible. In our view, a report of a clinical trial must give enough information to enable readers to understand the basic properties of the patients studied and to be assured that the groups being compared are similar in all respects other than the treatment under trial. The information requested by Dr B G Parsons-Smith (9 December, p 1640) was indeed provided in our original text but was excluded by the Editor for reasons of space. We have made this table available to colleagues who have requested it, but this now makes any subsequent discussion in the pages of the journal difficult to conduct, because some of the letter writers can refer to information which the other correspondents and the general readers have not seen. We believe that this is a general problem and that correspondence about many other papers illustrates the point well. In short, there is a limit to the condensation which can be applied to a paper without depriving the reader of information which we, as authors, feel he should have.

We turn now to specific points from the letters. Dr Parsons-Smith states that dexamethasone is often effective if given in large doses immediately after the onset of stroke, but this has not been confirmed by controlled trials. Moreover, many stroke victims are not seen by a doctor immediately