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 butyl bromide 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 I, 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 duration[3] and this makes it unsuitable for long-term use. The controversial reports about the spasmolytic effects of oral hyoscine butylbromide[2] 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.

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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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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-gastroduodenal 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"