analgesic action for opiates is strong. The clinical results, while not absolutely conclusive, grow steadily more convincing as further information becomes available. The onus remains with us—that is, with clinicians and clinical investigators—to unravel the remaining uncertainties concerning these substances when used in human subjects.

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¹ Pert CB, Kuhar MJ, Snyder SH. *Proc Natl Acad Sci USA* 1976;73:3729-33.

² Yaksh TL, Rudy TA. *Science* 1976;192:1357-8.

³ Wang JK, Nauss LA, Thomas JE. *Anesthesiology* 1979;50:149-51.

⁴ Cousins MJ, Mather LE, Glynn CJ, Wilson PR, Graham JR. *Lancet* 1979;i:1141.

⁵ Jones RDM, Jones JG. *Br Med J* 1980;281:645-6.

⁶ Houck JC, Kimball C, Chang C, Pedigo NW, Yamamura NI. *Science* 1980;207:78-9.

⁷ Snyder SH. *Sci Am* 1977;236:44-56.

⁸ Chang K-J, Cuatrecasas P. *J Biol Chem* 1979;254:2610.

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Cimetidine and ranitidine in duodenal ulcer

SIR,—Dr Janet D Elashoff (8 November, p 1284) suggests that our conclusion that ranitidine and cimetidine give equivalent results in duodenal ulcer¹ is unjustified. She bases her claim on a statistical analysis of data carried out at a single fixed point, after four weeks' treatment, and by doing so she ignores the information accumulated during the rest of the trial. Ultimately all except one (95%) of the cimetidine-treated patients' ulcers healed and all except two (89%) of the ranitidine-treated patients', and these two failed to respond to cimetidine. Furthermore, we know that the only material difference between cimetidine and ranitidine is in potency rather than in method of action. Since in terms of ability to suppress acid secretion they were being given in roughly equipotent doses, it would have been surprising if equivalent results were not obtained.

Dr Elashoff refers in her letter to a recent article of hers which emphasises the very large size of patient groups needed if distinctions are to be made between drugs.² However, in that same article she and her co-author say: "This would require large multicentre trials that are difficult to administer. . . . The advisability of such a massive undertaking early on in the evaluation of a new drug is debatable."

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¹ Langman MJS, Henry DA, Bell GD, Burnham WR, Ogilvy A. *Br Med J* 1980;281:473-4.

² Peterson WL, Elashoff JD. *Gastroenterology* 1980;79:585-8.

Palpable spleen and bleeding oesophageal varices

SIR,—Following the report last year by Dr J Bull and others (24 November 1979, p 1328) on upper gastrointestinal haemorrhage in patients with known oesophageal varices, a retrospective study was carried out to test the author's conclusion that the absence of a palpable spleen makes it unlikely that the bleeding is from varices.

Endoscopy was performed on 16 patients presenting to the University Hospital of Wales with known oesophageal varices and upper gastrointestinal haemorrhage. Fourteen had cirrhosis (nine alcoholic, three primary biliary, and two cryptogenic) and two had portal vein obstruction. Out of the 16, 12 had bled from their varices and only seven of these had palpable spleens. The other four patients had bled from another source (two from peptic ulceration and two from erosions) and two of these had palpable spleens. There was no significant difference in age, results of liver function tests, or clotting screens between the two groups.

This study shows that reliance on the presence or absence of a palpable spleen to determine the source of haemorrhage would have resulted in erroneous management in seven out of the 16 cases—that is, greater than 40%. This unfortunately means that all patients with oesophageal varices who are bleeding should have a definitive investigation in the form of endoscopy or barium studies so that the source of haemorrhage can be accurately identified and correct therapy therefore established.

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Neurological Examination in Clinical Practice

SIR,—In your 15 November issue (p 1342), you published an excellent review by Dr E M Critchley of our book by Dr Edwin Bickerstaff, *Neurological Examination in Clinical Practice* (4th ed). It contains one misleading comment, in that he compares the £18.00 price of the fourth edition with the £2.50 price of the "paperback third edition." The only paperback version was that which we produced for the Government-subsidised ELBS scheme for sale in various Third World countries. The only version of the third edition generally available was the hardback, which rose in price from £6.00 on publication in 1972 to £9.50 with the last reprint in 1978.

Since such an apparently enormous leap in the price is bound to have an adverse effect on sales, I should be most grateful if you could either publish this letter or some suitable correction.

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Statistics in medical research

SIR,—The least enjoyable part of a research project is often the struggle to calculate a *t* value in order to state with confidence the difference between two sets of figures whose means are clearly miles apart, $p < 0.05$, or to try to fit recalcitrant numbers into some analysis which will confirm what one knows in one's bones to be true. Insult is added to injury when in the *BMJ* of 8 November, which incidentally is carrying an instalment of the series "Statistics and Ethics in Medical Research," the first paper (p 1237), after using χ^2 statistics, contains the statement "Neonatal mortality was higher (though not significantly so) in infants born at King's Mill Hospital than in those born at University College Hospital, London." The second paper (p 1241) uses the Kolmogorov Smirnov test, analysis

of variance, F tests, and Spearman's test for coefficient of correlation (non-parametric). After all that, it concludes, "Chlorthalidone produced a decrease in blood pressure that was not statistically significant" and "Plasma renin activity rose with chlorthalidone and decreased with atenolol though this was not statistically significant." The third paper (p 1243) breaks the pattern, perhaps because it comes from an epidemiology unit.

If we are to be allowed to ignore statistics after we have gone through the laborious task of calculating them, could we not skip them altogether?

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Occupational hazards of anaesthesia

SIR,—The recent review by Professor M P Vessey and Dr J F Nunn of occupational hazards of anaesthesia (13 September, p 696) provides a thoughtful and balanced analysis.

We would like to elaborate, however, on certain methodological objections raised by the reviewers relevant to the referenced dental study to which they refer.¹ To our mind, availability of a group of non-anaesthetic users among dentists and dental assistants using anaesthetics provided a unique study opportunity for comparing groups exposed with groups unexposed to such agents. Although certain age differences were subsequently noted between groups, the age distributions were completely overlapping, and several statistical approaches were used to adjust for the differences found. Furthermore, other possible differences in the exposed and unexposed groups were studied concerning geographic distribution, mercury use, smoking habit, overall response rates, response to individual mailings, and so forth. Statistical analyses were carried out to ensure that these variables could not be responsible for the apparent differences between the two groups. Although there may be a hidden explanatory factor other than exposure, no such indication is known to us or suggested by the data.

On another point, we agree with the reviewers that a response rate less than 100% is "disappointing"; however, return rates of 74-78% in large-scale surveys are realistic and as high as can be achieved without exorbitant cost. Bias is, of course, always a serious concern in terms of experimental design and in responder response. We took great pains to distinguish early responders from late and to attempt to measure the differential changes in endpoint rates among the subgroups. Our analyses suggested differential trends but in the direction of minimising rather than exaggerating the differences seen. It remains possible that non-responder bias entered our study despite strong efforts to minimise it, but we can find no evidence for such in our data. It is of interest that the original postcard survey represented participation in a routine effort by the American Dental Association to update its membership file and had no health assessment objectives. A single question asked whether or not the dentist used inhalation anaesthetics in his practice.

Finally, we concur with Professor Vessey and Dr Nunn in their conclusions that sufficient evidence exists to warrant continued efforts to reduce anaesthetic contamination in

the operating theatre, and that it remains for future prospective studies to confirm the direct association we and others suggest as present between exposure to anaesthetic gases and increased health hazards.

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Atenolol and chlorthalidone for hypertension in black South Africans

SIR,—Although I have not practised medicine in South Africa, I feel that Professor Y K Seedat's otherwise excellent study (8 November, p 1241) leaves certain crucial questions unanswered. Being a Zulu physician myself and having lived in both Zululand and Durban prior to coming to Britain to study medicine, I would like to take issue with his conclusions.

Professor Seedat's article seems to imply that race may be an important factor in an individual's response to beta-blocker therapy for hypertension. But the conclusion that beta-blockers alone are of little value in the management of a black hypertensive patient appears to have been arrived at without any consideration of diet. I find this a serious omission. Salt (NaCl) consumption among the Zulus appears empirically to be much higher than that of whites or Asians. The typical Zulu breakfast of soft mealie-porridge is salted in addition to being sugared. Putu (stiff porridge), which a Zulu has for lunch and supper, is highly salted, quite apart from the highly salted meat and vegetables or other relish. Indeed, black South Africans demand additional salt when served Western foods. This Zulu "craving" for salt has been observed by several missionary doctors throughout South Africa.

Until this factor of salt consumption is taken into account, the implied importance of race in so far as the value of beta-blockers is concerned cannot be taken seriously. Further strictly controlled studies are awaited on the effect of beta-blockers alone on Zulu hypertensive patients put on an entirely Western diet.

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Comparison of various treatment for irritable bowel syndrome

SIR,—I read with interest the report by Drs J A Richie and S C Truelove comparing various treatments for irritable bowel syndrome (15 November, p 1317). Irritable bowel syndrome and related disorders are certainly in need of careful study. However, I think that the choice of Motival (nortriptyline and fluphenazine) for the study was unfortunate.

The similarity between results obtained with lorazepam and Motival is probably due to the anxiolytic effect of the small dose of fluphenazine in the preparation. The lack of effect on depressed patients is probably due to the fact that the therapeutic dose of nortriptyline is known to be between 50 and 100 mg daily and not 20 mg as was given in this study. If enough Motival is given to produced adequate antidepressant levels then

the patient usually refuses to take the medication because of oversedation due to the fluphenazine component.

Our own work¹ suggests that a number of patients with irritable bowel syndrome will certainly be suffering from anxiety or depression. However, the availability of blunderbuss preparations such as Motival does not circumvent the need for adequate diagnosis.

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¹ Macdonald AJ, Bouchier IAD. *Br J Psychiat* 1980; **136**:276-83.

Renal embolisation in Glanzmann's thrombasthenia

SIR,—The short report by Dr E Briët and others (18 October, p 1039) concerning the correction of a renal bleeding in Glanzmann's thrombasthenia by renal embolisation was most interesting. The blood group specificity of the platelet-specific alloantibodies demonstrated in the serum of this patient, however, was not correctly described.

The alloantibodies were not directed against Zw^a antigen but against antigenic determinants on the membrane glycoproteins IIb and/or IIIa, independently from the Zw-antigen system. They were reactive with Zw (a+, b-) as well as with Zw (a-, b+) platelets, but not with platelets from other patients with Glanzmann's thrombasthenia.¹ This is in complete accordance with the findings of Degos and others,² and Muller and others,³ who described the same kind of antibodies in other patients with Glanzmann's thrombasthenia. Therefore it is to be expected that in patients with these kinds of alloantibodies against platelets neither HLA-compatible Zw (a+, b-) nor HLA-compatible Zw (a-, b+) platelets will be of any benefit.

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¹ Leeuwen EF van, Borne AEG Kr von dem, Ries LE von, Nijenhuis LE, Engelfriet CP. *Blood* (in press).
² Degos L, et al. *J Clin Invest* 1975;**56**:236.
³ Muller JY, Patereau C, Soulier JP. *Rev Fr Transfus Immunohematol* 1978;**21**:1069.

Spironolactone prophylaxis of mountain sickness

SIR,—With reference to your correspondence on spironolactone prophylaxis in mountain sickness (14 June, p 1453; 30 August, p 618) I should like to report the following case.

An experienced trekker, known to acclimatise slowly, used spironolactone in a dose of 75 mg daily as prophylaxis against mountain sickness on a walk to a maximum height of 5500 metres. On previous walks he had experienced acute pulmonary oedema at 4000 m, Cheyne-Stokes respiration at 3000 m, and early mountain sickness at 3700 m. With longer acclimatisation he had walked to 5500 m with no symptoms other than extreme dyspnoea. Lung function as tested by the Airflometer had shown progressive deterioration with altitude, beginning at 2500 m.

While taking spironolactone he felt very well, was free of headache and nausea, maintained an excellent appetite, observed no nocturnal disturbance of breathing rhythm, and slept well. Dyspnoea on steep grades became noticeable at 3000 m, severe at 4000 m, and very severe at 4600 m,

though there was no cough, sputum, or wheeze. Lung function test by the Airflometer, expressed as a percentage of the figure at sea level, was 92 at 1500 m and 83 at 3700 m, this deterioration beginning earlier than that recorded on a previous trek after a similar period of acclimatisation. A week later, during several hill climbs in the course of the second half of the trek, acclimatisation was much better and dyspnoea considerably less. By this time spironolactone had been discontinued. On return to 1000 m the Airflometer reading was 105% of the original figure.

Whether spironolactone is of any use at all in the prophylaxis of mountain sickness remains uncertain. While it may contribute to a sense of wellbeing and help to prevent headache and nausea, in this instance it appeared to be of no value in lessening dyspnoea; and lung function as measured by the Airflometer deteriorated early despite its use.

Now that the importance of taking rest days above 3500 m is generally appreciated, it will be more difficult to carry out adequate studies of the use of this or other drugs in the prophylaxis of mountain sickness, the incidence of which should decrease. It is clear, however, that spironolactone cannot be relied on to protect the lungs, and that there is no substitute for a slow rate of ascent, especially in persons going to high altitude for the first time, whose tolerance for height is an unknown quantity.

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Mental Health Review Tribunals

SIR,—Mr Larry Gostin never loses an opportunity to publicise his own somewhat idiosyncratic views of the working of the Mental Health Act 1959, and in so doing to air his criticisms of doctors and in particular psychiatrists.

In his letter (25 October, p 1142) in reply to mine (27 September, p 872) he makes a number of statements which demand contradiction. Of paramount importance is that in which he alleges that "The Act is concerned almost exclusively in withdrawing rights which other citizens enjoy..." This is just not true. One of the major principles on which the Act is based is that wherever possible patients suffering from mental disorder should be treated informally—that is, voluntarily. Indeed, it is explicitly stated in the documents concerned with compulsory admissions under sections 25 and 29 that "informal admission is not appropriate in the circumstances of this case." Compulsory treatment, it follows, should be a method of last resort. So successful, indeed, has this been that over 90% of all patients admitted to mental hospitals are "informal" and virtually 100% of outpatients are likewise. Those who are under compulsory orders are, as I stressed in my letter, committed to hospital in the interests of their own health or safety or the safety of others. The periods for which they are committed are, I insist, determinate. Renewal of sections 26 and 60 by the responsible medical officer is by no means a rubber-stamp operation. It is only undertaken where, unfortunately, the patient has not responded satisfactorily to treatment and therefore needs to be further detained for the very same reasons that justified his original detention.

Mr Gostin further refers to the "one safeguard provided in the Act, which is the right of access to an independent mental health review tribunal." Here again this is far from being a true statement of fact. In addition to the right of access—which, I agree, is most important—the Act sets out precisely the rights of those who are compulsorily detained. For example, in the case of those detained under part IV, it clearly lays down the persons