Nedocromil sodium: a new drug for the management of bronchial asthma

SIR,—Such scant information as was provided about the pharmacology of this drug by Dr S Lal and others (November 1984;**39**:809–12) suggested that it had properties similar to those of sodium cromoglycate. It is thus extremely strange, to say the least, that there was no mention of that drug in their article.

The clinical trial it reported was claimed to show that nedocromil sodium was superior to placebo in the management of asthma. Even that simplistic conclusion is, however, open to question because the numbers of patients in the two trial groups were small (13 on active drug and 17 on placebo), and no attempt seems to have been made to match them for atropic status, which might well have influenced the response to treatment. As for the results, the three tables show p values for 28 separate comparisons of the effects of nedocromil sodium and placebo, but in no less than 16 there were no significant differences between the two treatments. In the other 12 the differences in favour of the active drug were no more than marginally significant ($p < 0.05$) in 11, leaving only one with a p value of < 0.01.

My object in inviting you to publish this letter is, however, not only to criticise some very shaky statistics, but also to ask the authors why the study did not incorporate a comparison with sodium cromoglycate as well as with placebo, which could easily have been done by recruiting perhaps 15 more patients. Nedocromil sodium may or may not be more effective than a placebo in the management of asthma. I would submit, however, that the publication in a prestigious journal of a clinical trial which omits comparison with a "reference" drug of a similar type, in this case sodium cromoglycate, could influence medical prescribing by facilitating the promotion of a new and probably expensive drug which has not yet been shown to have any therapeutic advantage over one of proved efficacy.

WB GRANT
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**This letter was sent to Dr Lal, who replies below.

SIR,—Ours was the first clinical trial to be completed on a drug whose therapeutic activity had so far been tested only under the artificial conditions of bronchial challenge, which is not necessarily predictive of activity in clinical asthma. Accordingly, our main objective was to investigate whether or not nedocromil sodium had any therapeutic activity in patients with asthma—hence the comparison with placebo.

Dr Grant comments on the number of comparisons in which nedocromil sodium was not significantly superior to placebo. These have to be taken in the context of the disease and its management. It is perhaps not surprising, for example, that our patients, who used significantly less inhaled bronchodilator when treated with nedocromil sodium, failed to show improvements in peak expiratory flow rate. Despite this, 12 comparisons attained the 5% significance level and, although no attempt was made to stratify the atopic and non-atopic status of the patients, they had an equal chance of receiving each treatment. Dr Grant will be pleased to know that the two groups were similar and there was no significant difference between them.

To add an active group of, say, 15 patients as Dr Grant suggests would have involved 15 more patients in the clinical trial, before it was known whether or not nedocromil sodium had any therapeutic activity.

Lastly and most importantly, in our paper we concluded that nedocromil sodium is worthy of further consideration in the management of bronchial asthma. As a first report, a journal like *Thorax* is more suitable for a study like ours, and we are gratified to know that it has aroused much interest in other workers. Only further trials will show if the drug has a place in the management of asthma.

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Notice

Confidential inquiry into perioperative deaths

The Association of Surgeons of Great Britain and Ireland and the Association of Anaesthetists of Great Britain and Ireland have jointly set up a Confidential Inquiry into Perioperative Deaths. This study has the support of the surgical colleges, the Royal College of Gynaecologists and Obstetricians, and the faculties of anaesthetists. The study is funded by the Nuffield Provincial Hospitals Trust and the King Edward's Hospital Fund. The project is to enumerate death rates within 30 days of operations in all specialties and to identify remediable factors in the practice of anaesthesia and surgery. The study is fully confidential, only the three coordinators having limited access to the identities of patients and clinical staff concerned, to enable the coordinators to process the data. The study is voluntary but has one novel feature—that is, that a system of feedback has been arranged so that participating individual clinicians who desire it can obtain the opinions of the assessors in person. The Association of Surgeons of Great Britain and Ireland discussed this study during the Reckitt and Colman symposium on quality control at the annual meeting in Birmingham on 27 March 1985. The Chairman of the Joint Working Party is Professor MD Vickers; Mr HB Devlin, Professor JSP Lumley, and Dr John Lunn have been appointed clinical coordinators. Further information and copies of the detailed protocol are available from Mr Nigel Buck, administrator of the confidential inquiry, 14 Palace Court, London W2 4HT.

Correction

Relative intakes of tar, nicotine, and carbon monoxide from cigarettes of different yields

There is an error in table 1 of the paper by Professor NJ Wald and others (May 1984;**39**:361–4). The estimated relative intake of tar in smokers of cigarettes in the fifth quintile should be 3·82 instead of 4·59. The authors regret this error; it does not alter the sense of remarks in the text.