between the three groups in initial anxiety scores, but the reduction in anxiety from first to second assessment was significant for group A ($P < 0.01$) and for group B ($P < 0.02$) but not for group C ($P > 0.1$). Moreover the Kruskal-Wallis test applied to the data (expressed as difference scores between the two assessments) yielded a statistically significant result. They state in their discussion that "the improvement in . . . anxiety [for group A] was not necessarily a result of reassurance given solely about anaesthesia . . . as a booklet containing the same information was less effective than the visit."

The point to be made is this. The Kruskal-Wallis test, like other parametric and non-parametric tests applied to more than two sets of data, can detect only whether all sets of data can reasonably be assumed to have come from the same population. It does not indicate where any significant difference lies. It is misleading to say, therefore, that there was "a significant difference in the reduction of . . . anxiety between the three groups," which implies that the data for all three groups differed significantly from each other. Nor is this substantiated by the fact that the confidence levels for the reduction in anxiety within each of the three groups were not identical. That the decrease was significant at $P < 0.01$ for group A and at $P < 0.02$ for group B does not necessarily mean that the magnitude of these decreases differed significantly as between groups A and B. The same argument applies to the differences between group C and groups A and B. Thus while inspection of the data presented by Dr Leigh and his colleagues does indeed suggest that the booklet was less effective in relieving anxiety than a personal visit, this cannot be considered established by the statistical analyses undertaken. It is possible that the result of the Kruskal-Wallis test was due to there being a significant difference only between the control group and group A and that the reduction in anxiety for group B may not have differed significantly either from group A or from the control group.

It must be acknowledged that the authors do not explicitly equate differences in confidence levels with differences in magnitude of anxiety reduction, but the wording of their paper is such that readers unfamiliar with statistical procedures may well fall into the trap to which I am drawing attention.

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Ipecacuanha as an emetic

SIR,—In your leading article (15 October, p 977) on emetics for acute poisoning I was disturbed to note that you mentioned ipecacuanha syrup, the preparation used in the USA, but not the equivalent preparation that is available in the UK—namely, ipecacuanha paediatric emetic draught of the *British Pharmaceutical Codex* and the *British National Formulary*.

The Codex Revision Committee considers that the use of the term "syrup" is misleading and might lead to misunderstandings because medicated syrups are usually syrupy stock solutions of drugs for use in extemporaneous preparations. The *BPC/BNF* title provides a precise description of the product, and its use

on labels avoids any possibility of misinterpretation, but there appears to be need of a shorter name for verbal use¹; the term "ipecacuanha emetic" is under consideration.

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Codex Revision Committee

Pharmaceutical Society of
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¹ Fraser, M S, *British Medical Journal*, 1975, 4, 647.

Post-marketing surveillance of new medicines

SIR,—The proposal of Dr A B Wilson (15 October, p 1001) to use FP10 prescriptions from the Prescription Pricing Authority to investigate adverse reactions to drugs is not as new as he implies. I used this technique to investigate the possible teratogenicity of meclozine in 1962,^{1 2} of pregnancy test drugs,³ and more recently of Debendox (dicyclomine, doxylamine, and pyridoxine in sustained-release tablets).⁴ These were small-scale studies carried out on shoe-string budgets. Given the scale of central resources which Dr Wilson's article implies, which the pharmaceutical industry might help the DHSS to fund, the prescription technique could be a powerful investigational tool.

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¹ Smithells, R W, *Bulletin de la Société Royale Belge de Gynécologie et d'Obstétrique*, 1963, 33, 117.

² Smithells, R W, and Chinn, E R, *British Medical Journal*, 1964, 1, 217.

³ Smithells, R W, *Practitioner*, 1965, 194, 104.

⁴ Smithells, R W, and Sheppard, S, *Teratology*. In press.

Oestrogens for menopausal flushing

SIR,—In recent months, Dr G P Mulley and Professor J R A Mitchell have repeatedly claimed that the superiority of oestrogens over placebo in the treatment of menopausal flushing is unproved.^{1 2} Previously in these columns³ we have answered this claim and referred to our two double-blind, randomised, crossover, placebo-controlled trials,^{4 5} which showed that oestrogens were statistically significantly better than placebo in alleviating hot flushes.

Undeterred, Dr Mulley and Professor Mitchell have recently reviewed both our studies^{4 5} and those of Coope⁶ and they concluded by repeating their original claim.⁷ As nearly every statement in this letter is incorrect the conclusion is invalid and we cannot allow such misrepresentation to pass unchallenged. Dr Mulley and Professor Mitchell state that we performed only a four-month trial; that all patients were given oestrogens before placebo; and that the placebo response was unimpressive. They further claim that our findings are at variance with those of Jean Coope, firstly because she observed an impressive placebo response and secondly because, according to Dr Mulley and Professor Mitchell, she observed no statistically significant difference in the flush count between oestrogen and placebo groups.

The facts of the matter are as follows. We divided our patients into two groups—

that is, those with severe menopausal symptoms and those with less severe symptoms. Patients with severe menopausal symptoms (two-thirds of whom had severe vasomotor symptoms) were allocated to a four-month trial as ethically a prolonged placebo study could not be justified. Oestrogens (Premarin, 1.25 mg) and placebo were each taken for two months. Patients with less severe symptoms were allocated to a twelve-month study as a prolonged placebo trial could be justified ethically and oestrogen and placebo were each taken for six months. Most of these patients also had vasomotor symptoms but they were of a less intense nature than those of the patients on the four-month trial and the majority presented with a different complaint.

Both double-blind, placebo-controlled crossover trials were randomised—that is, one-half of the patients were given oestrogen first and placebo second, the other half receiving placebo before oestrogen. All patients were assessed two-monthly and in patients on the twelve-month trial the urinary oestrogen excretion was measured at each visit. The mean oestrogen excretion according to whether oestrogen or placebo was being ingested is shown in the figure. The crossover effect after six months from oestrogen to placebo or vice versa is clearly demonstrated.

Mean 24-hour urinary oestrogen excretion at each two-monthly visit according to whether the patient was on oestrogen or placebo therapy. (Reproduced by permission of the publishers of *Clinics in Obstetrics and Gynaecology*.)

During placebo therapy, with respect to pretreatment values there was a non-significant reduction in hot flushes in patients on the four-month trial and in patients on the twelve-month trial this reduction was significant ($P < 0.05$). However, during oestrogen therapy with respect to placebo values the reduction in hot flushes was statistically significant in patients in both the four-month ($P < 0.001$) and the twelve-month ($P < 0.001$) trials.

Our findings are not at variance with those of Coope. She and her coworkers in both their publications^{6 8} plainly state that "the proportional reduction in hot flushes on oestrogen compared with placebo reached significance ($P = 0.04$)" and these results confirm our findings. We observed a statistically significant placebo response in our twelve-month trial, thus confirming her results. The lack of placebo response in our four-month trial is logical for when compared to an efficacious therapy the placebo effect can be expected to vary inversely with the severity of symptomatology. Therefore our patients with severe symptoms (four-month trial) derived little benefit from placebo when compared with the beneficial oestrogen therapy; a reduction in the severity of symptomatology resulted in a relative increase in the placebo response (twelve-month trial).

Our studies, which we believe to be definitive, are scientifically valid and have shown