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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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

oestrogens to be statistically significantly better than placebo at relieving hot flushes. Sound and well-argued criticism of any scientific work is valid but the gross misrepresentation of our studies by Dr Mulley and Professor Mitchell is inexcusable.

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¹ Mulley, G, and Mitchell, J R A, *Lancet*, 1976, **1**, 1397.
² Mulley, G, and Mitchell, J R A, *British Medical Journal*, 1976, **2**, 944.

³ Campbell, S, and Whitehead, M I, *British Medical Journal*, 1977, **1**, 104.

⁴ Campbell, S, et al, in *The Management of the Menopause and Post-Menopausal Years*, ed S Campbell, p 149. Lancaster, Medical and Technical Publishing, 1976.

⁵ Campbell, S, and Whitehead, M, in *Clinics in Obstetrics and Gynaecology*, Vol. 4, No 1, ed R Greenblatt and J Studd, p 31. Philadelphia and London, Saunders, 1977.

⁶ Coope, J, in *The Management of the Menopause and Post-Menopausal Years*, ed S Campbell, p 159. Lancaster, Medical and Technical Publishing, 1976.

⁷ Mulley, G, and Mitchell, J R A, *British Medical Journal*, 1977, **2**, 766.

⁸ Coope, J, Thomson, J M, and Poller, L, *British Medical Journal*, 1975, **4**, 139.

Campylobacter enteritis

SIR,—We have followed with great interest the correspondence on campylobacter enteritis since the original article by Dr M B Skirrow (2 July, p 9). During a three-month period, from the end of June 1977, we have examined 563 faecal samples for potential intestinal pathogens. Of these, 280 were from patients with recent acute gastrointestinal symptoms, 117 from contacts of these cases, and 156 from asymptomatic patients. The table below summarises our results.

Campylobacters of the *C jejuni*-*C coli* group were isolated on the selective blood agar medium incubated at 43°C under micro-aerophilic conditions as described by Dr Skirrow. Our isolation rate of 14% in patients with symptoms is higher than previously reported in your columns. We found that 38% of our patients with campylobacters were children under 10 years of age; five patients had another intestinal pathogen isolated in association with the campylobacter. In addition, over the same period examination of 63 chicken carcasses from a common source yielded 39 (62%) positives for the *C jejuni*-*C coli* group by direct culture technique; enrichment methods were not employed. Similarly, 167 caecal samples from apparently previously healthy poultry gave 114 (68%) positive isolates. Antibiotic disc diffusion tests of the human and avian strains were identical for aminoglycosides and erythromycin (all sensitive), and trimethoprim and cephaloridine

(all resistant); but they differed in the case of ampicillin (25 µg disc). Here we consistently found that the avian strains were resistant, while 29 of 33 human strains were sensitive.

The epidemiology of campylobacter enteritis remains uncertain, although chickens have been considered as a primary source, and indeed serum from one of our patients with symptoms agglutinated both human and avian strains, thus suggesting a common antigen. Our results show poultry are a reservoir for campylobacter, but until a reliable scheme of strain identification is developed the place of avian strains in the epidemiology of human campylobacter enteritis may not be easily established. Our high isolation rate may be explained by the fact that Herefordshire is predominantly a rural area and people may more frequently be exposed to campylobacters from a variety of potential animal reservoirs, or indeed from the environment.

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SIR,—While campylobacters are increasingly reported as a cause of gastroenteritis the epidemiology remains unclear, though the finger of suspicion is pointed regularly at chickens and other birds as sources of the organisms.^{1 2} We investigated a series of cases of gastroenteritis due to campylobacter occurring after a wedding reception. So far as we are aware this is the first report of a common-source outbreak.

Of 29 people from different parts of the country who attended a wedding breakfast, five fell ill with colicky abdominal pain and profuse watery diarrhoea. Three of them were also pyrexial and had rigors. The diarrhoea persisted for about three days. The incubation periods ranged from 48 to 84 h, with a mean of 62 h. A campylobacter was isolated from one patient at the height of her illness, but by the time the extent of the outbreak had become apparent all other patients had fully recovered and the organism was not isolated from their stools. Blood taken one month after the illness from four of those affected, including the patient from whom a campylobacter had been isolated, was tested for agglutinating antibodies. The index case showed a titre of 1/320, as did one of the others, while the other two had titres of more than 1/640, suggesting that these patients had all been infected by the same organism.

The wedding breakfast consisted of several types of cold cooked meats, salmon, salad, cheesecake, fruit, and sweets. The meats were chicken, ham, beef, tongue, and Scotch eggs. No food was available for examination and no single dish was common to all sufferers. The chicken was supplied as uncooked portions from a large wholesaler on the day before the reception, refrigerated overnight, cooked early the following morning, and allowed to cool before serving. It had not been deep-frozen. A similar pack of chicken from the same manufacturer received a month later was opened on arrival at the restaurant and a portion taken for culture. A campylobacter was isolated from the chicken skin but not from the meat. Agglutinins to this organism were not detected in the serum of our patients, but it is likely that there is wide

distribution of serotypes in the chicken population³ and the human sera were therefore tested against four other isolates of campylobacter obtained from local chickens. With two of the chick isolates titres were just as high as against the human strains; with the others no cross-reaction was demonstrable. The evidence for the involvement of chickens in the outbreak, though presumptive, is strong.

Cooking should kill these organisms and it is unlikely that the chicken was itself the sole final vehicle for infection in this outbreak, as one of those taken ill had not eaten any. Before being cooked the chicken pieces had been skinned on a working surface upon which other cooked meats were later prepared. It therefore seems likely that in this case cross-contamination had occurred between uncooked and cooked food and several different dishes may have finally become contaminated.

Henceforth campylobacter must be considered as a possible cause of food poisoning.

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¹ Skirrow, M B, *British Medical Journal*, 1977, **2**, 9.

² Pearson, A D, et al, *British Medical Journal*, 1977, **2**, 955.

³ Cruickshank, J G, unpublished observations.

SI units and acidity

SIR,—I hope that many correspondents have already suggested the most obvious solution of the problem described by Dr P J Tomlin (24 September, p 833)—the discrepancies that are found when the same laboratory measurement is expressed in different units and then the mean and standard deviation are used in determining clinically "normal" values. The appropriate method of presenting the measurements is the old but often neglected percentile technique, which "is a simple way of obtaining understandable information from any sample of measurements or counts."¹ It requires only the arrangement of the observed values in rank order, which would be the same whether the SI or the "old" units had been used, and it does not depend on any information or assumption regarding the shape (Gaussian or other) of the frequency distribution.

Readers who are not familiar with the applications and potentialities of the method could find much discussion in the textbook just cited and in three more recent publications²⁻⁴ which discuss clinical norms. Those who find it difficult to transfer their allegiance from the mean and standard deviation to the median and percentiles may be helped by knowing how the mean-SD allegiance probably came about. Dr Feinstein² suggests that it arose because the mean and variance (or its square root, SD) are fundamental to the *t*-test and related tests of "statistical significance." Having been involved in medical statistics since 1928 and at one time a worshipper of *t* and its relatives, I agree with Dr Feinstein's diagnosis. Indeed, I think it is possible to detect a time of change in the writings of Sir Ronald Fisher. An article⁵ that was published in 1921 discussed the variation among individual measurements without invoking Gaussian-curve assumptions, but in 1925 there appeared the first edition of the book⁶ that was the starting-point for the wide

Potential pathogen isolated	No (%) positive samples from		
	280 patients with symptoms	117 contact patients	156 asymptomatic patients
<i>Campylobacter</i> sp	39 (13.9)	2 (1.7)	1 (0.6)
<i>Salmonella</i> sp	12 (4.3)	2 (1.7)	0
<i>Shigella sonnei</i>	11 (3.9)	14 (12.0)	1 (0.6)
Enteropathogenic <i>E. coli</i>	5 (1.8)	0	2 (1.3)
Parasites	8 (2.9)	0	0