terminated to be a coccidian of cats. In one such classical case¹ the mother always had very close contact with cats, since when I have always warned midwives and doctors of this danger even though it is a remote one.

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¹ Morris, D., Levin, B., and France, N E, *Lancet*, 1955, 2, 1172.

SIR,—Another danger from cats (16 December, p 1700) is toxoplasmosis. Admittedly only about one in 100 cats sheds the oocysts at any one time, but that one may shed a vast number and they are very hardy.

C P BEATTIE

Sutton in Ashfield

"Lecture Notes on Medical Statistics"

SIR,—Dr J F Osborn (13 January, p 123) describes as "bad" an example in what he calls my "otherwise good, if brief, book."¹ I am grateful that he should have noticed my little book with such measured praise. It is therefore with diffidence that I write to question his opinion of the example.

This concerned the number of accidents that occurred during parachute jumps at two localities on a windy day. The number of accidents at one locality "seems unduly high," so a medical officer in the RAMC investigated the disparity in the relative numbers of accidents at the two localities. Dr Osborn says the example is bad "because the decision to perform the test is made *because the results look extreme*" (his italics). However, this is not quite what I said.

Not having set up a prospective trial—and to do so must be only slightly less uncommon in peacetime today than when I was a wartime parachutist—the medical officer must be content with a retrospective study. If the accident rates had been nearly the same he would not have devoted his valuable time to testing the statistical significance of the difference between them. To all but professional statisticians, whose job it is to weigh everything in the balance, some judgment must go into whether to spend time and energy on a significance test or not.

Nor do I entirely agree with Dr Osborn that Fisher's exact test "is certainly very clumsy to perform without a table of logarithms of factorials." It is true that if the numbers are large and disparate the test may be—to use Shelley's phrase for sexual intercourse between males—"an operose and diabolical machination," but in practice it is often not such a taxing performance.

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¹ Swinscow, T D V, *Statistics at Square One*, 4th edn. London, British Medical Association, 1978.

Miniature peak-flow meters

SIR,—Dr B M Wright is to be congratulated on designing a new peak-flow meter (9 December, p 1627) which combines accuracy with portability. In reviewing previous small devices for measuring peak-flow he refers *inter alia* to the Pneumometer Minimus.¹ It is perhaps worth mentioning that I tested this instrument² and found it accurate. Its correla-

tion coefficient with the standard Wright meter was 0.902 and with the FEV₁ it was 0.942. It weighs more than the new Mini-Wright at 284 g (10 oz), but is remarkable for its compactness, measuring 8.5 × 5.7 × 2.7 cm apart from the blow-tube mouthpiece. The leather case in which it packs is 14 × 10 × 4.5 cm. Small size is of major importance to those who must carry a bagful of instruments around.

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¹ Hildebrandt, G., and Hanke, O, *Ärztliche Wochenschrift*, 1956, 11, 493.

² Freedman, B J, *British Journal of Diseases of the Chest*, 1972, 66, 53.

Thyroid disease and pregnancy

SIR,—The recent reports in your columns of the effects of pregnancy on thyroid function (25 November, p 1496; and leading article, 7 October, p 977) and of the spontaneous transition of hyperthyroidism to hypothyroidism (2 December, p 1535) and vice versa (2 September, p 666) prompt us to record an unusual case in which fluctuating thyroid function has been well documented through a pregnancy.

A 21-year-old Indian woman was admitted to hospital in May 1977, having taken a small overdose of paracetamol. She had a smooth, diffuse goitre, whose weight was estimated clinically at 45 g, and she was taking 0.1 mg of L-thyroxine daily. Hashimoto's disease had been diagnosed two years previously in India, and her clinical appearance and biochemical profile (table) were consistent with Hashimoto's thyroiditis under treatment. Having been frightened by her experience of taking too many tablets, she resolved to stop all tablets, including thyroxine and the contraceptive pill. She was next seen in the outpatient department in December 1977, having been off all medication for six months, and at this time she was three months' pregnant. She was clinically and biochemically euthyroid (the elevation of thyroxine being consistent with this stage of pregnancy), and was delivered of a normal baby boy in May 1978. On review in June 1978, though still clinically euthyroid, she was biochemically toxic and was therefore recalled. After a delay caused by her being on holiday, she attended in September 1978, when she was clinically hypothyroid, having taken no medication in the interim. Formal thyroid function testing confirmed that she was severely hypothyroid, and following the reintroduction of L-thyroxine (0.1 mg/d) she became clinically and biochemically euthyroid.

If we assume that the original diagnosis of hypothyroid Hashimoto's disease was correct, a number of interesting possibilities arise. How did this hypothyroid (and, presumably, damaged) gland become toxic? The development of a chorionic thyroid stimulator during pregnancy is one possibility, although there is little evidence for this.¹ Alternatively, the microsomal antibody present may have exerted

some reversible effect on the gland, which remitted as the titre of the antibody fell (perhaps as a result of the immunosuppressive effect of the pregnancy). This speculation is supported by the recurrence of the hypothyroidism coincident with a return of the antibody titre to its former level at the end of pregnancy.

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¹ Hall, R., Rees-Smith, B., and Mukhtari, E E, *Clinical Endocrinology*, 1975, 4, 213.

Labetalol and urinary catecholamines

SIR,—Correspondence in this journal has dealt with the effect of labetalol on urinary excretion of catecholamines (CA) and their metabolites.^{1,2} Appreciable increases of urinary total CA,¹ adrenaline,³ normetadrenaline (NMA), and metadrenaline (MA)² have been described in patients being treated with labetalol. However, it remained to be clarified whether this is a chemical or a metabolic effect of the drug.

We have measured urinary CA, MA plus NMA, and vanillylmandelic acid (VMA) in 11 patients before and after treatment with labetalol (300-900 mg/day) using various methods.⁴⁻⁸ Pretreatment values of urinary CA were highly correlated ($r = 0.96$, $P < 0.001$) when fluorimetric⁴ and radioenzymatic⁵ assays were used. CA excretion did not change after labetalol when measured by the radioenzymatic method. In contrast, higher excretion values were measured when the fluorimetric assay was used owing to the presence of substances interfering with the determination. The interfering material showed an excitation spectrum with a fluorescence peak at 414 nm. Stock solutions of labetalol and urine with various concentrations of labetalol³ did not affect the fluorimetric procedure, suggesting that a metabolite or metabolites of the drug yield the spurious fluorescence.⁹

Pretreatment values of total (free and conjugated) MA and NMA measured by a photometric⁶ and a fluorimetric⁷ method were highly correlated ($r = 0.91$, $P < 0.001$). During labetalol treatment significantly higher values of MA + NMA were found with the photometric assay, which were due to an interfering substance as evidenced by the absorption spectra. In contrast, MA and NMA excretion did not change when measured by the fluorimetric method. VMA excretion did not change after treatment.

Using appropriate methods we can demonstrate that combined α - and β -adrenoreceptor blockade with labetalol does not affect urinary excretion of CA and their major metabolites. Previously described increases of urinary Ca,

Biochemical profile of patient with fluctuating thyroid function

Date	ETR	Plasma T4 (nmol/l)	Plasma T3 (nmol/l)	Serum TSH (mIU/l)	Microsomal antibody titre
26 May 1977	0.97	135	1.29	0.5	1/80 ²
22 December 1977	0.97	286	3.56	2.1	1/60 ²
1 June 1978	1.23	294	4.30	0.5	1/20 ²
7 September 1978	0.79	35	1.05	72	1/80 ²
19 October 1978	0.87	101	2.15	34	1/80 ²

ETR = effective thyroxine ratio; TSH = thyroid-stimulating hormone.

Normal ranges: ETR = 0.86-1.13; T4 = 45-160 nmol/l (3.50-12.43 mg/100 ml); T3 = 0.85-3.85 nmol/l (0.55-2.51 mg/100 ml); TSH = 0.5-4.0 mIU/l.

All values in this table were determined in the same assay run to minimise variation caused by assay differences.

adrenaline, or MA plus NMA are due to a chemical rather than to a metabolic effect of labetalol and represent falsely high values. Adequate methods should be employed in future studies evaluating the effects of labetalol on the sympathetic nervous system. Furthermore, our findings may prevent errors in the differential diagnosis of phaeochromocytoma.

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¹ Harris, P M, and Richards, D A, *British Medical Journal*, 1977, **2**, 1673.

² Chapman, B O, Veitch, A B, and Shepherd, B, *British Medical Journal*, 1978, **1**, 364.

³ Weidmann, P, et al, *American Journal of Cardiology*, 1978, **41**, 570.

⁴ Crout, J R, in *Standard Methods of Clinical Chemistry*, ed D Seligson, vol 3, p 62. New York, Academic Press, 1961.

⁵ Peuler, J D, and Johnson, G A, *Life Sciences*, 1977, **21**, 625.

⁶ Pisano, J J, *Clinica Chimica Acta*, 1960, **5**, 406.

⁷ Bigelow, L B, and Wil-Malherbe, H, *Analytical Biochemistry*, 1968, **26**, 92.

⁸ Pisano, J J, Crout, J R, and Abraham, D, *Clinica Chimica Acta*, 1962, **7**, 285.

⁹ Miano, L, Kolloch, R, and DeQuattro, V, submitted for publication.

Naming of drugs

SIR,—As a psychiatrist working in Germany and trying against unequal odds to correlate advances in drug therapy in this country and in Britain, I welcome the discussion stimulated by Dr G A MacGregor concerning the naming of drugs (18 November, p 1433).

Why not require the drug companies to display the approved name directly after the proprietary name and at least two-thirds as large? This would apply to advertisements as well as labels on containers, and to combinations of drugs as well as simple compounds. Even non-myopic doctors and nursing staff would then be able to readily associate the two names and pick out whichever is relevant. It would still be allowed to use the approved name with the manufacturer's name in brackets after it as an alternative, but I do not consider it realistic to expect drug companies to give up their cherished brand-names without a long struggle.

The system which I suggest is one which we could reasonably demand be used throughout the EEC.

M H BALL

W Germany

Plasma lipoproteins in renal transplant patients

SIR,—The report on plasma lipoproteins in renal transplant patients by Dr D B Evans and the late Dr P Ghosh (6 January, p 21) invites several comments.

They suggest that the reduction in plasma lipid concentrations was due to a reduction of the mean prednisolone dose from 21 mg/day to 11 mg/day. However, in their original paper¹ lipids were measured in 17 asthmatics receiving a mean dose of prednisolone of 9 mg/day. The cholesterol and triglyceride levels were 6.0 mmol/l (232 mg/100 ml) and 2.38 mmol/l (211 mg/100 ml) respectively, values very similar to those in the transplant patients on the higher dose of prednisolone rather than the lower one. Clearly, then, hyperlipidaemia is not related to the steroid dose alone.

The 17 long-term survivors analysed in 1978 constitute a different population from the original 32. The transplants with poorest function in 1971 would be likely to have failed by 1975, leaving a group of survivors with well-functioning grafts. (The fact that the rise in glomerular filtration rate over the four-year period was not statistically significant does not exclude this possibility.) It has been suggested² that some lipids, including triglyceride, especially in females, are related to graft function. With the progressive elimination of the worst-functioning grafts one would expect the mean triglyceride level of the group as a whole to fall.

The change in lipid profile could be further explained in part by the death of those of the 1971 cohort with the worst lipid profile. In one series of 101 transplant recipients,³ occlusive arterial disease was observed only in those with untreated hyperlipidaemia, while the 29 nonlipidaemic patients remained free of arterial disease over a mean three-year observation period.

It is inevitable that the long-term survivors of renal transplantation will tend to have low steroid requirements, good graft function, and absence of arterial disease; the other transplanted patients will have fallen by the wayside through death or graft failure. Other workers⁴ have followed renal transplant recipients for up to 13 years, and have found that the percentage of survivors with hyperlipidaemia progressively falls in the years following transplantation. However, the clustering of low steroid dose, good graft function, freedom from arterial disease, and normal lipid levels does not necessarily imply a causal relation between any of these factors as Drs Evans and Ghosh suggest.

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¹ Ghosh, P, et al, *Transplantation*, 1973, **15**, 521.

² Abbott, L K, et al, *Atherosclerosis*, 1978, **30**, 97.

³ Ponticelli, C, et al, *Kidney International*, 1978, **13**, suppl 8, S72.

⁴ Thomas, F T, and Lee, H M, *Annals of Surgery*, 1976, **184**, 342.

Oesophageal reflux and its myths

SIR,—Your leading article "Oesophageal reflux and its myths" (6 January, p 3) commendably stresses the importance of treating reflux oesophagitis, rather than a sliding hiatus hernia, which may be no more than a chance radiological finding.

The editorial is perhaps guilty, however, of oversimplifying the significance of lower oesophageal sphincter pressure in the aetiology of reflux. As DeMeester and Johnson¹ have shown, 24-hour oesophageal pH monitoring is possibly the most sensitive method of monitoring reflux currently available. Their studies have also shown that reflux occurs in normal subjects and that, even in symptomatic patients, its occurrence depends on a number of factors other than posture. Price and Castell² point out that, while in general people with reflux have lower resting lower oesophageal sphincter pressures than those without, there is much overlap between populations with and without reflux. Furthermore, although the work of Cohen and Harris³ on the influence of gastrointestinal hormones on sphincter pressure has greatly increased understanding of the lower oesophageal sphincter mechanism, it remains true that hiatus hernia repair, by whichever method

may be chosen, prevents reflux by restoring the anatomical position and relations of the lower oesophageal sphincter without altering its hormonal sensitivity. It is probably the case that measurement of lower oesophageal sphincter pressure as currently performed is a relatively indirect indicator of reflux, which may be the result of prolonged periods of sphincter relaxation occurring in response to a variety of alterations in anatomical and hormonal environment.

It is also worth stressing the point that surgical procedures for hiatus hernia repair are, in fact, methods of treating reflux oesophagitis, and that without evidence of reflux oesophagitis there is no indication for repairing a sliding hiatus hernia.

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¹ DeMeester, T R, et al, *Annals of Surgery*, 1976, **184**, 459.

² Price, S, and Castell, D O, *Journal of the American Medical Association*, 1978, **240**, 44.

³ Cohen, S, and Harris, L D, *New England Journal of Medicine*, 1971, **284**, 1053.

SIR,—Following your leading article (6 January, p 3) entitled "Oesophageal reflux and its myths" I must express interest as well as concern. Myths usually stem from ancient fables and the article by Price and Castell¹ serves only to perpetuate these. It is well known that reflux can occur without evidence of hiatal hernia. "True oesophageal reflux" cannot be merely defined as a combination of radiological reflux and endoscopic abnormality.

There may be no radiological reflux and at endoscopy the oesophageal mucosa may look macroscopically normal. These tests are well recognised to be only 50-60% diagnostic.² You mention the acid perfusion test and intraluminal pH test as being useful in the detection of gastro-oesophageal reflux but fail to mention the most important, which is the standard acid reflux test.³ Only a thorough history, examination, elimination of biliary dyspepsia, and the appropriate use of oesophageal function tests can discriminate between "medical" and "surgical" reflux. There is no reason why in this modern era we should not apply our "sophisticated technology" to the diagnosis of oesophageal disorders and put the many "myths" on the shelf with the Cyclops and Hercules.

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¹ Price, S, and Castell, D O, *Journal of the American Medical Association*, 1978, **240**, 44.

² Clark, J, Moossa, A R, and Skinner, D B, *Surgical Clinics of North America*, 1976, **56**, 1.

³ Skinner, D B, and Booth, D J, *Annals of Surgery*, 1970, **172**, 627.

Disrespect for language

SIR,—Pleased at being able to answer one or two of the questions in your Christmas Quiz (23-30 December, p 1778), I looked up the answers. You should not state that claudication is "thought to have originated from the limp of the emperor Claudius." *Claudicare*, to limp, was used often by Lucretius and by Cicero, both of whom were dead before Claudius was born.

And Claude Bernard was not the "discoverer