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.