a method which calls to mind the methods of the tailors of Laputa.—I am, etc.,

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Malignant Hyperpyrexia

SIR,—I should like to make a few comments on your leading article (30 November, p. 488) on malignant hyperpyrexia. Denborough and Lovell¹ were the first to report a case of malignant hyperpyrexia in 1960. They followed this with a more detailed report in 1962,² well before Saidman *et al.* in 1964.³ However, Saidman *et al.* can claim to be the first to treat malignant hyperpyrexia successfully with the help of steroids. They cured a patient whose temperature had risen to 108.5°F (42.5°C) with an arterial pH of 6.82, and reduced his temperature within an hour to 97.2°F (36.2°C) using icepacks and prednisone.³

You imply that myotonia congenita is a myopathy that commonly underlies malignant hyperpyrexia. This is not so: the association between myotonia congenita and malignant hyperpyrexia is extremely rare. Saidman's case of malignant hyperpyrexia (No. 2 in his report) was described as suffering from a generalized muscle weakness diagnosed as myotonia congenita.³ However, no clinical sign of myotonia was mentioned, and muscle weakness is not a common sign of myotonia congenita. Histology at necropsy showed generalized polymyositis. Thus the diagnosis in this case is in doubt.

Harriman *et al.*⁴ reviewed patients that recovered from malignant hyperpyrexia and their relatives. The only clinical signs of myopathy that they found were hypertrophy and slight weakness of the lateral parts of the thigh and absent ankle jerks—no clinical sign of myotonia was seen nor was there any histological evidence. Certainly Britt *et al.*⁵ could find no evidence of myotonia in their investigations. Other reports^{6,7} confirm that myotonia congenita is not usually the underlying myopathy. To put things in perspective, King *et al.*⁹ have reported one patient who developed malignant hyperpyrexia who came from a family affected by myotonia congenita. None of the other 17 patients or their relatives who were investigated were affected by myotonia congenita.

It would not be surprising if there is a small rise in temperature associated with the generalized muscle spasm that sometimes follows the administration of suxamethonium to a patient with myotonia. Cody¹⁰ described such a case in which the temperature reached 99.4°F (37.5°C)—hardly characteristic of malignant hyperpyrexia. Reports of cases with clinical myotonia (both dystrophica myotonica and myotonia congenita) undergoing anaesthesia do not mention complications from pyrexia.¹¹⁻¹³ Thus there is one report of a patient with myotonia congenita developing malignant hyperpyrexia. The evidence at present suggests that this association may be purely one of chance rather than significance.—I am, etc.,

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Diagnostic Test for Multiple Sclerosis

SIR,—In refuting the specificity of the linoleic acid test for multiple sclerosis,¹ Mertin *et al.*² maintain that they have repeated the work "under conditions which were not . . . changed in any material respect." While it is true that one of us (B.K.S.) made the measurements upon which their paper is based, there were important differences.

(1) Absence of E.J.F. with his personal supervision of the animal supply.

(2) Failure of adequate checking for guinea-pig sensitization during the relevant November-December period. A major part of the trial was carried out during (influenza-ridden) December—when only one check was made. Indeed, Mertin *et al.*'s pretty, but largely irrelevant, fig. 2 serves mainly to show how checking lapsed after June, when E.J.F. relinquished control. Unfortunately, Professor A. M. Thomson was not able to give the time at which animal house precautions³ were allowed to lapse, though the need for them had long been known to Mr. E. A. Caspary.⁴

(3) The finding of occasional spontaneous sensitization to P.P.D. in concomitant macrophage migration inhibition tests carried out by Mr. D. Hughes⁵ on the stock of normal guinea-pigs used as the source of normal macrophages. This direct experimental evidence of presensitization, vital in the present context, is omitted from Mertin *et al.*'s presentation. Successful operation of the macrophage electrophoretic mobility (M.E.M.) test requires the use not only of Analor grade chemical reagents but also of a similar grade of the most complicated reagent of all, the macrophage cell.

(4) Use of P.P.D. as test antigen in place of thyroid¹—a substitution without importance if non-sensitized guinea-pigs are used as the source of macrophages but one which experimental test shows to lead to bizarre results if animals are presensitized.⁵

Mertin *et al.*, in quoting Shenton,³ stop short of reference to "certain other sources of error which may have been operating."³ For example, Professor Thomson was unable to give an assurance that detergents had not been reintroduced into the glassware cleaning process. This too may lead to random results (including those from duplicate specimens). A recent test carried out in another laboratory showed that merely drawing macrophages five or six times through a Decon-cleaned pipette—

perfectly adequate for other purposes—added one second to the migration time of the cells.

In experiments involving the M.E.M. test specimens have from the very beginning been randomized and presented to the observer in numbered bijou bottles^{6,7} so that it would require a paranormal feat of some magnitude on the part of B.K.S. to know upon which specimens to bring to bear his "subjective bias." In many family studies he did not, in fact, know which was the multiple sclerosis patient.

The consistency of the method is attested by the series of control figures published by Mr. Caspary⁷ and by Shenton *et al.*⁸ The latter (Mr. Hughes being a coauthor) have eliminated some of the "subjective element" in the measurements. For each result the statistical significance has been calculated (from the raw data) and with present expertise (B.K.S.) percentage differences as low as 7.8% correspond to a P value of <0.01 (as opposed to the 15% needed two or three years ago). Increasing accuracy has also been a feature of Mr. Caspary's own later results.

Finally, the result of just such a "double-blind" trial advocated by Mertin *et al.*, in which the observer does not know the provenance of the bloods from which his scrambled numbered bottles have been prepared, was published by Jenssen *et al.*⁹ on the same day as Mertin's denial. In a first series they clearly differentiated multiple sclerosis patients on the one hand from patients with other neurological diseases and normal subjects on the other. With increasing experience they reported (in a second series⁹) figures almost identical with those of Field *et al.*¹—a clear encouragement to those prepared to exercise the attention to detail that the method demands. It might be added that these authors had previously confirmed the cancer test¹¹ greeted (not unnaturally) with so much scepticism when it first appeared but now substantiated in several laboratories.¹²—We are, etc.,

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Pericarditis and Peritonitis Associated with Practolol Therapy

SIR,—There have been increasing reports of side effects of practolol, including pericarditis and "sclerosing or plastic peritonitis."¹ The following case may represent another of these unusual reactions.

A 48-year-old man was seen in February 1973. He had had palpitations for eight

years and these had been worrying him more recently. E.C.G. showed ventricular extrasystoles, right bundle-branch block, and left axis deviation. He was started on 50 mg practolol twice a day. In January 1974 the palpitations were still persisting and his practolol dosage was increased to 100 mg twice a day.

In April 1974 he was admitted to hospital with a four-week history of pericardial pain, malaise, fever, and some dyspnoea. On examination there was a loud pericardial rub and mild cardiomegaly. E.C.G. showed atrial flutter with 2:1 block. E.S.R. was 23 mm in 1 hour. The practolol was continued and he was started on digoxin. The atrial flutter reverted, his heart size returned to normal, and he was discharged from hospital in one week on 200 mg practolol and 0.25 mg digoxin a day.

In August 1974 he was readmitted with a four-day history of colicky abdominal pain and vomiting. There was no hernia or previous abdominal surgery. He was thought to have an upper small-bowel obstruction and a laparotomy was performed. Two generations of adhesions were found. One firm, well-organized adhesion was causing obstruction distal to the duodenojejunal flexure. There were more recent diffuse, filmy adhesions over the lower 4 ft (1.2 m) of ileum and a small amount of free peritoneal fluid was present. The omentum was swollen, firm, and oedematous. These findings were unexpected and unexplained in view of the fact that there had been no previous laparotomies and no source of peritonitis was found. An omental biopsy showed rather prominent vessels and fairly numerous clumps of lymphocytes both on the surface and deeper within the omentum suggestive of chronic inflammation. An E.S.R. four weeks after surgery was 57 mm in 1 hour. He was started on prednisolone and two weeks later the E.S.R. had fallen to 6 mm in 1 hour. Practolol has been discontinued and he is now feeling well.—We are, etc.,

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¹ Proctor, C. R., *Interim Report on Adverse Reactions Associated with Practolol*. I.C.I. Australia Ltd., 1974.

Uticillin

SIR,—In their letter Drs. H. R. Ingham and J. B. Selkon (9 November, p. 344) comment on the unjustifiability of testing the sensitivity of organisms isolated from the urinary tract to carfecillin (Uticillin), since this is an oral compound absorbed and hydrolysed to the active carbenicillin.

We began testing such isolates with both carbenicillin and carfecillin discs each of 100 µg and during the first two weeks encountered two strains of *Escherichia coli* which were apparently sensitive to carfecillin but resistant to carbenicillin. Further testing by tube dilution methods showed that both these strains had minimum inhibitory concentrations to carbenicillin of greater than 800 mg/l (µg/ml) and one would have expected from this that though high-dosage carbenicillin may have been effective in therapy carfecillin, with a manufacturers' stated achievable concentration in the urine

of the order of 800 mg/ml, would not.

These preliminary findings suggest that testing isolates from urinary tract infections for carfecillin sensitivity is not only unjustifiable but also unreliable and misleading, and that carfecillin may have antibacterial properties which are not shared by carbenicillin.

Your correspondents have expressed the arguments for retaining carbenicillin for *Pseudomonas pyocyanea* infections and few would disagree with these views. These arguments, our findings of *E. coli* strains showing a high degree of resistance to carbenicillin, and the failure of carfecillin disc testing to detect these suggest that it would be reasonable for carfecillin to be reserved for the treatment of pseudomonas infections of the urinary tract in patients for whom oral therapy is suitable and from whom organisms have been isolated which have been shown by adequate laboratory testing for carbenicillin sensitivity that such therapy is likely to succeed.—We are, etc.,

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Visual Evoked Potentials and Transient Ischaemic Attacks

SIR,—Transient ischaemic attacks are not usually associated with permanent brain damage. Brain scan, E.E.G., and clinical examination are generally normal after an attack. We have correlated the findings of visual evoked potential (V.E.P.) recordings with the results of conventional E.E.G. to find out if the former are more sensitive than the latter in giving information about brain lesions in these cases.

Twelve men and eight women aged from 39 to 62 years (mean 50 years) who suffered from transient cerebral ischaemic attacks were studied. In 11 of the patients the attacks were internal carotid in origin and in nine vertebro-basilar. A diagnosis of transient ischaemic attack was made only when the symptoms lasted for less than 24 hours, and carotid and vertebrobasilar cases were differentiated according to the criteria adopted by the National Institute of Neurological Diseases and Blindness.¹ The E.E.G.s and V.E.P.s were recorded on average 20 days after the last attack, 10 of them within 20 days of it. The V.E.P.s were recorded at the beginning of the routine E.E.G., the E.E.G. activity being monitored simultaneously. During the recording the patients were lying in a dimly-lit room with closed eyes. They received 100 successive flash stimuli with a frequency of 2 Hz. The duration of a flash was 1 ms and the intensity 0.42 J. The analysis time was 500 ms. The stroboscope was placed in the midline 30 cm above the eyes. The derivations used were frontal, central, parietal, and occipital referred to the ipsilateral ear. On the basis of our own control material and the findings of others^{2,3} V.E.P.s were judged abnormal by the following criteria: (1) no single deflection before 80 ms after the stimulus (complex I); (2) no biphasic deflection between 80–300 ms after the stimulus (complex II); (3) unilateral lack of a V.E.P. deflection recorded in the homologous brain area; (4) amplitude difference between homologous deflections, the lower potential complex being less than 50% of the higher complex amplitude; and (5) unilateral total lack of the rhythmic after-activity.

As is evident from the results (see table) the V.E.P.s were more informative than the E.E.G., especially during the first three weeks after the attack. In the cases of hemispherical attacks in which the lateralization of the ischaemia could be determined the abnormal V.E.P.s were on the ischaemic

Findings of E.E.F. and V.E.P. Examinations in 20 Patients Related to Interval between Examination and Attack

Interval (days)	No. with Focal or Lateralizing E.E.G.	No. with Abnormal V.E.P.
<21 days (n = 10)	4 (40%)	10 (100%)
≥21 days (n = 10)	3 (30%)	5 (50%)

side. It seems that transient ischaemic attacks may be followed, at least in some cases, by permanent brain tissue damage but that the lesion, either because of its small size or its location in a "silent" region, may escape detection in a clinical examination. The V.E.P. recording seems to be more sensitive than the E.E.G. in detecting possible brain damage in these cases.—We are, etc.,

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Deaths during Dentistry

SIR,—In answer to Dr. P. J. Tomlin (14 December, p. 655), let me first make clear that when using the terms "faint" or "fainting" I refer to nothing other than the common fainting attack.¹ Dr. Tomlin rightly values facts above opinions, but in the case under dispute he has been somewhat selective about the facts he discloses, restricting himself to quotations from the pathologist's necropsy report. He makes no mention of the clinical facts. It is the clinical facts attending the administration leading up to the cardiac arrest that are usually the more informative ones when a death has occurred with an anaesthetic and necropsy fails to reveal a specific cause. It was these facts in this case that led the anaesthetist, the pathologist, and me to attribute the death to fainting, the pathologist believing with me that the faint probably came on at the start of induction, immediately after the application of the nasal mask. Briefly, the clinical facts were as follows.

The boy was anaesthetized sitting up by one of the most experienced dental anaesthetists in the country. Induction seemed uneventful. He went under smoothly, there was no difficulty with the breathing, no asphyxia, no shortage of oxygen, and no mistake in the administration of the anaesthetic. Two deciduous teeth were quickly and easily extracted, the mask was removed, and the head was held forward for recovery. There was noticeably little bleeding and there was concern over delay in recovery; cold water was splashed on his face, but there was no response. Then suddenly, unaccountably, there was cardiac arrest.

The case exactly matches other reported cases^{2,3} in which young, healthy patients collapsed and died in the dental chair under anaesthetics—given in several of the cases by consultant anaesthetists. It also matches a case that occurred at my own hands^{4,5} in a man who fainted during induction while his blood pressure was being continuously recorded. He was being closely watched by five of us, four doctors and a dentist. None