letter (16 April, p 1033) long-term studies are needed to investigate the effects of β -blockade in such patients.

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- ¹ Deacon, S P, *British Journal of Clinical Pharmacology*. In press.
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- ¹⁰ Ghosh, P, et al, *Lancet*, 1975, **1**, 9.

Bruising in thyrotoxicosis

SIR,—I wish to report briefly the case of a woman with long-standing thyrotoxicosis whose presenting complaint was of bruising in order to inquire whether similar patients have been encountered.

The patient, aged 47, was suspected of having thyrotoxicosis some four years before hospital consultation, which was delayed because, although her goitre and eye signs were typical, she had lost very little weight. However, in this time she had started to bruise spontaneously and often excessively on the limbs. Her serum thyroxine concentration was elevated at 245 nmol (19 μ g/100 ml) and her 4-h radioiodine tracer uptake was 48%. The platelet count was $180 \times 10^9/l$ (180 000/mm³) and her prothrombin time and other coagulation tests normal. The factor VIII level was 1.5 g/l and that of factor IX 1.1 g/l. The antinuclear factor and latex tests were negative.

Mild spontaneous bruising in some women is not uncommon. In this case I wonder whether continued catabolism has resulted in a thinning of her basement membranes. The Hess test produced a very florid petechial reaction. Indeed, in the converse situation of myxoedema it is recognised that the lamina densa of the vascular basement membranes is thick and dense.¹

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- ¹ McFadden, P M, and Berensen, G S, *Circulation*, 1972, **45**, 808.

Cephalic motor responses in brain death

SIR,—Working as clinical neurologists we are consulted routinely in cases of probable brain death. We have welcomed the newly issued codes of practice, such as the Harvard criteria,¹ those of the Conference of Medical Royal Colleges and their Faculties,² and those of the collaborative study sponsored by the US National Institutes of Neurological Diseases and Stroke³ as guidance in this very delicate matter. Recently, however, certain clinical findings have disturbed us.

While some patients have indisputably fulfilled the criteria of brain death, including the unequivocal diagnosis of the cause of structural brain damage, lack of spontaneous respiration, absence of certain brainstem reflexes (fixed, unresponsive pupils, absence of corneal, vestibular, and gag reflexes), and, in some cases, flat EEG, still some motor responses have been present, even shortly after the

cardiac standstill which has eventually resulted from the disconnection of the patient from the artificial respirator. Tapping of the area above the eyebrows has repeatedly elicited noticeable contraction of the frontal muscle, indicated by upward movement of the eyebrow. Also tapping of the body of the masseter muscle has repeatedly caused a sharp upward movement of the chin as a reflection of contraction of the muscle. Chvostek's sign has been present in all these cases.

According to established neurophysiological knowledge at least, the contractions of the frontal and masseter muscles represent normal muscle stretch reflexes, which reflect patency of the reflex arc and thus also normal function of the motor nuclei of the trigeminal and facial nerves in the brainstem. Chvostek's sign, on the other hand, is considered to be a sign of local tetany reflecting low serum calcium content. But nevertheless it is a motor response.

It would be interesting to know whether other clinicians have had similar experiences and how the appearance of the phenomena described above should be interpreted. Should the patients be cared for as long as these signs are present, even though all the other brainstem reflexes had long been gone? Or should some revisions still be made in the criteria for the diagnosis of brain death?

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- ¹ Conference of Medical Colleges and their Faculties in the United Kingdom, *British Medical Journal*, 1976, **2**, 1187.
- ² Ad Hoc Committee of Harvard Medical School, *Journal of the American Medical Association*, 1968, **205**, 337.
- ³ Collaborative Study, *Journal of the American Medical Association*, 1977, **237**, 982.

Gonadotrophin deficiency and adrenocortical insufficiency in children

SIR,—I can confirm the suggestion of Dr W F Kelly and his colleagues (9 July, p 98) that this syndrome "will . . . be recognised more frequently now that cortisone-treated children will be surviving long enough to manifest the hypogonadal component."

In 1974 we examined a 21-year-old boy because of eunuchoid gigantism. At the age of 4 years he had been referred to the paediatric department for abdominal pain, vomiting, profound fatigue, and hypoglycaemia which had developed in the course of acute bronchitis. Hypocortisolism was confirmed biochemically and treatment with hydrocortisone was instituted. At the age of 20 his height was 201.8 cm and weight 105.5 kg. There were no signs of puberty and the testes did not show pubertal growth. The following results of endocrinological examinations were obtained.

Plasma testosterone 4.2 nmol/l (0.12 μ g/100 ml) (normal 17–28 nmol/l (0.5–0.8 μ g/100 ml)). Basal serum luteinising hormone 3 IU/l (normal 5–20 IU/l); after luteinising hormone-releasing hormone (LH-RH) (100 μ g intravenously) 7.5 IU/l (normal maximal increase 20–80 IU/l). Basal serum follicle-stimulating hormone 2.1 IU/l (normal 5–15 IU/l); after LH-RH 2.4 IU/l (normal maximal increase 1–6 IU/l). Serum thyroxine 116 nmol/l (9.0 μ g/100 ml) (normal 70–160 nmol/l (5.4–12.4 μ g/100 ml)). Basal serum thyrotrophin (range) 4.7–7.0 mU/l (normal <8.0 mU/l); after thyrotrophin-releasing hormone (TRH) (200 μ g intravenously) 20 mU/l (normal maximal increase 4–15 mU/l). Basal serum prolactin (range) 7–15 μ g/l (normal

<15 μ g/l); after TRH 26 μ g/l (normal maximal increase 15–40 μ g/l); after chlorpromazine (25 mg intramuscularly) 9 μ g/l (normal maximal increase 15–60 μ g/l). Growth hormone 1 μ g/l (normal <5 μ g/l); after insulin (0.1 U/kg body weight intravenously) 8 μ g/l (normal peak value >7 μ g/l); after levodopa (500 mg by mouth) 10 μ g/l (normal peak value >7 μ g/l). Basal plasma cortisol at 7 am 168 nmol/l (6.1 μ g/100 ml) (normal 140–690 nmol/l (5–25 μ g/100 ml); after synthetic ¹⁻²⁴corticotrophin (0.25 mg intravenously) 146 nmol/l (5.3 μ g/100 ml). Urinary 17-hydroxy-corticosteroids unmeasurable (normal 17–48 μ mol/24 h (5–14 mg/24 h); after metyrapone (4.5 g by mouth) 2.42 μ mol/24 h (0.7 mg/24 h); after synthetic ¹⁻²⁴corticotrophin (0.25 mg in 8-hour infusion for three days) unmeasurable. Steroid examinations were performed while the patient was temporarily on fludrocortisone.

I believe that this is another case of the syndrome of gonadotrophin deficiency and adrenocortical insufficiency. Moreover, there was a lack of prolactin stimulation by chlorpromazine with preservation of stimulation by TRH. This finding may support the presumed hypothalamic aetiology of the gonadotrophin deficiency and indicate a disturbance of the hypothalamic dopaminergic system.

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Primary cutaneous actinomycosis

SIR,—Despite the fact that 20–40 cases of actinomycosis are reported annually in the United Kingdom,¹ primary cutaneous actinomycosis is extremely rare. The following is the fourth case to be added to the literature.²

A 60-year-old Negro woman presented with a seven-week history of a growing abdominal mass. Eleven years previously an uncomplicated truncal vagotomy and pyloroplasty had been carried out for chronic duodenal ulceration. She looked well and was healthy generally and orodentally. The abdominal mass was 3.5 cm in diameter; it was situated in the abdominal wall at 10 o'clock to the umbilicus. It was tender and soft centrally but hard peripherally. Routine haematological and biochemical tests were normal, as was the chest x-ray. An initial diagnosis of a necrotic and malignant secondary was made.

At exploration yellow pus with obvious "sulphur granules" was obtained. A search for foreign bodies and for intraperitoneal and umbilical connections was negative. A biopsy specimen of the abscess wall was taken and the cavity drained. Whole pus was examined immediately and the diagnosis of actinomycosis confirmed. Pus culture later on grew *Actinomyces israeli* and anaerobic streptococci. Histological examination of the abscess wall also showed classical "sulphur granules." The pus swab taken at operation, on the other hand, proved of no significant bacteriological value as compared with the examination of the whole pus. This, in fact, may explain some of the failures to diagnose actinomycotic infections. Intramuscular penicillin, 2 MU daily for one week followed by 1 MU daily for six more weeks, was given. The abscess showed no sign of recurrence on review one year later.

It is accepted that the source of actinomycotic infection is almost invariably endogenous, although it has been reported after a human bite.³ Haematogenous spread from a primary focus is well documented.⁴ *A. israeli* does not cross intact gastrointestinal mucosa and hence abdominal infections with this organism are usually associated with surgery, trauma, or viscus perforation. It is possible that the abscess in this case was secondary to the operation performed 11 years previously;

if it was so, this would be the longest latency period recorded. Moreover, unlike other cases occurring after surgery,⁵ no communication between the abscess and the previous field of surgery was demonstrated.

I wish to thank Mr J Spencer for his permission to publish this case.

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¹ *British Medical Journal*, 1973, **1**, 365.

² Minocha, V R, et al, *Australian and New Zealand Journal of Surgery*, 1975, **45**, 66.

³ Emmons, C W, et al, *Medical Mycology*, 2nd edn, p 76. Philadelphia, Lea and Febiger, 1970.

⁴ Davies, M, et al, *British Journal of Surgery*, 1973, **60**, 18.

⁵ Adar, R, et al, *Israel Journal of Medical Science*, 1972, **8**, 143.

Treatment of acute paracetamol poisoning

SIR,—Some of the statements in your leading article on the treatment of acute paracetamol poisoning (20 August, p 481) need qualification.

(1) Oral methionine has been recommended for the routine treatment of paracetamol overdose by the poisons unit at Guy's Hospital for all cases reported since 1974.¹ During 1975 they received 755 inquiries relating to paracetamol poisoning. Methionine treatment was recommended for all patients reputed to have taken more than 15 g of paracetamol (presenting within 10 hours of ingestion). The total number given methionine is not recorded, but the results from 36 treated cases admitted to the liver unit at King's College Hospital and to the Guy's Hospital intensive care unit have been reported by Crome *et al*.² Thus, although the use of cysteamine has been more widely reported than that of methionine, the adoption of methionine as the recommended treatment of paracetamol poisoning in the south of England has led to its widespread use.

(2) Cysteine and methionine increase the amount of glutathione in the liver. However, cysteamine does not,³ but appears to act mainly through inhibiting a cytochrome P450 mixed-function oxidase, thus reducing the oxidation of the paracetamol to the toxic intermediate.

(3) The relationship between hepatic damage and paracetamol half lives was originally reported by Prescott in 1971.⁴ However, a more accurate method of predicting possible hepatic damage based on the pharmacokinetics of paracetamol has been designed and reported.⁵ This method relies on rapid and accurate methods of blood level estimation of paracetamol, such as the blood paracetamol estimation kit,⁶ a technique for determining paracetamol levels on the ward not mentioned in your article.

(4) Cysteamine injection is not commercially available. Cysteamine is rapidly oxidised in solution to cystamine, but stable formulations of cysteamine injection have been developed.⁷⁻⁹ Nevertheless, as these formulations have not been developed commercially the preparation requires a pharmacy with a sterile products production unit. (Prescott *et al*¹⁰ use a freeze-dried preparation prepared jointly by the pharmacy and the blood transfusion unit.) Thus cysteamine injection is not available in all hospitals. Methionine is readily available as powder or tablets and, as

it can be given orally, poses no such pharmaceutical manufacturing problems.

The report of the Royal College of Physicians of London symposium on paracetamol and the liver¹¹ lists the majority of these comments and gives the rationale behind the development of the treatments for acute paracetamol poisoning.

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¹ Volans, G N, *Journal of International Medical Research*, 1976, **4**, suppl 4, p 7.

² Crome, P, et al, *Journal of International Medical Research*, 1976, **4**, suppl 4, p 106.

³ Andrews, R S, et al, *Journal of International Medical Research*, 1976, **4**, suppl 4, p 39.

⁴ Prescott, L F, et al, *Lancet*, 1971, **1**, 519.

⁵ Recommended Management of a Case of Paracetamol Overdose, *Journal of International Medical Research*, 1976, **4**, suppl 4, p 157.

⁶ Kendal, S E, Lloyd-Jones, G, and Smith, C F, *Journal of International Medical Research*, 1976, **4**, suppl 4, p 83.

⁷ Prior, F G R, *Pharmaceutical Journal*, 1974, **1**, 578.

⁸ Brouwers, J R B J, and Vermeij, P, *Lancet*, 1976, **2**, 965.

⁹ Prior, F G R, *Lancet*, 1977, **1**, 315.

¹⁰ Prescott, L F, et al, *Lancet*, 1974, **1**, 588.

¹¹ Symposium on Paracetamol and the Liver: Overdose and its Management, *Journal of International Medical Research*, 1976, **4**, suppl 4.

Ventricular arrhythmias caused by prenylamine

SIR,—With reference to the paper by Dr R Puritz and others (3 September, p 608) we would like to comment that their recommendations are in line with our own, which stress that prenylamine should be used with caution in patients taking certain other cardioactive drugs or drugs likely to induce hypokalaemia.

Our data sheet states that "prenylamine should be used with caution and in reduced dosage when combined with negative inotropic drugs—for example, β -adrenergic blocking agents, quinidine, etc, or drugs likely to produce hypokalaemia. Isolated reports indicate that on rare occasions such combinations are capable of producing paroxysmal ventricular tachycardia or fibrillation. Under such circumstances a marked increase in the duration of the Q-S or Q-T interval above the rate-adjusted norm is an indication of the need to withdraw treatment with prenylamine."

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Skeletal scintigraphy in carcinoma of the breast

SIR,—Your leading article (3 September, p 592) does well to draw attention to the need for a diagnostic imaging strategy in the evaluation of metastatic breast cancer.

Skeletal isotope scanning followed by conventional radiology of abnormal areas so demonstrated¹ is a realistic and economic approach. Patients with positive scans and negative radiographs then pose a problem. False-positive isotope scans of the spine may be due to degenerative joint disease of intervertebral or costovertebral origin or osteophyte formation. Plain radiographs may be unhelpful.

This dilemma is the subject of an ongoing study in this department² employing computed tomography (CT) with the EMI whole-body scanner. CT enables a precise analysis to be made of horizontal cross-sections 8 or 13 mm in thickness. Preliminary observations³ on 30

patients with breast cancer and positive isotope scans of the spine suggest that differentiation by CT between metastatic and degenerative joint disease even when the two are coincident in the spine is readily made. Lytic deposits unsuspected on conventional radiographs are demonstrable by CT.

It would seem that where whole-body CT is available it could be used in the "positive scan, negative radiograph" situation and certainly unnecessary bone biopsy avoided.

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¹ Roberts, J G, et al, *Lancet*, 1976, **1**, 237.

² Best, J J K B, et al. In preparation.

³ Isherwood, I, and Best, J J K B, Third International Symposium on Computer Tomography, Miami, April 1977.

Hygiene in NHS hospitals

SIR,—We have read the letters from Dr G A J Ayliffe and Mr B J Collins (2 July, p 48) and Mr G Aston and Dr H Gordon (27 August, p 579) with interest and would like to draw attention to the fact that for a considerable time Cuckfield and Crawley Health District has been aware of the importance of kitchen hygiene.

For a number of years past an open invitation has been extended to environmental health officers of the three local authorities within the health district boundary to visit, without prior notice, any of the hospital kitchens within the district for inspection purposes. After each visit a report is forwarded to district headquarters. A working party, consisting of the medical officer for environmental health, general administrator (support services), the local authority environmental health officer concerned, the unit catering manager, the unit administrator, and a representative of the works department, meets to discuss and where possible implement recommendations of the report. By this process not only is progress made towards achieving a high standard of kitchen hygiene but the local authority environmental health officer is aware of any financial constraints which might delay the early implementation of any of the recommendations. The essential rapport between officers of differing authorities and disciplines is also beneficially maintained.

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Bell's palsy and herpes simplex

SIR,—Herpes simplex virus (HSV) has been suggested, on theoretical grounds, as a possible cause of Bell's palsy.^{1,2} I am able to find only one report of clinical HSV infection associated with Bell's palsy and that describes an HSV type II infection in a man with genital and oral ulcers immediately after the development of facial palsy.³ The present report describes a case of primary herpes stomatitis followed by mild Bell's palsy.

A European male aged 36 became unwell with a high temperature, multiple generalised mouth ulcers, and cervical lymphadenopathy. There was no suggestion of hand, foot, and mouth disease (more correctly, hand, foot, mouth, and bumps-a-