ted in the first few days of the disease in adequate doses four-hourly, is accompanied in the first 4-6 hours by a characteristic reaction which we termed the diagnostic penicillin-leptospirosis response.²

The highest concentration of leptospirosis is in Malaysia and Indonesia.⁵ Nevertheless, the presence of leptospirosis in Malaya, now Western Malaysia, was first noted by Fletcher in 1928.⁶ Yet in the 1950s it was reported that in the British armed Forces in Malaya 35% of all fevers, excluding malaria, were due to leptospirosis.⁷

I suggest that the number of cases of leptospirosis now being diagnosed in the United Kingdom at present represents only the tip of the iceberg if 85% or so of all cases are mild to moderately severe, and misdiagnosed as they were in Malaya in Fletcher's time and much later. The many confusing manifestations of this disease, or leptospirosis syndromes as they have been called, have been repeatedly stressed.^{1,2,8,9}

I believe that leptospirosis in the United Kingdom and the Republic of Ireland will be diagnosed more frequently in the future when, in febrile illnesses of apparently indeterminate origin, the overall history includes, in every case, not only the occupational history but a history of contact with cattle, pigs, dogs, rats, mice, and voles as well as with soil and water polluted with their infected urine. When such a history becomes routine there is bound to be an increasing awareness of leptospirosis in the United Kingdom. With that there will be earlier provisional diagnosis of leptospirosis, with the immediate early institution of adequate parenteral penicillin four-hourly for the first 24 hours and thereafter six-hourly. When such treatment begins in the first few days of the illness there is the inevitable appearance of the diagnostic penicillin-leptospirosis response; such is my experience and that of my colleagues.—I am, etc.,

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Adrenal Failure in Bronchial Asthma

SIR,—We appreciate that there are problems associated with oral corticosteroid reduction and the substitution of beclomethasone in the treatment of asthma, but we think that the dangers have been misrepresented and hope that this will not prevent the continued use of a promising form of treatment, whose main advantage is that it permits reduction of the dose of oral corticosteroids.

The real danger is that beclomethasone may not be so effective as oral corticosteroids and that the asthma may relapse, a risk that arises whenever effective treatment is withdrawn in any disease. This risk is present

regardless of hypothalamo-pituitary-adrenal (H.P.A.) function.

Drs. Ruth M. Clayton and P. Howard (2 June, p. 547) suggest that corticosteroid reduction exposes the patient to the possibility of failure of the adrenal to respond to stress, but this risk is already present in any patient who has H.P.A. suppression, and could be guarded against only by continually providing corticosteroids in a quantity equivalent to the maximal output of the normal adrenal—300-400 mg of hydrocortisone daily—which is obviously absurd. If the actual dose is reduced from 15 to 7.5 mg prednisolone daily and severe stress should occur either from status asthmaticus or some unrelated condition, high-dose replacement would be necessary and it would make little difference whether the patient was receiving 15 mg or 7.5 mg, as both of these are inadequate for stress replacement. The higher dose, however, will perpetuate H.P.A. suppression, whereas the lower dose may allow some function to return. If gradual reduction and withdrawal is possible, H.P.A. function will return to normal, often by the time the steroid is completely withdrawn or within a short time afterwards.^{1,2} Thus continuation of the higher dose actually increases the risk of adrenal failure.

It is difficult to draw any conclusion from the case quoted by Drs. Clayton and Howard in which the patient died within six hours of onset of a mysterious illness. Adrenal failure does not usually lead to such rapid death, and we do not believe that an extra 7.5 mg of prednisolone would have significantly altered the outcome.

We agree with Dr. A. O. Robson (30 June, p. 781) that the response to tetracosactrin has a loose correlation with the response to stress, but failure of the upper end of the H.P.A. axis is present in a significant proportion of corticosteroid-treated patients in whom the response to tetracosactrin is normal.^{2,3} The insulin hypoglycaemia test is the only adequate way of testing the integrity of the whole axis, and should be used if worthwhile conclusions are to be drawn.⁴—We are, etc.,

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Mediterranean Anaemia in Antiquity

SIR,—Dr. W. T. Menke's interesting case from the Hippocratic collection (26 May, p. 489) was not, I think, one of sickle-cell thalassaemia. Lehmann and Cutbush¹ suggested 20 years ago that the sickle cell had an Indian origin and came west comparatively recently, and I² put forward the view that its distribution in Africa might be explained by a migration during the Christian era which also left behind the shorthorn zebu breed of cattle. If this is so, there were not many sickle-cell genes in the Aegean in

the period during which the Hippocratic corpus was composed. The case may well have been one simply of thalassaemia, in which the spleen is characteristically large and leg ulcers, though not the rule, do sometimes occur. But the Greeks, I am sure, would have had a different word for it; the term thalassaemia ought surely to apply to the dilution of the blood with sea-water, such as occurs—for all I know—in those drowned at sea.—I am, etc.,

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Hazards of Laparoscopy

SIR,—I was interested to read Mr. M. McD. Usherwood's account of the breakage of Palmer's diathermy forceps (30 June, p. 773). I have had the same problem during a laparoscopic sterilization. Another pair of Palmer's forceps was not immediately available, but fortunately it was possible to remove the broken claw of the forceps by means of sigmoidoscopy biopsy forceps through the cannula, and after a short interval the sterilization was completed by the laparoscopic method.

The forceps were almost new, and I wonder if these were isolated incidents or whether some of the current instruments available are not strong enough for this purpose.—I am, etc.,

T. D. ANDERSON

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The Suspended Retractor

SIR,—The deep-chested patient who needs a vagotomy and the patient with a high, small liver and adherent gall bladder present exposure problems which are very much helped by the suspended retractor. With the aid of the normal lithotomy poles and cross-bar, a Doyen retractor lifts up the chest cage and is suspended by tape from the cross-bar with a small Durham retractor.

This technique was developed by Mr. G. Dimopolous, of Durban. I have found it extremely valuable but have failed to secure the interest of manufacturers. I am therefore writing in the hope that surgeons will try it out—their assistants will be grateful and perhaps for the first time will be able to see for themselves what is going on, while the anaesthetist will raise no objection at all.—I am, etc.,

D. W. BRACEY

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High-altitude Oedema Presenting as Coma

SIR,—The syndrome of high-altitude oedema has been increasingly documented over the past 10 years¹⁻⁶ Typically the disease presents with respiratory symptoms following on from severe mountain sickness. Cerebral forms are recorded, but according to Singh et al.,¹ unconsciousness takes days to appear. The patient recorded by Foster⁵ was unconscious, but this was in terminal pulmonary oedema. Pine's patient⁶ became comatose, but details of timing are not recorded.

On Mount Kenya this year I witnessed high-altitude oedema presenting as coma. The patient, a 25-year-old European, had walked from 6,500 feet (1,980m) to 15,500 feet (4,724 m) altitude in a day and a half—he had proved to be the fittest member of the party. On the next day he developed headache and nausea, causing him to rest. He was rational till night. During that night he had loud but not alarming breathing. Next morning he was unrousable, with temperature of 38.5°C, tachycardia, tachypnoea, and frothy saliva. Cyanosis was not present at any stage of the illness. After first-aid treatment (parenteral digoxin, frusemide, chlorpromazine, and penicillin, with oxygen) he was evacuated by stretcher and helicopter. Chest x-ray showed pulmonary oedema. His fundi later showed retinal haemorrhages. C.S.F. pressure was high. After a week of treatment including positive-pressure ventilation, diuretics, dexamethasone, and antibiotics he recovered consciousness. A spastic quadriplegia gradually resolved, leading to complete recovery after about two months.

The mechanism of the cerebral "oedema" is uncertain. It is clearly not just due to hypoxia. Cerebral arteriolar constriction (due to hypocarbia), with or without diffuse thrombosis or haemorrhage, must be a partial explanation.

My thanks go to Dr. Ponte of the Consolata Mission, Nyeri, and Dr. Henderson of the Nairobi Hospital for permission to describe the care with which they provided the definitive medical treatment; also to Mr. Woodley, Warden of Mount Kenya and Aberdare National Parks, for the rescue and much information.

—I am, etc.,

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Medical Schools in Italy

SIR,—With reference to the report on "Medical Research in Europe" (24 March, page 733) I should like to amend two figures referring to Italian medical schools. The update, figure for the number of medical schools in Italy is 27, and, much more relevant to a correct picture of our current situation, the number of medical students has reached 120,000 in 1973. With only some 6,000 teachers (1,000 professors and 5,000 lecturers) it is easy to imagine how happy and efficient the teaching may be.—I am, etc.,

RODOLFO SARACCI

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Spontaneous Periodic Hypothermia: Diencephalic Epilepsy

SIR,—With reference to the article by Dr. R. H. Fox and others (23 June, p. 693), I would like to express my admiration for the extremely thorough investigation in this unusual condition.

It is a pity however, that, among all the investigations carried out, the most important one of all was not illustrated. I

refer to the report of the abnormal electroencephalogram. Surely a short page of a typical discharge, as described, would have added a great deal more to the paper's value? All those who are involved in interpretation of EEGs realize the fallacies of relying on a verbal report. Furthermore, the paper raises the question of what is epilepsy, and though I searched diligently, I found nothing in the discussion to substantiate the basic concept as stated in the title.—I am, etc.,

H. JACOBS

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Sick Sinus Syndrome

SIR,—We agree with your leading article (23 June, p. 677) that the sick sinus syndrome is of clinical importance and that it is commoner than generally realized. However, we were surprised that the one clear recommendation for therapy was for prophylactic anticoagulants. No reference was given for the alleged high incidence of systemic embolism in patients with the sick sinus syndrome, though cerebral embolism was inferred by Samarasinghe and Senanyake¹ in two cases of the syndrome and Rubenstein *et al.*² recorded systemic embolism in eight out of 33 patients. Our own experience is different; indeed, no instances of embolism were seen in the 46 patients we described in 1971,³ nor have any occurred during subsequent follow-up. We would advise against the wholesale adoption of anticoagulant therapy in patients with the sick sinus syndrome on the present data.

We were disappointed that though the basic pathology of the sick sinus syndrome was described authoritatively as "usually degenerative change in the sino-atrial node (and other specialized conduction tissue)," again no relevant source was quoted. We have had difficulty in finding detailed pathological descriptions of the sino-atrial node in the literature and would have welcomed further references.

We would agree that the time has come for a more anatomical title than "sick sinus syndrome" and, though we were guilty of adopting the term "lazy sinus syndrome" some years ago,^{4,5} the term "sinu-atrial disorder" suggested by Oram *et al.*⁶ would seem to be the best available.—We are, etc.,

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Grades of Hypothyroidism

SIR,—We have read the recent article by Dr. D. C. Evered and his colleagues (17 March, p. 657) with great interest. The key group of patients in the series described was that said by the authors to be suffering from "subclinical hypothyroidism." Most of

these patients had circulating antibodies to thyroid tissue and were distinguished from other patients with antibodies solely on the basis of a raised serum thyroid-stimulating hormone (TSH) concentration. Nowhere in their paper do the authors give the absolute upper limit of serum TSH concentration measured by their assay in the normal population. Without this information patients with "subclinical hypothyroidism" cannot, by definition, be categorized. In the discussion reference is made to an earlier paper¹ in which "the range of serum TSH concentrations in normal subjects has been defined." In fact a range is not given in the paper to which reference is made but only the arithmetic mean values for two relatively small groups of men and women. The "95% confidence limits" (sic) for these means are given but they have been calculated on the incorrect assumption that the data are normally distributed. Inspection of fig. 6 of the present paper shows that the authors themselves have ignored the upper calculated confidence limit to which they refer (2.8 μ U/ml) and have fixed on one nearer to 4 μ U/ml. This latter figure approximates to the highest value (4.2 μ U/ml) in a group of 29 normal patients described by the same workers in an earlier publication.² As the lower normal values are below the limit of sensitivity of the assay employed and the data are therefore truncated, it is very difficult to predict the true distribution without a very much larger sample. It is possible that if a large population were to be sampled values in excess of 4.2 μ U/ml would be encountered in some normal subjects.

The authors have therefore not provided a sound basis for their division of patients with autoimmune thyroid disease into those with and those without "subclinical hypothyroidism." Furthermore this arbitrary division into two groups may serve to conceal a determinant of TSH secretion which is active in some patients. It is apparent from the data in this paper, and from the work of others, that in some euthyroid patients with damage to the thyroid gland the TSH concentration may be abnormally elevated by any criteria. If the plasma concentrations and effects of thyroxine and triiodothyronine are indeed normal in such patients, then the raised TSH must be sustained by a factor operating independently of the physiological negative feedback of the thyroid hormones on the hypothalamus and the pituitary. This factor could be related either to a reduction in the mass of thyroid tissue capable of synthesizing hormone or to something released from the damaged gland.

The classification that Dr. Evered and his colleagues have proposed does not, therefore, seem to us to be either valid or useful. Indeed the use of the term "subclinical hypothyroidism" is inappropriate as the patients, on the evidence presented, are neither subclinical nor hypothyroid.—We are, etc.,

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