("an observation not previously made") Hillyer⁵ wrote in 1971: "the results suggest that auto-immune and/or localised in vivo antigen-antibody reactions may play a significant role in the pathogenesis of schistosomiasis. . . ." In 1930 Muller and Stender reported a similar case.⁶

EEG, EMG, and spinal cord evoked response studies of the reported case must be most relevant. It is regrettable that these studies were not mentioned in the article. The treatment given to this patient (niridazole 25 mg/kg twice daily for 14 days and then prednisolone 10 mg three times daily, reducing to 5 mg daily after one week) must be considered too little and too late. Why were hycanthone and higher doses of prednisolone not tried in this utmost neurological emergency? What could have been the relative or absolute contraindications?

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- ¹ Ross, G L, Norcross, J W, and Horray, G, *New England Journal of Medicine*, 1959, **246**, 823.
² Phillips, T M, and Draper, C C, *British Medical Journal*, 1975, **2**, 476.
³ Wakefield, G S, et al, *Brain*, 1962, **85**, 535.
⁴ Bird, A V, *Neurology*, 1964, **14**, 647.
⁵ Hillyer, G V, *Proceedings of the Society for Experimental Biology and Medicine*, 1971, **136**, 880.
⁶ Muller, H R, and Stender, A, *Archiv für Schiffs- und Tropenhygiene*, 1930, **34**, 527.

Professorial pulchritude

SIR,—Referring to the obituary tribute to the late Professor M F Lucas Keene (28 May, p 1422) in which this comely teacher is described as "the first woman professor of anatomy," I am prompted to draw attention to the following fact.

In Wilfred Blunt's book *Sebastiano* about the travels of a Bolognese priest to Paris and back in 1664-5 it is stated that "Bologna was the first university to institute a chair of anatomy, and the first perhaps to have a woman professor—Novella d'Andrea, in the fourteenth century. (Such, however, was that lady's beauty that she was obliged to deliver her lectures behind a curtain.)" Similar restrictions were not practised 600 years later when the histrionic Professor Lucas Keene gave her lectures, which, no doubt, were a conspicuous success.

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Megaloblastic anaemia associated with sulphasalazine treatment

SIR,—Drs R E Schneider and Linda Beeley (25 June, p 1638) report a case of anaemia with megaloblastic change in the marrow which, they feel, resulted from treatment with sulphasalazine. The use of this agent may be questioned in a patient in whom a diagnosis of ulcerative colitis was excluded by normality of the rectal mucosa. The symptoms reported may merely have been the result of an irritable bowel syndrome and haemorrhoids.

The microbiological serum folate level would be invalidated by concurrent antibacterial therapy,^{1,2} and only an isotope dilution technique would have been acceptable.² However, the serum vitamin B₁₂ level (presumably measured by the *Euglena gracilis* or isotope dilution method) would be resistant to antibacterial interference and was low compared with stated normal ranges. Since no details of gastric antibodies, peak acid output, or Schilling test are reported B₁₂ deficiency

cannot be excluded, and the response to high-dose folate therapy is not specific to folate depletion. It has been suggested that patients with B₁₂ deficiency may be especially prone to sulphonamide-induced blood dyscrasias.³

More information, including adequate documentation of dietary folate and some investigation of the small bowel, is required before sulphasalazine is blamed for the megaloblastic anaemia in this patient.

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- ¹ Herxheimer, A, *Journal of Antimicrobial Therapy*, 1975, **1**, 346.
² Bateson, M C, Hayes, J P L A, and Pendharkar, P, *Lancet*, 1976, **2**, 339.
³ Chanarin, I, and England, J M, *British Medical Journal*, 1972, **1**, 651.

Bites from house martin parasites

SIR,—Insect bites are common but often the causative insect is not identified.

In late April neighbours started to suffer a series of severe insect bites, with bullae and marked surrounding erythematous induration, principally around the ankles but also elsewhere on the limbs. The pruritus lasted for over a week despite treatment with local and systemic antihistamines. One of the insects was identified by Dr S F Barnett, of the Department of Clinical Veterinary Medicine, Cambridge, as *Oeciacus hirundinis*. These small brown parasites of swallows and martins are similar to bed bugs. There have been no recent published reports of this insect emerging from house martins' nests to bite humans.

It appears that the insects over-wintered in the remains of last year's nests and became active at the start of spring, just before the martins returned from Africa. Many of the insects entered the houses around the window frames and, usually at night, crawled over the ceiling, falling on to the bed and biting their human victims. Hiding from light by day they were not initially apparent.

The victims had not suffered similarly in previous springs, although the martins had nested under the eaves within inches of the windows for two years past. The succession of good summers and mild winters may have allowed the bugs to build up to large numbers, such that with the coming of the warmer weather they spread further afield in search of their usual prey and found humans instead.

This year attacks abated with the complete clearance of all traces of old nests and extensive spraying of the area with domestic fly spray, to which the bugs are susceptible. As an ornithologist may I ask that the nests are not knocked down till after the end of the breeding season?

N I MCNEIL

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Beckett on biofeedback

SIR,—Your informative leading article (11 June, p 1491) on biofeedback considers some recent publications on this concept, but perhaps the most extreme example of voluntary cardiac control was vividly described as long ago as 1938.¹

"Murphy had lately studied under a man in Cork called Neary. This man, at that time, could stop his heart more or less whenever he liked and keep

it stopped, within reasonable limits, for as long as he liked. This rare, faculty, acquired after years of application somewhere north of the Nerbudda, he exercised frugally, reserving it for situations irksome beyond endurance, as when he wanted a drink and could not get one, or fell among Gaels and could not escape, or felt the pangs of hopeless sexual inclination."

It is, perhaps, not surprising in a land in which the heart more often than not rules the head, that Murphy himself should have some cardiologist peculiarities, but Beckett's insight into cardiology—or, perhaps more correctly, into cardiologists—is fascinating; might not Neary have as easily created the words inotropy, chronotropy, or bathmotropy?

"Murphy's purpose in going to sit at Neary's feet was not to develop the Neary heart, which he thought would quickly prove fatal to a man of his temper, but simply to invest his own with a little of what Neary, at that time a Pythagorean, called the Apmonia. For Murphy had such an irrational heart that no physician could get to the root of it. Inspected, palpated, auscultated, percussed, radiographed and cardiographed, it was all that a heart should be. Buttoned up and left to perform, it was like Petrushka in his box. One moment in such labour that it seemed on the point of seizing, the next in such ebullition that it seemed on the point of bursting. It was the mediation between these extremes that Neary called Apmonia. When he got tired of calling it the Apmonia he called it the Isonomy. When he got sick of the sound of Isonomy he called it the Attunement. But he might call it what he liked, into Murphy's heart it would not enter. Neary could not blend the opposites in Murphy's heart."

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- ¹ Beckett, S, *Murphy*. London, Routledge, 1938.

Zinc, acrodermatitis, acne, and prostaglandins

SIR,—You have twice recently drawn attention to the importance of zinc in human metabolism.^{1,2} In zinc poisoning there are gastrointestinal upsets, fever, muscle pain, hypotension, cardiac arrhythmias, and renal and hepatic damage.¹ In acrodermatitis enteropathica there is a zinc deficiency.^{2,3} Acrodermatitis responds to treatment with either halogenated 8-hydroxyquinolines or zinc.³ In one patient zinc treatment brought the plasma level of the metal from 400 µg/l up into the normal range of 700-1150 µg/l.³ A patient with acrodermatitis and acne showed improvement in both conditions during zinc treatment⁴ and zinc has been shown to bring about improvement in other acne patients.⁵

In acrodermatitis enteropathica there is evidence of abnormal essential fatty acid metabolism and prostaglandin deficiency.⁶ Using a rat vascular preparation we have recently shown that zinc is a powerful stimulator of the production of a substance which has the characteristics of prostaglandin E₁. The threshold zinc concentration for the effect was 500 µg/l, which is very close to the threshold for a therapeutic effect in acrodermatitis. Excess stimulation of prostaglandin synthesis could account for a number of the features of zinc poisoning. It suggests that prostaglandin synthesis inhibitors, like aspirin and indomethacin, and prostaglandin antagonists might be of value in this situation.

We have not tested the halogenated 8-hydroxyquinolines, but we have shown that the related compounds chloroquine and quinine can act as either prostaglandin agonists

or antagonists depending on the test condition.⁷ The 8-hydroxyquinolines may be acting as imitators of prostaglandin action in acrodermatitis.

It is possible that a prostaglandin deficiency may be involved in acne. Diphenylhydantoin is a drug whose long-term use is frequently associated with acne-like eruptions. Because we have shown that membrane-stabilising drugs can have prostaglandin antagonist actions⁷ and because diphenylhydantoin is known to be a membrane stabiliser we have recently tested it and shown it to be a competitive prostaglandin antagonist. We suggest that zinc is effective in acne because it stimulates prostaglandin synthesis and that this is also the basis of its action in acrodermatitis.

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¹ Brocks, A, Reid, H, and Glazer, G, *British Medical Journal*, 1977, **1**, 1390.

² *British Medical Journal*, 1977, **1**, 1493.

³ Neldner, K H, and Hambridge, K M, *New England Journal of Medicine*, 1975, **292**, 879.

⁴ Michaelsson, G, Juhlin, L, and Vahlquist, A, *Archives of Dermatology*, 1977, **96**, 283.

⁵ Michaelsson, G, Vahlquist, A, and Juhlin, L, *British Journal of Dermatology*, 1977, **96**, 283.

⁶ Evans, G W, and Johnson, P, *Lancet*, 1977, **1**, 52.

⁷ Manku, M S, and Horrobin, D F, *Prostaglandins*, 1976, **12**, 789.

Propranolol in thyrotoxic heart failure

SIR,—We welcome the important paper by Dr H Ikram (11 June, p 1505) showing that propranolol may be deleterious in patients with thyrotoxicosis and heart failure for we have recently had two patients who died in whom there was a probability that the administration of propranolol was a factor in their deaths.

Case 1—A coloured woman aged 58 of West Indian origin was admitted from the outpatient department with rapid atrial fibrillation 160/min, settling to 120/min in the ward. There was clinical evidence of tricuspid and mitral incompetence, with severe oedema to the top of the thighs and widespread expiratory wheezes in the chest but no basal crepitations. The blood pressure was 130/80 mm Hg. There were no abnormal eye signs and the thyroid was not palpable. She was known to have had atrial fibrillation and mitral incompetence, presumed due to ischaemic heart disease, for some years and there was also a history of chronic bronchitis being treated with salbutamol. Thyrotoxicosis had recently been diagnosed, serum thyroxine being 224 nmol/l (17.4 µg/100 ml) and triiodothyronine (T₃) 4.1 nmol/l (0.27 µg/100 ml). At 10 pm she was given digoxin 0.25 mg, propranolol 40 mg, salbutamol 4 mg, and nitrazepam 5 mg orally. Three and a half hours later she became urgently dyspnoeic and distressed owing apparently to severe asthma, which was treated with intravenous salbutamol and aminophylline with some improvement in her clinical state. After another three and a half hours—that is, seven hours after propranolol had been given orally—she had a sudden cardiac arrest, from which she was immediately resuscitated, but she ultimately died after a further five hours of aggressive treatment. After the cardiac arrest there was ECG evidence of myocardial infarction and the serum hydroxybutyrate dehydrogenase was 337 IU/l after the episode of cardiac arrest.

Case 2—A 21-year-old English girl was admitted as an emergency with a 12-h history of increasing drowsiness preceded by two weeks' history of shortness of breath and palpitations. On examination she was confused and disorientated, temperature 39°C, pulse 180/min. There was exophthalmos and a diffuse goitre was present.

There were focal signs of pneumonia in the right upper chest. A diagnosis of thyrotoxic crisis provoked by right upper lobe pneumonia was made and confirmed by chest x-ray. Serum thyroxine was 300 nmol/l (23.3 µg/100 ml) and T₃ 7.3 nmol/l (>0.48 µg/100 ml). The ECG showed sinus rhythm. At 2 pm on the day of admission she was given propranolol 40 mg orally and an intravenous infusion of dextrose saline was started. At 5 pm she was given intravenous ampicillin and 10 min later she collapsed with severe wheezing, hypotension, and skin mottling. Anaphylactic shock was diagnosed and she responded to intravenous hydrocortisone and antihistamine. However, she still had extreme agitation and tachycardia so 2 mg of propranolol was given intravenously. Immediately after this she had an exactly similar collapse and she subsequently required artificial ventilation. Carbimazole, digoxin, gentamicin, and potassium iodide were then given. The thyrotoxicosis came under control but neurological activity did not return and she had an asystolic arrest after 14 days on the ventilator.

It was unfortunate that in case 1 the patient was given propranolol in view of the history of chronic bronchitis, and, although it was over three hours before she had the acute episode of asthma, we feel that this was probably provoked by the administration of the drug. It is not possible to be sure of the exact cause of the subsequent sequence of events and unfortunately necropsy was refused, but in the light of Dr Ikram's paper it is quite possible that a fall in cardiac output following this single oral dose of propranolol was a factor that led to myocardial infarction and cardiac arrest and her ultimate death. In case 2 there was no previous history of allergy to penicillin or anything else and in view of the immediate collapse following intravenous propranolol we think that this drug was the more likely cause of both episodes and that the initial diagnosis of penicillin anaphylaxis was incorrect. The hypotension and the hypoxia at the time of the collapse were contributory to her death. Although these two patients were quite different in their clinical presentation it did seem that propranolol was an important factor in their deaths and we shall be interested to hear whether anyone else has similar cases to report.

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Mumps orchitis and testicular tumours

SIR,—We would like to comment on your leading article on mumps (11 June, p 1489), in which you suggest that there may be "at best a tenuous relationship" between mumps orchitis and malignant testicular tumours and urge an inquiry "in large numbers of patients."

We have investigated the incidence of testicular tumours in the population of Hamburg. During the period 1966-76 294 patients with such tumours were collected (3.0 cases per 100 000 males) in Hamburg and 200 further cases from other parts of Germany (total 494). Only two cases of unilateral mumps orchitis were found in which a testicular tumour had later developed: a man 76 years old with seminoma (orchitis in the same testicle at 22 years) and a patient 45 years old with the identical diagnosis (orchitis in the diseased testicle at 21 years). It is interesting that 24 patients with testicular tumours (4.9%) had suffered from epididymitis on the affected side some years ago (median 8.6 years). We could not find any patient with a

history of epididymitis in the non-affected testicle. Since it is well known that epididymitis can very occasionally be the only symptom of mumps¹ this seems worth recording. Sixty-one patients (12.3%) had simultaneous atrophy of the diseased testicle; in addition, 28 patients (5.7%) had a palpable atrophy of the contralateral testicle. This fact seems to be of interest since Beard *et al*² also found atrophic testes in their patients with previous mumps orchitis and testicular tumour.

From our data on a larger series of patients with testicular neoplasms we conclude that mumps orchitis itself is seldom found in the past history of these patients. On the other hand, if one speculates that the previous epididymitis in the testicle in which a tumour subsequently developed in 4.9% of our patients was in fact a manifestation of mumps the situation is different.

We have also checked 87 cases of mumps orchitis treated between 1960 and 1970 in Hamburg hospitals. On screening the records of the urology and x-ray departments of the city none of these patients was found to have developed a testicular tumour up to 1977.

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¹ Christie, A B, *Infectious Diseases: Epidemiology and Clinical Practice*, p 469. Edinburgh and London, Churchill Livingstone, 1974.

² Beard, C M, *et al*, *Mayo Clinic Proceedings*, 1977, **52**, 3.

Getting close to the patient

SIR,—Has any aspect of the reorganisation of the Health Service resulted in any benefit to anyone except those who appear to enjoy endless committee work? Were they not typical of the ineptitude of the system that has been created, the following excerpts from one of those circulars from the local area health authority would have been treated as a joke. Instructing hospital staff on the management of violent patients it says, after some initial platitudes about peaceful persuasion:

"If this fails [that is, if he refuses to co-operate] stay close to the patient. . . . If he has abandoned the weapon or instrument but appears likely to attack you or anyone else in the vicinity or do injury to himself, approach him, still talking to him, and when close enough grasp his arms at elbow level and pull him towards you. Quickly change your grasp and encircle him with your arms but continue to pull him towards you. . . . Then quickly get behind the patient, push him towards a nearby wall, retain your grip, lean on him, press him to the wall or floor and remove his footwear. . . . Make sure the relevant incident forms are filled in as soon as possible."

What can we do to alter the system?

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Diagnostic amniocentesis in early pregnancy

SIR,—You state in your leading article (4 June, p 1430) that "anti-Rh(D) immunoglobulin should be given [following amniocentesis] to patients with a significant fetomaternal transfusion as indicated by the Kleihauer technique." If this recommendation is followed some untreated mothers will become sensitised with serious risks to their babies.