Cyclophosphamide in Nephrotic Syndrome

SIR,—In your account of the recent joint B.M.A./B.P.A. meeting at Cheltenham you state (2 November, p. 319): "Dr. Martin W. Moncrieff described treatment by Dr. R. H. R. White and himself of 46 children with the nephrotic syndrome using cyclophosphamide." We would like to point out, as we did when giving the communication, that this was a collaborative study, with almost half of the patients treated by Drs. J. S. Cameron and C. S. Ogg at Guy's Hospital, London.

Also, it is incorrectly stated that some of our patients have been in remission for four years; our longest remission, to date, is 23 months.—We are, etc.,

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Malabsorption and the Skin

SIR,—In their article on dermatitis herpetiformis and coeliac disease (5 October, p. 30) Dr. N. G. Fraser and others come to the conclusion that the relationship between the two diseases is uncertain. We do not think it is nearly as uncertain as they make out. Indeed, we are astonished that in the short time that has elapsed since our original description of the enteropathy of dermatitis herpetiformis[1] so much confusion has arisen, in our opinion quite unnecessarily, over this and other issues.

First of all dapsone as the cause of the enteropathy[2] was always a non-starter, as a number of patients in our original study had never taken the drug.[1] Secondly, folate deficiency[2] never had to be considered seriously as the explanation of an enteropathy as severe as this and could in any case be excluded on the basis of our original data. The finding of folate deficiency in the patients studied by Fry and his colleagues did not surprise us. On the contrary, we should have been amazed if patients with malabsorption, and with haemolysis from dapsone, had not been found to be folate deficient.

The confusion which arose over these two points is, however, relatively insignificant when it is compared with the muddled thinking which followed concerning the role of gluten. It is now absolutely beyond dispute that the enteropathy of dermatitis herpetiformis improves with gluten withdrawal in a number of cases.[3–6] Our further observations that an inflammatory response can be invoked by gluten instilled into previously normal bowel and that the severity of the enteropathy is greatest in the upper part of the small intestine[6] provide still more evidence of the similarities between the enteropathy of dermatitis herpetiformis and the coeliac syndrome. The fact that in some cases of dermatitis herpetiformis the enteropathy has not yet responded to gluten-withdrawal does not alter these facts, and it is well known that a number of patients with the coeliac syndrome unassociated with dermatitis herpetiformis do not respond either.[7] The observation that the rash of dermatitis herpetiformis has improved in a few patients while on a gluten-free diet[3–5] has in our opinion been misinterpreted, as there is no evidence that the improvement is due to other than the natural history of the dermatosis. The present observations of Dr. Fraser and his colleagues add weight to our finding that treatment of the enteropathy does not improve the rash.[6]

We are still a long way from knowing the answers to all the questions about the syndrome we described,[1] but it is a pity to ignore the facts which exist. The conclusion of Dr. Fraser and his colleagues that the relationship between the rash and the enteropathy is uncertain is a confusing over-simplification of these facts. We can say with confidence that there is a clear statistical relationship, that this relationship is an indirect one, and that the evidence is very suggestive that it is genetic.—We are, etc.,

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SIR,—The paper by Dr. N. G. Fraser and others (5 October, p. 30) has prompted us to mention two further patients with coeliac disease and dermatitis herpetiformis.

A man aged 27 was diagnosed as having coeliac disease at the age of 22 months, and a "restricted" diet was ordered. He resumed a normal diet at 9 years old. At the age of 13 he received a gluten-free diet in hospital and before diet was started the faecal fat was 17.5 gm./day. He never received a strict gluten-free diet thereafter but had no symptoms of malabsorption since the age of 14. He developed severe dermatitis herpetiformis in 1967. Jejunal biopsy prior to treatment showed a completely flat mucosal surface (subtotal villous atrophy). After three months' dapsone therapy (100 mg. daily) biopsy appearances were unchanged, although his skin was free of lesions, and following this biopsy a gluten-free diet was commenced.

A man aged 36 developed an irritant blistering eruption in 1955. He first complained of anorexia and diarrhoea in 1962, and jejunal biopsy at that time showed subtotal villous atrophy and absorption of fat, xylose, and vitamin B_{12}, was impaired. Treatment with A.C.T.H. relieved his symptoms, but small bowel histology remained unchanged. Gluten-free diet was instituted and bowel histology and all parameters of absorption returned to normal over the next two years. He returned with weight loss in 1967 having discontinued his diet in 1965. Gluten-free diet was restarted and at this time dermatitis herpetiformis was diagnosed and confirmed by skin biopsy. In the years prior to diagnosis of dermatitis herpetiformis his skin neither improved on a gluten-free diet nor showed any deterioration when it was withdrawn. Eruption rapidly responded to dapsone and is controlled on 100 mg. daily.

Our first patient is the only patient so far reported with evidence of coeliac disease in infancy, dermatitis herpetiformis appearing 24 years later. Jejunal biopsy appearance did not alter following treatment with dapsone in distinction to dermatogenic enteropathy and skin therapy. A gluten-free diet taken over a period of some years had no effect on dermatitis herpetiformis in our second patient, a finding in keeping with the view of Shuster *et al.*[1] Our two further cases tend to confirm the association of true coeliac disease with dermatitis herpetiformis, though more cases will need to be studied to ensure that this is not a chance association. However, the occurrence together of two uncommon diseases is not usually due to chance.

The high incidence of jejunal abnormalities but low incidence of malabsorption in dermatitis herpetiformis does not necessarily reflect a genetic association of this condition with asymptomatic coeliac disease. The degree of malabsorption may be dependent upon the extent of small bowel involvement.[2,3] If mucosal abnormality of any cause is localized to the upper jejunum, malabsorption might be expected to be minimal.

We thank Dr. Peter Borrie and Dr. A. M. Dawson for permission to publish details of their patients.

—We are, etc.,

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Acute Epiglottitis

SIR,—Dr. J. D. Andrew and others (31 August, p. 524) reported four cases of acute epiglottitis seen in Newcastle upon Tyne during a six-year period. This report would suggest that epiglottitis is a relatively uncommon condition and that there is some uncertainty concerning its management.

During the last three years we have seen 22 cases of this condition at the Royal Children's Hospital, Melbourne. One arrived at the hospital moribund and could not be resuscitated. Thirteen required tracheostomy soon after admission, and it is our experience that about 70% of children with this condition require tracheostomy. A number of points can be made concerning the diagnosis of this condition. The sudden onset of upper respiratory obstruction with an inspiratory stridor, softer than that in acute laryngo-tracheitis, and an intermittent low-pitched expiratory snort is characteristic. The child is invariably toxic and the degree of illness is out of proportion to the respiratory embarrassment. The cough and voice are usually not hoarse. Direct examination of the pharynx is usually not necessary to confirm the diagnosis, and this examination can precipitate acute respiratory obstruction. It should never be performed unless facilities to establish an artificial airway are immediately available.

Chloramphenicol and penicillin are the drugs of choice in the management of this condition, and they should be administered parenterally. Penicillin should be used, as occasional cases

are due to β haemolytic streptococci. There is usually dramatic improvement four to six hours after the first dose of the drugs, so if it is possible to avoid the establishment of an artificial airway during this period the crisis is over.

Tracheostomy and nasotracheal intubation by a skilled anaesthetist are both satisfactory methods for the relief of the airways obstruction. The choice of method will be determined by the skill of the team responsible for the care of these patients.—We are, etc.,

PETER D. PHELAN.
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Urinary Tract Infections

SIR,—In this practice we find that the great majority of new cases of bacterial urinary infections are caused by organisms sensitive to sulphonamides. Thus, in the last four months, of all midstream urine specimens sent to the laboratory 53 were reported as having a significant bacterial growth (that is, more than 10^5 organisms/ml.) and of these 42 were sensitive to sulphonamides. Of the 11 sulphonamide-resistant specimens five were from patients already known to have chronic or recurrent urinary disease, leaving only six resistant specimens from new cases. These figures obviously apply only to those cases in which urine was sent to the laboratory. For various reasons a number of cases are treated without laboratory examination and the actual incidence of sulphonamide resistance is thereby probably exaggerated.

When confronted with a patient having symptoms suggesting urinary infection, our routine is to look at an uncentrifuged specimen with a 1/6th objective, and to send a mid-stream specimen of urine to the laboratory. If we find no pus cells no treatment is given. If pus cells are present in significant amount and if vaginal squames are absent, treatment is started with a sulphonamide. When the laboratory report returns, if the infection appears sulphonamide-resistant the patient is recalled, the urine is re-examined, and the patient asked about symptoms. If the infection seems to be responding sulphonamide treatment is continued; if not, treatment is switched to an appropriate alternative. On the whole there is close correlation between clinical results and in vitro sensitivity, but with the occasional case of in vitro resistance responding to sulphonamide treatment.

Our figures therefore support the opinion of your leader that a sulphonamide is a reasonable drug of first choice.

We are grateful to the laboratory staff at Queen Mary's Hospital, who have carried out all the examinations.

—We are, etc.,

J. H. S. HOPKINS.
K. BOHEIMER.
M. HENRY.
London S W.14.

SIR,—We were interested in your expert's contribution to this subject (7 September, p. 600) and the subsequent comments of Dr. D. Brooks (21 September, p. 745), Dr. M. H. Robertson (12 October, p. 121), and others.

The Mansfield Area Laboratory serves some 1,700 acute and chronic beds, and just under half (42%) of the coli–Proteus infections appear to be resistant to sulphonamides. The coli–Proteus ratio, however, is now below 2:1. The most marked change in resistance in yearly checks since 1963 has been the increased resistance in the last three years of *Proteus* spp. to nitrofurantoin. The most recent figures show the continued low resistance of 165 *Escherichia coli* and coliforms to the other three commonly used urine antibacterial agents compared with that of 200 *Proteus* spp.

	Resistant Organisms		
	Ampicillin	Nalidixic Acid	Nitrofurantoin
Esch. coli	4%	2%	2%
Proteus spp.	39.5%	20%	45%

In the autumn of 1967 the resistance of 149 *Proteus* spp. to nitrofurantoin was as much as 68%, compared with an average of 25% for 1963–5. It will be of interest to know the experience of other clinicians in this field.—We are, etc.,

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Hypnosis for Asthma

SIR,—While not decrying Dr. Monica K. McAllen's warning concerning the indiscriminate use of hypnosis in severe asthma (26 October, p. 251), I cannot agree with some of the assumptions she makes. I fail to see the logic when she infers that because a patient feels better, even though his respiratory function is unchanged, he will lower the dosage of his steroid but at the same time increase the use of his bronchial dilator drugs. In my opinion the indiscriminate use of steroids in mild asthmatics, and particularly in children, leads to far more danger than indiscriminate use of hypnosis in severe asthma. I deplore the fact that patients are subjected to steroids and never have the chance of having hypnotic therapy. I am quite sure that we will see far fewer patients on long-term steroids in the future if hypnosis is more widely used. I should like to point out that hypnosis was only used as suggestive therapy in the trial.

Finally, I would like to say that the indiscriminate use of hypnosis in any condition is to be deplored, as is the indiscriminate use of drugs which are so widely prescribed today.—I am, etc.,

London W.1. D. ZIMMERMAN.

Sudden Death in Asthma

SIR,—I wish to draw attention to the possible dangers of "asthma cures" sold over the counter.

The patient was an educated woman of 48 years who had suffered from bronchitis with asthma from the age of 5. Throughout her life she was treated along contemporary lines and had been thoroughly investigated and well advised by various chest physicians. She was treated with corticosteroids for the first time in 1965 on an intermittent basis at times of crises. In January 1966 she was given A.C.T.H. 20 units twice weekly. During these two years she improved dramatically in her mental outlook and physical abilities. She put on reasonable weight and, for the first time in years, was able to take on social activities outside the home.

On the day before her death she was seen in surgery because, although she had increased her A.C.T.H. to 20 units on alternate days as advised in exacerbations, she was still somewhat wheezy. She was also having her normal ephedrine, and although there was little cough she wondered if there might be an infective element. She was not worried, appeared happy, and was apyrexial with a good pulse. There was no cyanosis, but some minimal rhonchi throughout the chest. I felt that reassurance was required and gave a prescription for oxytetracycline, as she complained of a slight cough in the morning. That night she went to bed at her normal time and slept with two pillows until 6 a.m., when she and her husband wakened. She sat up in bed and took two inhalations of orciprenaline sulphate. She then emptied "about an eggcupful" of compound lobelia powder (lobelia and stramonium) into a saucer, ignited it, and inhaled the smoke for 5–10 minutes. She then made some gasping sounds and collapsed. When seen by me 5–10 minutes later she was pale, slightly cyanosed, the skin was moist, pupils dilated, the bladder had been voided, and heart and breath sounds were absent. Efforts at cardiac and respiratory resuscitation were to no avail.

At first the husband did not mention lobeline, and it was only on direct questioning afterwards that he told me of it. I had no knowledge that she ever used it, but learned that she had used it in this way for 20 years, but she had never previously been unwell as a result. Had I not questioned the husband in detail I should never have known of her habit. If I had known of it I might well have dismissed it as a relatively harmless herbal mixture. The sale of "old-fashioned" herbal compounds may increase if the asthmatic finds himself short of supplies after surgery hours. Needless to say, I hope that the sale of these old remedies will be stopped immediately.—I am, etc.,

Hatch End, Middx. GEORGE MCLAREN.

Conference Bureau

SIR,—I am sure that many others in the medical profession have had cause to regret that either they could not attend a meeting because of commitment to another conference or, as secretaries of a meeting, found their proposed date clashing with another. This seems to be an ever-increasing problem and perhaps a conference bureau at B.M.A. House might be the answer.

Here, for a fee, conferences might be booked so that the dates did not clash with a similarly related specialty, and lists of good hotels in the area and facilities for the entertainment of accompanying wives could be available. I am sure that many medical societies, associations, and large postgraduate centres would use such a service. Undoubtedly there would be requests from foreign visitors for the next year's consolidated United Kingdom list of medical meetings, and the bureau could supply them with the date and location of any meeting, and the name and address of the particular secretary.—I am, etc.,

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