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 herpetiformis¹ so much confusion has arisen, in our opinion quite unnecessarily, over this and other issues.

First of all dapsone as the cause of the enteropathy² was always a non-starter, as a number of patients in our original study had never taken the drug.¹ Secondly, folate deficiency² 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 intestine⁶ 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 diet³⁻⁵ 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 B₁₂ 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