Fig. 2 Patient aged 7 years: (x-rays of abdomen). After more than 2 years of treatment with alpha-mercaptopropionyl glycine, total dissolution of bilateral calculosis.

for the treatment and prevention in homozygotes for the disease. Alpha-mercaptopropionyl glycine may be safer than D-penicillamine.

Reference

- ¹ Ruysch van Dugteren G, Wiggelinkhuizen J. Dissolution of bilateral staghorn cystine renal calculi. *Arch Dis Child* 1979; **54**: 795-8.

AGOSTINO BERIO
Paediatric Clinic,
University of Genoa,
Via 5 Maggio 39,
Gaslini Institute,
Genoa, Italy

Dr Ruysch van Dugteren comments:

D-penicillamine has been, until recently, the only thiol readily available for the treatment of cystine stone-forming patients. Potentially serious side effects have necessitated the withdrawal of this drug in 50% of patients.

Since 1973 alpha-mercaptopropionyl glycine has been used in a number of (presumably) adult patients.¹⁻³ In a total of 26 patients so treated for up to 5 years no serious side effects were observed, and the effectiveness of the drug in reducing cystine excretion in the urine equalled that of D-penicillamine.

Professor Berio's letter provides further clinical evidence that alpha-mercaptopropionyl glycine may prove to be the drug of choice in children with cystinuria. It must be stressed however that a 3-pronged attack with (1) an increased fluid intake, (2) alkalinisation of urine, and (3) a thiol such as alpha-mercaptopropionyl glycine, has a far better chance of succeeding in dissolving stones than any one of these methods on its own.

References

- ¹ Remien A, Kallistratos G, Burchardt P. Treatment of cystinuria with Thiola (α -mercaptopropionyl glycine). *Eur Urol* 1975; **1**: 227-31.
- ² Terhorst B, Stuhlsatz H W. Cystinsteinterapie mit Mercaptopropionylglycin (MPG) (Thiola). *Urologe (A)* 1975; **14**: 190-3.
- ³ Hautmann R, Terhorst B, Stuhlsatz H W, Lutzeyer W. Mercaptopropionyl glycine: a progress in cystine stone therapy. *J Urol* 1977; **117**: 628-30.

G RUYSCH VAN DUGTEREN
Renal Clinic,
Red Cross War Memorial Children's Hospital,
Rondebosch 7700, Cape Town,
South Africa

Cows' milk protein-sensitive enteropathy

Sir,

In 1978 we proposed the following criteria for the diagnosis of cows' milk protein-sensitive enteropathy.¹

- (1) Clinical disease (diarrhoea with or without vomiting) while receiving cows' milk protein.
- (2) Clinical improvement on a diet free of cows' milk protein.
- (3) Normal or mildly abnormal histology of jejunal mucosa when taken 6-8 weeks after symptoms subside.
- (4) Histological relapse, with or without clinical relapse, after re-exposure to cows' milk protein.

We have now studied a further 60 infants. In analysing the clinical, histological, and enzymological results we have found that cows' milk protein can cause depletion of the mucosal oligosaccharidases, and malabsorption of xylose in the absence of mucosal damage visible under the light microscope.

These 60 infants were clinically suspected to have intolerance to cows' milk protein. After their fluid, electrolytes, and acid-base imbalance had been corrected, they were started on a lactose- and cows' milk protein-free formula which was maintained for 6-8 weeks. After this they were readmitted for milk challenge which was performed as has been described.² The clinical features of these 60 infants at admission have been described.²

From clinical, histological, and enzymological response to cows' milk protein, after milk provocation, each infant could be placed in one of 4 groups.

Group 1 consisted of 22 infants with significant histological changes associated with pronounced reductions in disaccharidase levels. All 22 infants developed diarrhoea, some of them with vomiting, fever, or lethargy, 17 of them within 24 hours and five 3 to 28 days after milk provocation. 11 of 12 infants tested had reducing sugar in the stools.

Group 2 consisted of 22 infants with significant histological changes and reduction in enzyme levels (except in

one in whom the levels of all 3 enzymes remained unaltered despite significant histological changes) but without clinical symptoms. At follow-up 4 weeks later, all 22 infants remained well on a cows' protein-based formula despite the histological findings.

Group 3 consisted of 6 infants with normal histological findings but with depressed enzyme levels. Five of them tolerated cows' milk but the 6th developed diarrhoea 48 hours after milk provocation, although the stools collected before and after milk provocation were positive for rotavirus.

Group 4 consisted of 10 infants in whom there was no histological, enzymological, or clinical relapse. Although some variability in the pre- and postchallenge enzyme values was observed, unlike 50 infants in groups 1, 2, and 3 there was no consistent fall in enzyme levels.

Although the reduction in the mean levels of the disaccharidases in group 1 was significantly greater than that in group 2 or 3, individual cases overlapped greatly.

The histological findings and enzyme values of the 4 groups have been described.²

Xylose absorption studies, using the method of Rolles *et al.*,³ performed in the 6 infants in group 3 showed a drop in the postchallenge compared with the prechallenge levels. It appears that cows' milk protein can cause enzyme depletion and xylose malabsorption without obvious histological changes. It is possible that the enzyme depletion is associated with subcellular changes that are

not visible under the light microscope. These observations now lead us to propose that our original combined clinical and histological criteria should be modified to include enzymological criteria:

- (1) Clinical disease (diarrhoea with or without vomiting) while receiving cows' milk protein.
- (2) Clinical improvement on a diet free of cows' milk protein.
- (3) Normal or mildly abnormal jejunal mucosa with normal oligosaccharidase levels 6–8 weeks after symptoms subside.
- (4) Histological or enzymological relapse with or without clinical relapse on re-exposure to cows' milk protein.

References

- ¹ Iyngkaran N, Robinson M J, Prathap K, Sumithran E, Yadav M. Cows' milk protein-sensitive enteropathy. Combined clinical and histological criteria for diagnosis. *Arch Dis Child* 1978; **53**: 20–6.
- ² Iyngkaran N, Abidin Z, Davis K, *et al.* Acquired carbohydrate intolerance and cow milk protein-sensitive enteropathy in young infants. *J Pediatr* 1979; **95**: 373–8.
- ³ Rolles C J, Kendall M J, Nutter S, Anderson C M. One-hour blood-xylose screening-test for coeliac disease in infants and young children. *Lancet* 1973; **ii**: 1043–5.

N IYNGKARAN AND ZAINAL ABIDIN
University of Malaya,
Department of Paediatrics,
Malaysia