LETTERS TO THE EDITOR

Fragile X syndrome

EDITOR,—Our experience in a special school in Newcastle upon Tyne lends support to the proposal by Slaney *et al* to screen for fragile X syndrome.¹ Many individuals with special educational needs have not had recent investigation. In a preliminary survey of records for the year 1992/3, of the 58 individuals (44 male and 14 female) who had statutory reassessment of special educational needs in Newcastle upon Tyne, 48 were considered to have mild learning difficulties, 10 severe. All those having severe learning difficulties had been fully investigated by this stage. Among those with mild learning difficulties, one individual was already known to have fragile X syndrome but in 41/48 there was neither known diagnosis nor record of genetic investigations. Over half of these children, 21/41, had a family history of learning difficulties.

On the basis of these findings, chromosome analysis and molecular investigations for the fragile X syndrome was offered at one special school as a part of the medical review undertaken for the statutory reassessment of special educational needs during the period September 1993–July 1994. None of the 34 children, aged 13–14 years, had a recognised diagnosis, although two had had previous genetic investigations. There were 32 pupils with no known diagnosis to whom testing was offered, after full discussion of the details and implications of such investigations with each family. Blood samples were obtained from three girls and 23 boys: the remaining six pupils declined testing on account of fear of venepuncture. One boy with fragile X syndrome, one boy with Klinefelter's syndrome 47,XXY, and one chromosomal deletion 46,XY del (18) (q22?2) were detected. A satellite Y chromosome was observed in one boy, which was thought to be a normal variant.

The families were referred for specialist genetic counselling. In the three cases where a diagnosis was given, parents were relieved to have an explanation for their child's learning difficulty. Liaison with educational and community provision was facilitated. Thus, in three out of 26 children tested, a previously unrecognised diagnosis was made. Not only did we detect previously unrecognised fragile X syndrome but, with the inclusion of cytogenetic analysis as recommended in screening of populations selected on the basis of learning difficulties (unlike the restricted study by Slaney *et al*), also detected other important abnormalities. In their study, counselling was retrospective. In practice, we found that the opportunity to counsel families before testing could easily assimilated by a school doctor within the procedure required for medical input associated with the Education Act 1981, when parental concerns about the aetiology and implications of their child's problems often need to be readdressed. We believe that the offer of genetic screening in this way is feasible, within both the existing community health and regional genetic service resources, and welcomed by those involved. The findings of our study would support an argument to retain medical input into the 'transitional review' (Education Act 1993) of

children who have statements of special educational needs, at least until the cohort of younger children, who are more likely to have been investigated, is reached.

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1 Slaney SF, Wilkie AOM, Hirst MC, *et al*. DNA testing for fragile X syndrome in schools for learning difficulties. *Arch Dis Child* 1995; 72: 33–7.

Do children with hepatic cirrhosis complicating cystic fibrosis receive too much pancreatic enzyme?

EDITOR,—Colonic strictures^{1 2} and thickening of the bowel³ have recently been recognised in children with cystic fibrosis receiving high doses of pancreatic enzymes. We are concerned that some children with the complication of hepatic cirrhosis in cystic fibrosis are receiving excessive doses of pancreatic enzyme supplements in an attempt to control their steatorrhoea.

In the past 4.5 years we have assessed 13 children with cystic fibrosis complicated by hepatic cirrhosis for liver transplantation. Twelve were malnourished with median body mass index 16.5 (range 13.4–23.3) and upper arm circumference measurements all under the 5th centile. Seven gave a history of steatorrhoea and six required regular laxatives to prevent distal intestinal obstruction. There was wide variation in the daily intake of pancreatic enzymes (table) but the mean for the group was 16 653 units/kg/day of lipase and 544 units/kg/day of protease. In a recent study Sweeney *et al* found that a daily protease intake of more than 265 units/kg was a risk factor for bowel wall thickening and that the risk rose 10 times if laxatives were taken in addition.³ Six of the children we report here had high daily intakes of protease (410–3688 units/kg/day), five received high strength pancreatic enzyme preparations, and three of these also required regular laxatives.

We did not assess the bowel wall thickness in these children, but, when investigated for abdominal pain by abdominal computed tomography, patient 6 was found to have 3 mm thickening of the walls of both the small and large intestine. Patient 5 developed a haemorrhagic colitis which resolved when his pancreatic enzyme intake was reduced. Both

these patients had received high strength enzyme preparations.

Nine of these children have now received liver grafts and their daily enzyme intake is greatly reduced (table). The average daily protease intake has fallen by 56% and the daily lipase intake by 61%. In spite of this reduction in pancreatic enzymes fat absorption has improved and none of the children now have steatorrhoea. All except one now receive normal strength pancreatic enzyme preparations.

In children with cystic fibrosis and hepatic cirrhosis steatorrhoea may be a symptom of both the hepatic disease and pancreatic insufficiency. There is little benefit to be gained from increasing the enzyme doses beyond the recommended amounts of 265 units/kg/day of protease³ and doing so may be associated with considerable risk of gut complications.

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- 1 Smyth RL, van-Velzen D, Smyth AR, Lloyd DA, Heaf DF. Strictures of ascending colon in cystic fibrosis and high-strength pancreatic enzymes. *Lancet* 1994; 343: 85–6.
- 2 Taylor CJ. Colonic strictures in cystic fibrosis. *Lancet* 1994; 343: 615–6.
- 3 Sweeney EJM, Oades PJ, Buchdahl R, Rosenthal M, Bush A. Relation of thickening of colon wall to pancreatic-enzyme treatment in cystic fibrosis. *Lancet* 1995; 345: 752–6.

Monoclonal IgA gammopathy in a well infant

EDITOR,—We report on an unusual case of monoclonal gammopathy in an infant with no evidence of an underlying disorder. A 15 month old girl was referred because of raised serum IgA concentration (3.50 g/l) and λ IgA paraprotein. The indication for the investigation had been recurrent upper respiratory tract infections: five to six per year since attendance at day school. Her perinatal and previous medical history were unremarkable, with no suggestion of immunodeficiency, serious infections, or malignant disorder.

Her physical examination was normal (weight: 25th centile, height: 50th centile). On follow up at 20 months she had remained well and had developed varicella at 19 months with no complications, suggestive of intact T cell function.

The λ IgA paraprotein was confirmed at 18 and 20 months by serum electrophoresis and immunofixation of the α and λ chain (1–2 g/l on both occasions). Investigations showed a haemoglobin concentration of 120 g/l, white

Details of children studied

Patient No	Sex	Age (years)	Before transplant			After transplant		
			Lipase (units/kg/day)	Protease (units/kg/day)	Steatorrhoea	Lipase (units/kg/day)	Protease (units/kg/day)	Steatorrhoea
1	F	14.3	7385	194	—	4634	122	—
2	M	11.5	7385	194	—	5538	145	—
3	M	14.0	4900	129	—	4000	264	—
4	F	8.4	22 727	425	+	5533	145	—
5	M	5.8	73 765	3688	+	15 238	400	—
6	F	16.4	19 286	360	+	8378	545	—
7	M	19.0	5263	98	+	2631	49	—
8	F	12.9	17 931	471	+			
9	F	13.4	5000	131	+			
10	F	15.8	8000	210	—			
11	F	13.0	6824	179	—			
12	M	10.5	22 400	588	—			
13	M	11.4	15 625	410	+			
Mean			16 653	544		6565	239	