LETTERS TO THE EDITOR

Byler's syndrome

EDITOR,—The report of Byler's syndrome with raised sweat electrolytes in an Irish traveller kindred[1] interests us, as we have observed raised sweat electrolytes in two members of the original Byler kindred who have Byler's disease. Neither has cystic fibrosis; both underwent liver transplantation in their second decade and subsequently developed pancreatic disease. One has had recurrent pancreatitis and the other has a fibrotic pancreas with exocrine insufficiency.[2] In the children without Byler's disease whom we attend, pancreatic disease after liver transplantation is not usual. Have affected traveller children, particularly older ones, had pancreatitis?

We can provide additional information on the sister and brother with progressive familial intrahepatic cholestasis and raised sweat electrolytes referred to by Bourke *et al*[1] and described by Lloyd-Still[3 4] (fig 1). Neither parent was of Irish or Amish background; the father (II.2) came of Norwegian and the mother (II.3) of Italian stock. At age 3.5 years, the boy (III.5) had normal serum γ-glutamyltranspeptidase activity (29 U/ml; expected, <40) and moderately raised cholesterol concentrations (8.0 mmol/l; expected 3.9–6.5; determination at age 1 year,[4] 1.6) with marked hyperbilirubinaemia (458 μmol/l; expected, 1.7–20.5). Fasting serum bile acid concentrations were not measured but at age 1 year had been 'markedly elevated'[4]; intense pruritus was present. Serum amylase and lipase activities were normal.

The (III.2) girl came to liver transplantation aged 8 years and the boy 4.5 years. Both died of infection within two months of surgery. On light microscopy, findings in the native livers resembled those in the older traveller children[1] and in the two Amish children who underwent hepatectomy.[5] Coarsely granular bile like that seen in Byler's disease ('Byler bile')[5] was found on transmission electron microscopy (fig 2).

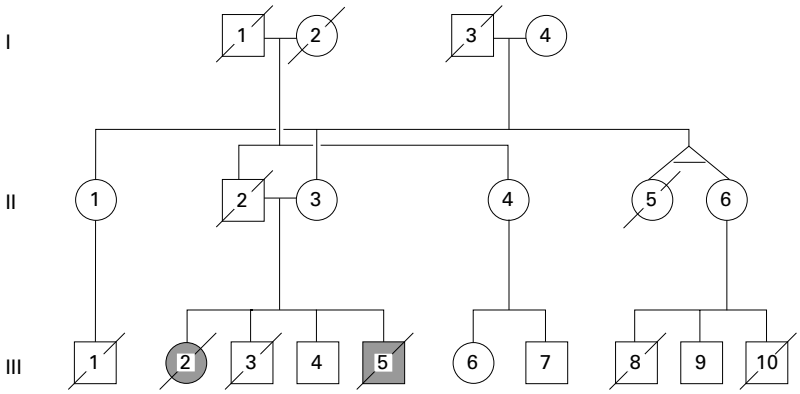

Figure 1 Pedigree of family with Byler disease-like progressive familial intrahepatic cholestasis described by Lloyd-Still.[3 4]

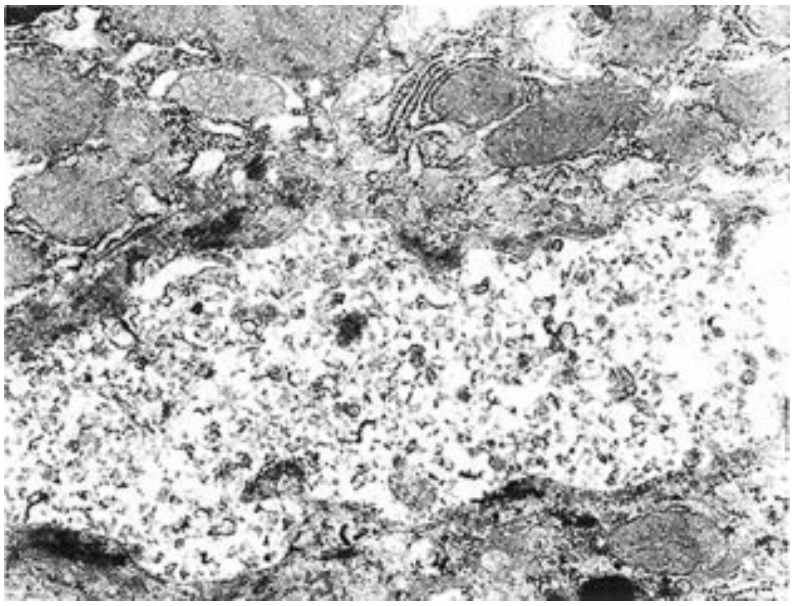

Figure 2 Transmission electron micrograph of coarsely granular bile, characteristic of bile from children with Byler's disease,[5] *within canaliculus of liver obtained at hepatectomy in affected boy (III.3); 4% paraformaldehyde/0.5% glutaraldehyde in Swenson's phosphate buffer, pH 7.3; OsO_4/uranyl acetate/lead citrate (original magnification × 18 000).*

Convergence of phenotypes leads us to believe that these children may have had a lesion at 18q21-q22, the Byler's disease locus,[6] to which the disorder in the traveller kindred also has been mapped.[7] We would like to know what was seen if liver tissue from an affected traveller child was examined by transmission electron microscopy.

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Dr Bourke and Professor Drumm comment:
We thank Dr Agostini and colleagues for their interest in our paper describing an Irish kindred with Byler syndrome.[1] As yet, we have not examined liver tissue from the traveller kindred using transmission electron microscopy. As these children likely will need further evaluation and/or transplantation in the coming years we will have the opportunity to undertake further studies including analysis of biliary bile acid content and examination of biopsy samples for the presence of 'Byler bile'.

We are aware of the report of Knisely *et al* describing pancreatic disease in members of the original Amish kindred with Byler's disease.[2] Although we have not observed pancreatitis or evidence of pancreatic dysfunction in the Irish traveller family with Byler's syndrome, one of us (BB) has encountered a child with progressive familial intrahepatic cholestasis and chronic pancreatitis at another institution (patient of E Roberts and R Superina, Hospital For Sick Children, Toronto). Whether this child has a mutation at 18q21-q22 is currently being evaluated.

The presence of raised sweat electrolytes and pancreatitis in a subset of these children with Byler's disease/syndrome is certainly intriguing and raises interesting questions about the function of the mutated allele at 18q21-22. Ongoing genetic studies of members of the original kindred and unrelated families such as this Irish family should soon provide answers to these questions.

1 Bourke B, Goggin N, Walsh D, Kennedy S, Setchell KDR, Drumm B. Byler-like familial cholestasis in an extended kindred. *Arch Dis Child* 1996;**75**:223-7.
2 Knisely AS, Boyle JT, Naylor EW, Klinger K, Freimer NB, Kocoshis S. Pancreatic dysfunction in Byler disease. *J Pediatr Gastroenterol Nutr* 1995;**21**:328 (abstr).
3 Lloyd-Still JD. Familial cholestatic syndrome with elevated sweat electrolytes. In: Sturgess JM, ed. *Proceedings of the 8th International Congress on Cystic Fibrosis.* Toronto: Imperial Press, 1980:25a (abstr).
4 Lloyd-Still JD. Familial cholestasis with elevated sweat electrolyte concentrations. *J Pediatr* 1981;**99**:580-3.
5 Bull LN, Carlton VEH, Stricker NL, *et al*. Genetic and morphologic findings in progressive familial intrahepatic cholestasis (Byler dis-

ease and Byler syndrome): evidence for heterogeneity. *Hepatology* 1997;**26**:155-64.
6 Carlton VEH, Knisely AS, Freimer NB. Mapping of a locus for progressive familial intrahepatic cholestasis (Byler disease) to 18q21-q22, the benign recurrent intrahepatic cholestasis region. *Hum Mol Genet* 1995;**4**:1049-53.
7 Barton DE, McQuaid S, Bourke B, *et al*. Familial progressive intrahepatic cholestasis (Byler disease): evidence that the disease haplotype in the Old Order Amish is also found in the Irish 'traveller' population. *Am J Hum Genet* 1996; **59**:A248 (abstr).

Intestinal neuronal dysplasia associated with cystic fibrosis

EDITOR,—The association between cystic fibrosis and intestinal neuronal dysplasia (IND) has been rarely described.[1] We report a case of full thickness, biopsy proved, IND type B of the ileum and colon associated with cystic fibrosis. The boy was born at full term to non-consanguineous parents. Because of obstructive symptoms, several resections were performed: 20 cm of distal ileum after birth; distal ileum and part of ascending colon at the age of 18 days; ileum, part of jejunum, and colon at the age of 2 months. A series of radiographs of the upper gastrointestinal tract series showed a normal duodenum at 16 months and no dilatations of the remaining intestinal tract. Contrast appeared in the rectum after 90 minutes. By histology, the proximal ileal tract had 6.25 neurons/mm of myenteric plexus, according to Smith's method (normal values: 2–4),[2] the ascending colon 16.0 neurons/mm, and the transverse colon 8 neurons/rnm. Acetylcholinesterase staining showed an increase of number of submucosal ganglia, neuronal heterotopy, and increase of positive fibres in circular muscular layer and lamina propria.[3]

NADPH-DH showed an increased number of neurons in myenteric and submucosal plexuses. The study with neurofilaments (NF65, NN18) showed a normal maturity of neurons. The results of two sweat tests were abnormal. An homozygosity for the delta F508 mutation was demonstrated and both parents were carriers of the allele. It is possible that there is an NID-B determining gene linked to the cystic fibrosis transmembrane conductance regulator locus for cystic fibrosis, localised on chromosome 7q.

We suggest that intestinal neuronal dysplasia should be considered as an underestimated, underlying cause in patients with cystic fibrosis having functional small bowel dysmotility and obstruction leading to emergencies, such as meconium ileus in neonates or meconium ileus equivalent in children and adults.

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1 Wildhaber J, Seelentag WKF, Spiegel R, Schoni MH. Cystic fibrosis associated with neuronal intestinal dysplasia ype B: a case report. *J Pediatr Surg* 1996;**31**:9411-4.
2 Smith VV. Intestinal neuronal density in childhood: a baseline for objective assessment of hypo- and hyperganglionosis. *Pediatr Pathol* 1993;**13**:225-37.
3 Milla PJ, Smith VV. Intestinal neuronal dysplasia. *J Pediatr Gastroenterol Nutr* 1993;**17**:356-7.

Legislation and drug trials

EDITOR,—In their recent leader, Walsh and Drumm point out important difficulties facing paediatricians wishing to conduct intervention trials where the aim is to prevent disease in children (or anyone incapable of giving fully informed consent) in Ireland.[1] It is worth pointing out that the Irish legislation that prevents such studies thereby prevents all vaccine studies in children from being conducted in that country. Vaccines against *Haemophilus influenzae* type b and more recently acellular vaccines against pertussis have been licensed and introduced in Ireland on the basis of immunogenicity and efficacy studies done elsewhere. While it is not necessary for each vaccine to be studied in every country, there is a clear need for all countries to be able to contribute clinical studies particularly as the number of new antigens and combinations grows. It is to be hoped that the current stranglehold on research into child health in Ireland is loosened in the near future.

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1 Walsh D, Drumm B. Legislation and drug trials. *Arch Dis Child* 1997;**76**:296-7.

Situs inversus and left sided pyloric tumours

EDITOR,—The case report by Harrington *et al*[1] reminded me of the procedure to examine for a pyloric tumour taught by Dr M J Simpkiss, based on an identical case he had seen decades previously. Namely, define the apex beat before examining the abdomen. This combination will occur again, just like the case of 'The glass eye...'.[2]

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1 Harrington B, Chambers T, Grier D. A diagnosis obscured: pyloric stenosis with situs inversus [letter]. *Arch Dis Child* 1997;**76**:385.
2 Gordon RM, Greene JM, Kassirer JP. Solution to a 'medical mystery'[letter]. *N Engl J Med* 1997;**336**:1393-4.

Head lice in schoolchildren

EDITOR,—I am grateful to Ibarra and Hall for reviewing a common problem in general practice.[1] I recently performed a Medline search of the literature regarding the role of hairdressers and head lice. To my concern no references existed and my personal experience compounds my view that some gentlemen's hairdressers do not wash, let alone sterilise their 'tools' or drapes between customers. Therapy has an important role in the eradication of head lice, but there is a more important public health issue in relation to prevention.

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1 Ibarra J, Hall DMB. Head lice in schoolchildren. *Arch Dis Child* 1996;**75**:471-3.