LETTERS TO THE EDITOR

Byler’s syndrome

Editor,—The report of Byler’s syndrome with raised sweat electrolytes in an Irish traveller kindred1 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.1 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?

![Pedigree of family with Byler disease-like progressive familial intrahepatic cholestasis described by Lloyd-Still.](image)

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

![Transmission electron micrograph of coarsely granular bile, characteristic of bile from children with Byler’s disease,](image)

Figure 2  Transmission electron micrograph of coarsely granular bile, characteristic of bile from children with Byler’s disease.1 Within canaliculus of liver obtained at hepatectomy in affected boy (III.5); 4% paraformaldehyde/0.5% glutaraldehyde in Swenson’s phosphate buffer, pH 7.3; OsO4/uranyl acetate/lead citrate (original magnification × 18 600).

We can provide additional information on the sister and brother with progressive familial intrahepatic cholestasis and raised sweat electrolytes referred to by Bourke et al1 and described by Lloyd-Still4 (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 (5.0 mmol/l; expected, 3.9–6.5; determination at age 1 year, 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’; 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 children1 and in the two Amish children who underwent hepaticectomy.1 Coarsely granular bile like that seen in Byler’s disease (‘Byler bile’)1 was found on transmission electron microscopy (fig 2).

Convergence of phenotypes leads us to believe that these children may have had a lesion at 18q21-q22, the Byler’s disease locus,2 to which the disorder in the traveller kindred also has been mapped.3 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.

5 Bull LN, Carlton VEH, Stricker NL, et al. Genetic and morphologic findings in progressive familial intrahepatic cholestasis (Byler dis-
Intestinal neuronal dysplasia associated with cystic fibrosis

**EDITOR—** The association between cystic fibrosis and intestinal neuronal dysplasia (IND) has been rarely described. 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/mm² of myenteric plexus, according to Smith’s method (normal values: 2–4), the ascending colon 16.0 neurons/mm², and the transverse colon 8 neurons/mm². Acetylcholinesterase staining showed an increase of number of submucosal ganglia, neuronal heterotopy, and increase of positive fibres in circular muscular layer and lamina propria.

**Legend to figures:**


**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. 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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