

- 3 Walker-Smith J, Hamilton JR, Walker WA. Practical paediatric gastroenterology. Norwich: Butterworth, 1983: 254–55
- 4 Williams CB, Nicholls S. Endoscopic features of chronic inflammatory bowel disease in childhood. *Baillière's Clin Gastroenterol* 1994; 8: 121–31
- 5 Ward AM, Riches PG, eds. PRU handbook of clinical immunochemistry, 4th ed. Sheffield: Hallmark: 1993: 157–66.

Sir—After reading Andrew Wakefield and colleagues' article<sup>1</sup> I did a simple Internet search and quickly found the *Society for the Autistically Handicapped*. (<http://www.mplc.co.uk/eduweb/sites/autism/index.html>) I downloaded a 48 page fact sheet produced for the society by Dawbarns, a firm of solicitors in King's Lynn.

It seems likely then that some of the children investigated by Wakefield et al came to attention because of the activities of this society; and information from parents referred in this way would suffer from recall bias. It is a pity that Wakefield et al do not identify the manner in which the 12 children investigated were referred (eg, from local general practitioners, self-referral via parents, or secondary/tertiary or international referral). Furthermore, if some children were referred, directly or indirectly, because of the activities of the Society for the Autistically Handicapped, Wakefield should have declared his cooperation with that organisation.

#### A Rouse

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- 1 Wakefield AJ, Murch SH, Anthony A, et al. Ileal-lymphoid-nodular hyperplasia, non-specific colitis and pervasive-developmental disorder in children. *Lancet* 1998; 351: 637–42.

#### Author's reply

Sir—D R Walker states that “biased selection of patients will influence what you hear”. Bias occurs in science when data are either wittingly or unwittingly concealed. Does he condone the exclusion of a potentially significant element of the history? He asks for virological evidence: we refer him to our abstract (*Gut* 1998; 42: A86). Sadly, Walker casts the value of the medical history, the process of peer review, and this paediatric diaspora to the scrapheap of bad science and anecdote.

Leonard Sinclair and Peter Richmond and David Goldblatt correctly point out the inappropriate use of adult reference ranges. We stated that IgA levels were low in four out of 12 affected children. The normal range for IgA in this age group is 0.5–2.4 g/dL, and, only one child was outside the normal range. Similarly, the appropriate age-related range for

alkaline phosphatase is 250–800 U/L. These errors do not affect the conclusions of the paper, particularly the identification of ileal lymphoid nodular hyperplasia and colonic inflammation in a group of children with developmental disorder.

A Rouse suggests that litigation bias might exist by virtue of information that he has downloaded from the Internet, from the *Society for the Autistically Handicapped*. Only one author (AJW) has agreed to help evaluate a small number of these children on behalf of the Legal Aid Board. These children have all been seen expressly on the basis that they were referred through the normal channels (eg, from general practitioner, child psychiatrist, or community paediatrician) on the merits of their symptoms. AJW had never heard of the *Society for the Autistically Handicapped* and no fact sheet has been provided for them to distribute to interested parties. The only fact sheet that we have produced is for general practitioners, which describes the background and protocol for investigation of children with autism and gastrointestinal symptoms. Finally all those children referred to us (including the 53 who have been investigated already and those on a waiting list that extends into 1999) have come through the formal channels described above. No conflict of interest exists.

The authors stand by their findings. We recommend that paediatric gastroenterologists investigate this problem further, since it is our belief that there is both a large unmet need in the community and a possible window-of-opportunity for some children with autism.

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Sir—Letters in *The Lancet* and the letter of March 27, 1998 (PL/CMO/98/2) to all doctors by Sir Kenneth Calman, Chief Medical Officer, Department of Health, on measles, mumps, and rubella (MMR) vaccine, Crohn's disease, and autism are in danger of completely obscuring the observation we made of an association between ileal lymphoid nodular hyperplasia, non-specific colitis, and autism in childhood. As the senior clinician on the study I would like to make several points.

We did not describe any increase in Crohn's disease or ulcerative colitis in children with autism so the observations of Eric Fombonne (March 28, p 255)<sup>1</sup> are not surprising. What we did describe was non-specific colitis with

ileal lymphoid nodular hyperplasia. The colitis we described was ignored in Robert Chen and Frank De Stefano's commentary accompanying our *Lancet* paper. Calman seeks to dismiss our findings concerning lymphoid hyperplasia and also makes no mention of colitis. Indeed, he selectively quotes from my own publications on this topic since 1983 but makes a number of false assumptions. Because our *Lancet* paper was a preliminary report we did not expand on the diagnostic term “ileal lymphoid nodular hyperplasia”. This is a term often used inexactly by radiologists and endoscopists to describe both a normal finding in children and a pathological finding which may be accompanied by abdominal pain and diarrhoea requiring therapy.

The 1983 Walker-Smith, Hamilton, and Walker reference cited by Calman does indeed state that ileal lymphoid nodular hyperplasia “has been termed benign” but we went on to say that recurrent abdominal pain and diarrhoea often prompt a diagnostic barium study to permit this radiological diagnosis. We also stated that symptoms could be so severe that steroids may be used and even that surgery might be contemplated (although is this not recommended owing to uncertain knowledge concerning outcome). Calman also cites a 1990 radiological study<sup>3</sup> which indicated that 24% of children referred for investigation of inflammatory bowel disease had a form of lymphoid nodular hyperplasia with a disorganised mucosal fold pattern. What was new was that this report distinguished two patterns of lymphoid hyperplasia. Lymphoid hyperplasia causing small nodular defects about 2 mm in diameter is considered a normal variant but there is a more exaggerated change, probably reflecting enlargement of Peyer's patches. This latter pattern can occur in yersiniosis and it could represent an early lesion of Crohn's disease. That paper referred back to our 1987 endoscopic study describing lymphoid follicles in the ileum of 23 children of whom only seven children had identifiable disease. Three cases were described as lymphoid nodular hyperplasia with recurrent abdominal pain and diarrhoea. This proportion (13%) accords with the 12% found in the endoscopic study of Lindley and Milla.<sup>4</sup> In their endoscopic study Williams and Nicholls<sup>5</sup> referred to the radiological diagnostic confusion.<sup>3</sup> They describe “1–5 mm nodules, usually pink and shiny . . . dotted singly or in coalescing masses. Localised conglomerations around 10–15 mm diameter are described as Peyer's