

STATEMENT

A statement by the editors of *The Lancet*

On February 18, 2004, serious allegations of research misconduct concerning an article by Dr Andrew Wakefield and colleagues published in *The Lancet* in February, 1998,¹ were brought to the attention of senior editorial staff of the journal.

The allegations are:

- (1) That, contrary to a statement in the *Lancet* paper, ethics approval for the investigations conducted on the children reported in the study, some of them highly invasive (eg, lumbar puncture), had not been given.
- (2) That the study reported in *The Lancet* was completed under the cover of ethics approval for an entirely different study of 25 children with “A new paediatric syndrome: enteritis and disintegrative disorder following measles/rubella vaccination”.
- (3) That, contrary to the statement in the *Lancet* paper that children were “consecutively referred to the department of paediatric gastroenterology” at the Royal Free Hospital and School of Medicine, children were invited to participate in the study by Dr Andrew Wakefield and Professor John Walker-Smith, thus biasing the selection of children in favour of families reporting an association between their child’s illness and the MMR vaccine.
- (4) That the children who were reported in the *Lancet* study were also part of a Legal Aid Board funded pilot project, led by Dr Wakefield—a pilot project with the aim of investigating the grounds for pursuing a multi-party legal action on behalf of parents of allegedly vaccine-damaged children, the existence of which was not disclosed to the editors of *The Lancet*.
- (5) That the results eventually reported in the 1998 *Lancet* paper were passed to lawyers and used to justify the multi-party legal action prior to publication, a fact that was not disclosed to the editors of *The Lancet*.
- (6) That Dr Wakefield received £55 000 from the Legal Aid Board to conduct this pilot project and that, since there was a substantial overlap of children in both the Legal Aid Board funded pilot project and the *Lancet* paper, this was a financial conflict of interest that should have been declared to the editors and was not.²

The editors of *The Lancet* have seen and reviewed the documentary evidence available in support of these allegations. In acting on this information we have followed the guidelines on dealing with alleged misconduct as set out by the UK Committee on Publication Ethics, on which representatives of *The Lancet* sit.³ We have presented this evidence to the senior authors of the 1998 *Lancet* paper (Dr Wakefield, Professor John Walker-Smith, Dr Peter Harvey, and Dr Simon Murch) in order to seek their responses. Dr Richard Horton, Editor of *The Lancet*, has also shared this information with Professor Humphrey Hodgson, vice-Dean and campus director of the Royal Free and University College Medical School, London, the institution at which the original work took place.

With this notice are accompanying statements from Dr Murch, Professor Walker-Smith, and Dr Wakefield, answering the allegations of research and publication misconduct, together with a statement from the Royal Free and University College Medical School.

Given these four statements, together with an evaluation of the available documents, we consider that:

Allegation 1

The evidence we have seen indicates that ethics committee approval was given for data collection from clinically indicated investigations in the children with an initially undiagnosed illness and who were described in the 1998 *Lancet* paper. This illness was at first believed to be enteritis combined with a disintegrative disorder. Subsequent detailed clinical investigations eventually showed this condition to be the syndrome finally reported in *The Lancet*. This course of events was not described in full in the *Lancet* paper, although the similarity of the behavioural changes with those of a disintegrative psychosis (Heller’s disease) were commented on in the discussion section of the 1998 *Lancet* paper. In summary, the evidence does not support this allegation.

Allegation 2

As described under Allegation 1, detailed clinically appropriate investigations led to a re-evaluation of the initial diagnosis of these children, as set out in protocol 172-96. The evidence we have seen indicates that there was no attempt by investigators to conduct the study of children reported in *The Lancet* in 1998 under cover of an entirely different investigation. In sum, the evidence does not support this allegation.

Allegation 3

Professor Walker-Smith notes that although the referral pattern was unusual—direct contact by patients with Dr Wakefield leading to referral to the Royal Free—the children were indeed consecutively referred. He reports that to the best of his recollection he did not invite any children to participate in the study. Thus, as far as the facts can be ascertained by a review of the case notes and from memory, children reported in the 1998 *Lancet* paper were consecutively referred to the Royal Free and were not deliberately sought by the authors for inclusion in their study based on parents’ beliefs about an association between their child’s illness and the MMR vaccine.

Allegations 4–6

Dr Wakefield had two roles in this work. First, he was the lead investigator of a Royal Free study into the nature of a new syndrome with bowel and psychiatric symptoms. Second, he was commissioned through a lawyer to undertake virological investigations as part of a study funded by the Legal Aid Board. At the time of submission and eventual publication of his 1998 *Lancet* paper, this second study had not been disclosed to the editors of *The Lancet* and his co-authors. We judge that it should have been so disclosed, irrespective of the number of children overlapping between the pilot project funded by the Legal Aid Board and the *Lancet* paper. Such a disclosure would have provided important information to editors and peer reviewers about the context in which this work was taking place—a context that would have been vital in making a final decision about publication. We believe that our conflict of interest guidelines at the time should have triggered such a disclosure, including the fact that a significant minority of the children described in

the *Lancet* paper were also part of the Legal Aid Board funded pilot project. These guidelines stated that: "The conflict of interest test is a simple one. Is there anything . . . that would embarrass you if it were to emerge after publication and you had not declared it?"

The difficulty of adopting a dual role as a clinical investigator and as a participant in an evaluation on behalf of the Legal Aid Board is revealed in Dr Wakefield's response to Allegation 5. Although it may be correct that "this [*Lancet*] publication . . . added nothing further to the issue of causation than that that was already well known to the lawyers", the perception of a potential conflict of interest remains. Editors and reviewers should have had an opportunity to take his dual role into consideration when assessing this paper for publication.

Finally, although the Legal Aid Board funding referred to a different aspect of Dr Wakefield's work from that reported in *The Lancet*, the perception of a conflict of interest nevertheless remains. This funding source should, we judge, have been disclosed to the editors of the journal.

Summary

The first three allegations of alleged research misconduct have been answered by clarifications provided by the senior authors of this work. The wording in the published paper regarding Ethical Practice Committee approval and patient referral was accurate, yet at the same time summarised obviously lengthy and complex institutional and clinical review and referral procedures. In the light of the public controversy surrounding this work and the allegations made to us, one could argue that more explanation could and should have been provided in the original paper. Although, with hindsight, this seems a reasonable criticism, all research papers published by all journals are inevitably concise accounts of often complicated research protocols. We do not judge that there was any intention to conceal information or deceive editors, reviewers, or readers about the ethical justification for this work and the nature of patient referral. We are pleased to have had the opportunity to clarify the scientific record over the matters raised by these serious allegations.

We regret that aspects of funding for parallel and related work and the existence of ongoing litigation that had been known during clinical evaluation of the children reported in the 1998 *Lancet* paper were not disclosed to editors. We also regret that the overlap between children in the *Lancet* paper and in the Legal Aid Board funded pilot project was not revealed to us. We judge that all this information would have been material to our decision-making about the paper's suitability, credibility, and validity for publication.

In considering what sanctions *The Lancet* should apply, the COPE guidelines³ give eight options in a ranked order of severity. Given the public-health importance of MMR vaccination, together with the public interest in this issue, we have decided to pursue a course of full disclosure and transparency concerning these allegations, the authors' responses, the institution's judgment, and our evaluation.

Richard Horton

Editor, *The Lancet*, 32 Jamestown Road, London NW1 7BY, UK
(e-mail: richard.horton@lancet.com)

- 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: 637-41.
- 2 In 1998, *The Lancet* required that: "The Editor needs to be informed [of any conflicts of interest] and will discuss with you [the authors] whether or not disclosure in the journal is necessary. All sources of funding must be disclosed, as an acknowledgment in the text."
- 3 See <http://www.publicationethics.org.uk/cope1999/gpp/dealing.phtml>.

A statement by Dr Simon Murch

These allegations concerning our 1998 study are extremely serious, and clearly require immediate clarification. I welcome the opportunity to do so. My comment relates to the alleged lack of Ethical Practices Committee approval. I refute the allegation absolutely on the basis of extensive documentary evidence.

The protocol for the 1998 *Lancet* paper was submitted on September 16, 1996, to what was then termed the Ethical Practices Sub-Committee. It was entitled "A new paediatric syndrome: enteritis and disintegrative disorder following measles/rubella vaccine". It was signed by Andrew Wakefield as lead investigator. Named consultants were John Walker-Smith and myself, with signed collaborators Peter Harvey, for the department of neurology, and Mark Berelowitz, for the department of child psychiatry. The application was initiated due to findings at colonoscopy of two children with behavioural disorders, which would now be classified within the autistic spectrum, and a history of chronic gastrointestinal symptoms, and recognition of a broadly similar clinical history among other referred patients. Specifically, for several years previously we had looked after an autistic child with severe ulcerative colitis who eventually required colectomy (not included in the study), and the second child colonoscoped (on September 2, 1996) had ileitis of sufficient extent that a diagnosis of probable Crohn's disease was made. Following this diagnosis, the child had been entered in good faith by our inflammatory bowel diseases fellow into an ongoing (ethically approved) study of polymeric enteral nutrition. He had already made remarkable symptomatic improvement, including apparent cognitive advance. We, thus, appeared to be dealing with a condition of significant severity, and had seen clinical improvement unprecedented in this child's history. News of this improvement was rapidly disseminated among parents of autistic children, which I believe led to many further referrals. This child was included in the study, with additional investigations performed after ethics approval was obtained.

The title of this submitted application is a point of contention, and should be clarified. Having taken initial advice from our psychiatric colleagues on the basis of referral letters, it was considered that these children demonstrated a form of autism called disintegrative disorder (Heller's disease). After full psychiatric assessment of each child seen, it was later concluded that the more accurate description for the submitted paper should be pervasive developmental disorder. Our working title for these cases had, however, remained disintegrative disorder, while some parents referred to their child as autistic, and others did not. The whole area of nomenclature in autistic spectrum disorders was notably difficult at that stage. As we saw more patients, we moved towards a more inclusive label of autism, which was used in subsequent correspondence after February, 1998, to the Ethical Practices Committee. Measles and rubella were singled out in the application since these conditions, but not mumps, had been linked to autism in previous isolated reports.

This application (172-96) was for permission for in-depth analysis of 25 patients, referred either by general practitioners or the vitamin B12 unit at the Chelsea and Westminster Hospital, who had been studying B12 absorption in children with regressive neurological disorders. The selection criteria explicit in this application were the presence of disintegrative disorder, symptoms and signs suggestive of gastrointestinal disease, and parental request for investigation. All patients reported met these criteria. The consultant paediatricians responsible for the children's care decided on the investigations, although advice was taken from colleagues at