

EDITORIALS

Institutional research misconduct

Failings over the MMR scare may need parliamentary inquiry

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It is now more than 18 months since the UK's General Medical Council found Andrew Wakefield guilty of dishonesty and other serious professional misconduct¹; and it is nearly a year since the *BMJ* concluded that his now retracted *Lancet* paper linking the measles, mumps, and rubella (MMR) vaccine with autism and bowel disease was an "elaborate fraud."^{2 3} At that time, January 2011, we called on Wakefield's former employer, University College London (UCL), to establish an inquiry into the scandal. Ten months on, no inquiry has been announced.

Our coverage in January showed how Wakefield manufactured the appearance of a link between the vaccine and regressive autism while employed by lawyers trying to build a case against the MMR vaccine,⁴ and while negotiating extraordinary commercial schemes that would succeed only if confidence in the vaccine was damaged.⁵ The articles, by investigative journalist Brian Deer, also showed that the conflicts of interest were not confined to Wakefield. They drew in his then employer, the Royal Free hospital and medical school. Now part of University College London, the Royal Free issued public statements of support for national immunisation policy while privately holding business meetings with Wakefield over purported diagnostic kits, single vaccines, and autism products meant to be sold on the back of the vaccine crisis.

Now we can report that it is not only Wakefield and UCL's administrators who have a case to answer. This week we publish new information that puts the spotlight on Wakefield's coauthors. Previously unpublished histopathology grading sheets apparently completed by Amar Dhillon, the senior pathologist on the paper, remove any remaining credibility from the claim that the Royal Free doctors had discovered a new inflammatory bowel disease associated with MMR. Along with UCL's failings during and after Wakefield's tenure, this evidence also raises wider concerns about the prevailing culture of Britain's academic institutions.

In 1997, Dhillon was asked to reassess intestinal biopsy specimens taken from children enrolled in Wakefield's research after the hospital's histopathology service, under consultant and fellow coauthor Susan Davies, reported most of the children's

biopsies to be normal. His 62 A4 grading sheets were sent to the *BMJ* by David Lewis, a self employed environmental microbiologist. Lewis says he was given them by Wakefield after they met at a vaccine safety conference in January. In his accompanying letter, Lewis concludes that a non-expert pathologist such as Wakefield could have thought they showed that the children had non-specific colitis.

The grading sheets are certainly interesting, but not for the reasons Lewis (or, it may be assumed, Wakefield, in giving them to him) intended. We sent them to two independent reviewers and supplied the data for comment to two further senior gastroenterologists. We also showed them to Brian Deer, the investigative journalist who over the past eight years has uncovered the secrets behind the MMR scare and who arguably knows more about this case than anyone apart from Wakefield. Our expert reviewers are in no doubt that Dhillon's findings—like Davies's before him—are almost all normal, or as near to normal that the changes they reported were likely to be physiological.^{6 7} In an accompanying feature article, Deer explains what they add to our knowledge of the Wakefield saga.⁸

The grading sheets, which we have made available on bmj.com in the public interest (web extra), present findings from the biopsies of 11 of the 12 children, scored on a scale of 0-3 for the appearance of various levels of inflammation. Each sheet has a box for indicating the presence and severity of Crohn's disease or ulcerative colitis, or for indicating other findings: "infection," "ischaemia," "non-specific," or "normal." In all but one child, "non-specific" is ticked for at least one biopsy.

Lewis also sent us slightly different grading sheets completed by another coauthor, Andrew Anthony, who was then a trainee pathologist. Anthony concluded that some of the children had "mild" or in one case "active" chronic colitis. But these sheets are dated either September 1998 or October 2001, so they were completed after the *Lancet* paper was published. Because of this we did not send them out for external review.

Assuming that the sheets are what they appear to be (and we have supplied them to Dhillon, who has not demurred), it is

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Extra material supplied by the author (see <http://www.bmj.com/content/343/bmj.d7284/suppl/DC1>)

A P Dhillon's biopsy score sheets

A Anthony's biopsy score sheets

impossible to reconcile them with what was published in the *Lancet*. The paper talks of enterocolitis and a new bowel disease involving a putative “unique disease process.” How could two consultant histopathologists have reported healthy biopsies and then put their names to such a text?

The paper’s first sentence reads: “We investigated a consecutive series of children with chronic enterocolitis and regressive developmental disorder.” The only truth in this sentence is that the patients were children. In May of last year, the five member GMC panel said that the paper’s claim that the case series was “consecutive” was a dishonest representation of patient selection. In January of this year, the *BMJ* revealed that of the 11 boys and one girl in the study, only one clearly had regressive autism, and three who were said to have this condition clearly did not. This week we show that, according to Dhillon’s own data, none had enterocolitis.

This new information does nothing to exonerate Wakefield of fraud, but neither does it reflect well on his 12 authors. And, as Deer reports, there were other holes in their paper that they should have spotted. These include its failure to mention the children’s main presenting gastroenterological problem (constipation), and the almost total absence of discussion about “ileal-lymphoid-nodular hyperplasia,” which were the first four words of the paper’s title. Were these doctors, like the rest of us, distracted by Wakefield’s exaggerated prose and the paper’s suggestion of a link with MMR? Or could the prospect of authorship in a high impact journal have dazzled them into silence?

Deer has uncovered another relevant aspect of the case, not included in his article. In its bid for funding during the 2001 research assessment exercise, UCL included two of the coauthors in its panel of top performers.⁹ One was John Walker-Smith, professor of paediatric gastroenterology, who is currently appealing after being struck off the medical register along with Wakefield. The other was Mark Berelowitz, consultant child psychiatrist, who told the GMC panel that the paper’s use of the word “regressive” was wrong. In a list of their best work over the past four years, Walker-Smith’s entry put Wakefield’s *Lancet* paper first. Berelowitz’s put it second, with another Wakefield paper third. The research assessment exercise’s main metric for research quality was the journal of publication. Soon after this, Wakefield was quietly sacked.

This brings us back to UCL, the institution at the heart of the scandal. In January, we wrote to John Tooke, vice provost for health, asking him to investigate Wakefield’s research. In May we sent more detailed information, including a list of at least six other papers involving Wakefield that we believe require investigation. We also identified, in addition to Wakefield’s 12 coauthors, six senior academics who we believe should be questioned about their role. Given the extent to which the institution’s own processes and personnel at the highest level would be under scrutiny, we stressed that the only credible inquiry would be independent.

In response we have received only vague assurances that something will be done. Nothing has been publicly announced. Worryingly, UCL has a history of trying to sweep this matter under the carpet. It failed to properly investigate Deer’s initial allegations in 2004 and, worse, reassured the world, in

statements published in the *Lancet*, that an investigation had been done and all but one of the allegations had been found to be unproved.¹⁰ It also took three years to provide Deer with documents requested under the freedom of information act, despite the matter being personally notified to its provost, Malcolm Grant. It released the documents only after direct intervention from the UK’s information commissioner.⁵

Institutional misconduct is too important to be left to the institutions themselves. In light of UCL’s failure to act, the *BMJ* has this week referred the matter to Andrew Miller MP, chair of the House of Commons Select Committee on Science and Technology. If UCL does not immediately initiate an externally led review of its role in the vaccine scare, we believe that parliament should do it. This is not a call to debate whether MMR causes autism. Science has asked that question and answered it. But we need to know what happened in this inglorious chapter in medicine. Who did what, and why?

Among the most pressing questions is the conduct of Wakefield’s coauthors and other senior colleagues at UCL. What does this tell us about the prevailing culture of our academic institutions and attitudes to the integrity of their output? What safeguards are in place to prevent and expose institutional conflicts of interest in the future? And perhaps most pressing, why does the United Kingdom still have no publicly accountable and adequately resourced mechanism for investigating allegations of research misconduct? After the effort and time it has taken to crack the secrets of the MMR scare, and the enormous harm it has caused to public health, it would compound the scandal not to heed the warnings from this catastrophic example of wrongdoing.

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