

The Lancet should Reinstate the Andrew Wakefield Paper



By Martin Hewitt

In the wake of the High Court judgment on Professor John Walker-Smith's appeal against the decision of the General Medical Council (the UK regulatory body for doctors) to delicense him, what should now happen to the retracted paper he co-authored with Dr Andrew Wakefield? The decision lies with *The Lancet* editor, Dr Richard Horton. But what are the grounds for reinstating the paper as a properly conducted clinical investigation into 12 children with autism and bowel disease admitted to the paediatric gastroenterology department at the Royal Free Hospital (RFH) London in the mid-1990s? The paper was the focus of the GMC's trial of the three senior authors on charges of serious professional misconduct which led to the delicensing of Walker-Smith and Wakefield.

Background

Few academic articles have been dogged by the controversy attending the now retracted [Lancet Paper](#) 'Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children' since its publication in February 1998. ([Another link to retracted paper here.](#)) In seeking to avert controversy *The Lancet* published an editorial accompanying the paper to warn against drawing the wrong conclusions that the paper had established that the MMR caused autism and bowel disease. The paper, which went through several cautious redrafts, said it "did not prove an association between measles, mumps, and rubella vaccine and the syndrome described", adding that "Virological studies are underway that may help to resolve this issue".

On publication the RFH took the exceptional step of holding a press conference to launch the paper in the hope of preventing the media and public from concluding that the MMR was unsafe and to avert a collapse in MMR take-up. When Dr Andrew Wakefield the lead writer

was asked by the press if he would personally support the three-in-one MMR vaccine, he responded by advising parents to choose the single measles, mumps and rubella vaccines spaced out at intervals. Whilst his comments were seized on by the press as evidence that the MMR was unsafe and by the medical establishment as highly irresponsible, his answer accorded with official government policy. At the time the government vaccination schedule offered the choice between MMR and the three separate vaccines, in accord with the Department of Health's express policy when the MMR was launched in 1988.

In March 1998, the then UK Medical Officer of Health convened a conference of selected experts under the auspices of the Medical Research Council to discuss the paper with Wakefield. One question asked was how the case series of 12 children with autism and bowel disease was selected. This began a further controversy that challenged the paper's statement that the children were "consecutively referred to the department of paediatric gastroenterology" and sought clarification of its statement that "Intestinal and behavioural pathologies may have occurred together by chance, reflecting a selection bias in a self-referred group". To many medical researchers it appeared that the child patients had been selectively chosen as a result of parents contacting Dr Wakefield to produce a biased sample.

The controversy reignited in February 2004 when the Sunday Times' published the findings of a five-month investigation by freelance investigative journalist Brian Deer into the paper's research and ethics. Deer's articles continued up to January 2011 and were then followed by further articles in the British Medical Journal. When Deer first presented *The Lancet* with his findings four days before publishing his first Sunday Times article, the journal began its own investigation publishing a summary of Deer's allegations and responses by the three lead authors Dr Wakefield, Professor John Walker-Smith and Dr (now Professor) Simon Murch and by the Royal Free and University College Medical School. *The Lancet* summarised Deer's allegations: the investigations, some highly invasive, did not have ethical approval; the study was completed under cover of an entirely different approved study; the children were selected by invitation from Wakefield and Walker-Smith to the parents, constituting selection bias and contrary to the paper's claim about consecutive referrals; and the *Lancet* children were part of a legal-aided and funded research project to investigate the feasibility of litigation for vaccine damages.

Having considered the responses of the senior authors and the medical school *The Lancet* judged that the first three allegations were unfounded. However, on the last allegation concerning Dr Wakefield's

involvement with a separate LAB-funded study from *The Lancet* study, it concluded that "the perception of a conflict of interest nevertheless remains. This funding source should, we judge, have been disclosed to the editors of the journal." Nonetheless the paper was not retracted.

Henceforth *The Lancet* paper entered into a period of unprecedented controversy much deeper than before, driven by the Sunday Times investigation and the personal involvement of Brian Deer, who used his website to make claims far beyond those made in the Sunday Times at the same time. Three days after Deer had published his first article, he sent a 6-page email to the GMC outlining the above allegations with the additional claim that Wakefield had committed scientific fraud. In effect this not only instigated the 3 year GMC investigation that led to the fitness to practice hearing begun in 2007, but also outlined the trajectory Deer was to follow in his serious attacks on Wakefield's reputation in the Sunday Times and on his website, and from 2011 onwards in the British Medical Journal. Currently both Deer and the BMJ appear to have adopted an expedient silence as they await the result of Wakefield's forthcoming libel action against them in Texas.

The final stage of controversy began with the GMC fitness to practice hearing of the three doctors which culminated on January 2010 with findings of serious professional misconduct against them. In July the GMC recommended the sanction against Wakefield and Walker-Smith of erasure from the medical practice register, to be applied on appeal to the High Court. For Wakefield an appeal was not feasible as the Medical Protection Society, the insurance fund providing legal cover for doctors accused of offending medical regulations, withdrew its support and he was unable to finance the appeal himself. He was thereby struck off. However Walker-Smith's appeal was heard by Justice Mitting in the High Court in London in February 2012.

On 2 February 2010 *The Lancet* fully retracted the paper "from the published record" on the grounds that "several elements of the 1998 paper by Wakefield et al are incorrect, contrary to the findings of an earlier investigation [see above]. In particular, the claims in the original paper that children were 'consecutively referred' and that investigations were 'approved' by the local ethics committee have been proven to be false". The statement hints at other concerns. We know from *The Lancet's* earlier investigation that the editor formed the view that Dr Wakefield should have declared a conflict of interest regarding his involvement in a separate legal-aided study. But, being a separate issue from Walker-Smith's appeal, this does not form part of Mitting's judgment. Wakefield himself has claimed throughout that the

legal-aided study was for different scientific purposes than those pursued in the *Lancet* paper.

The Mitting Judgment and the *Lancet* paper

Having digested much of the hearing's 149 days of submissions and evidence and many other related papers, and heard Queens Counsels for Walker-Smith and the GMC, on 7 March J Mitting quashed all charges against the Professor.

Inevitably the thorough and irrevocable negation of the charges against Walker-Smith and of the GMC's legal case, based on its deep misunderstanding of *The Lancet* paper, raises an important question of the status of the Wakefield et al paper, which is still listed as retracted, to which we now turn.

There is no doubt that the Mitting judgment goes to the heart of the way the GMC exercised its regulatory powers in this case. He outrightly criticises the "universal inadequacies" and "inadequate and superficial reasoning" of the disciplinary panel's approach, and recognised the personal suffering the GMC had inflicted on Walker-Smith. "It would be a misfortune if this were to happen again" he concluded on delivering his judgment.

More specifically, the Mitting judgment rejects the two fundamental grounds the GMC gave for finding the three doctors guilty of serious professional misconduct and so undermines *The Lancet's* argument for retraction based on these grounds; out go the claims that the patients were not consecutively referred to the department of paediatric gastroenterology and that the investigations did not have ethics committee approval.

On the issue of referral, J Mitting rejects the GMC's charge against Walker-Smith that a consecutive referral meant "a routine referral to the gastroenterology department...in which the investigators had played no active part". Mitting says, "Thus construed, this paper does not bear the meaning put upon it by the panel. The phrase 'consecutively referred' means no more than that the children were referred successively, rather than as a single batch, to the Department of Paediatric Gastroenterology. The words did not imply routine referral." Moreover, he notes that "The general reader of that paragraph would note the author's [Dr Wakefield's] caution about the possibility of selection bias in the self-referred group. Taken together with the comments already cited made about the temporal coincidence

of the onset of symptoms and MMR vaccination in the case of eight children, the author has made it clear that this was not a routine referral. It was a referral generated by the concerns of parents about a possible link" (para 157 [here](#)).

On the issue of whether the paper had ethical approval, Mitting's findings are more complex. First he rejected the GMC's view that the paper was research. Summarising, he says, "At the heart of the GMC's case against Professor Walker-Smith were two simple propositions: the investigations undertaken under his authority on eleven of the twelve *Lancet* children were done as part of a research project – Project 172-96 – which required, but did not have, Ethics Committee approval; and they were clinically inappropriate" (9). However, contrary to the GMC's position, Mitting concludes that the investigation was clinically driven. Addressing the inadequate thinking of the GMC's fitness to practice panel, he concludes that "What the panel's stated reasons do not do, however, is to justify its conclusion that the investigations were for the purposes of [research] Project 172-96 and not for the purpose of a developing clinical project." On the panel's findings on the individual *Lancet* children, he says, "The detailed findings of the panel...did not fill the obvious gaps in its general conclusions.... In no case did it address the indications in the medical notes which supported the oral evidence of the clinicians that they were undertaking a programme of diagnostic and therapeutic investigations, not research; or give adequate reasons for rejecting that account in the case of each individual child" (148). In relation to the individual children, Mitting found clear evidence that they were referred for clinical reasons and not for research.

Secondly, on the question of paper's approval, the GMC had found that the paper was governed by research approval 172-96, which set a start date for the investigation of 18 December 1996 and that children included in the study should have Disintegrative Disorder and be vaccinated by Measles Mumps vaccination – conditions that the investigation had not followed. However, contrary to the GMC, Mitting found that the panel had given no grounds for saying the paper was approved by 172-96: "On any view, that was an inadequate explanation of the finding" (20). Further Mitting notes that a letter of 11th November 1996 from Professor Walker-Smith to Dr Pegg, chair of the ethics committee, "contained an unmistakable implied statement: that investigations under Project 172-96 had not yet begun" (17). The investigation was undertaken for clinical reasons and not covered by approval 172-96. In conclusion the paper was a case series of 12 children and did not require research ethics approval.

On the issue that the children did not have the approved condition Disintegrative Disorder and the Measles Mumps vaccination, Mitting concludes that "The only ground upon which [the panel] found that the investigations lacked Ethics Committee approval was that child 7 did not meet the inclusion criteria because he had had MMR vaccination and had not been diagnosed with disintegrative disorder. Those findings were correct, but could not have justified a finding of serious professional misconduct. As far as I know the reason for including the first criterion has never been explained. The second was treated by gastroenterologists in the clinical team as shorthand for a disorder on the autistic spectrum" (138).

The finding that the children were admitted for clinical reasons also puts paid to GMC allegations that the children were subject to inappropriate invasive procedures and that the study did not comply with 172-96's administrative requirements for start date, consent forms, etc.. (For a AoA discussion of these requirements go [here](#).) The GMC prosecution trick was to claim that the paper was covered by approval 172-96, and thereby to introduce a set of conditions that would condemn the doctors were 172-96 accepted as the appropriate approval. In the light of Mitting's judgment, this trickery is now out in the open and the GMC's attempt to shift the goal posts declared null and void. However, the current injustice is that these spurious charges still apply to Dr Wakefield and Professor Simon Murch unless the GMC recants and accepts that in the light of Walker-Smith's successful appeal they must now withdraw these charges on the grounds of consistent justice for all three doctors.

On the paper's approval status, Mitting concludes that the statement in the paper – that "Ethical approval and consent: Investigations were approved by the Ethical Practices Committee of the Royal Free Hospital NHS Trust, and parents gave informed consent." – was "untrue and should not have been included" (153). He notes that this was a change made to the previous draft which stated "This clinical investigation has been approved by the Ethical Practices Committee of the Royal Free Hospital NHS Trust" – itself inaccurate as a clinical paper would not need ethical committee approval. In focusing on Walker-Smith's case alone, as was his brief, J Mitting appears to ignore the fact that ethical approval 162-95 – giving Walker-Smith generic approval to take two additional tissue samples for research from children undergoing clinical colonoscopy – applied to the paper. The published statement of approval refers to 162-95. When examined by his QC on 49th day of the GMC hearing, Dr Wakefield clarified his reasoning for publishing

the approval statement. He responds in the negative to the question, "Were you, from your standpoint, at any stage seeking ethical approval in respect of what you have described as 'the clinical elements'?" (page 19). In short ethical approval was not necessary for a clinical study. However, when asked about his research responsibilities for the paper, Wakefield explains, "In respect of what I was doing, which was research, then ethical approval would have been required. And, when asked "Did you have it?", says "Yes, I did...Under 162/95".

Conclusion

Mitting's judgment should allay *The Lancet* editor's concerns based on the GMC's now fallacious findings on the children's referral and the paper's ethical approval. However, Mitting raises a new, and we have argued mistaken, concern about the ethics approval statement printed in *The Lancet*. Mitting's findings apply to Walker-Smith and not to Dr Wakefield who has not had the opportunity to appeal the GMC's findings and sanctions. Mitting accepts that the paper was for clinical purposes and we know from Wakefield's testimony that, although this is the case, generic approval 162-95 also applied. Even if this proved not to be correct, it would be unreasonable to make this a serious sticking point for continuing the paper's retraction after Mitting's judgment.

Further clarification on the findings against Wakefield and Murch must await the GMC's publication of 'lessons learnt' from the Mitting's judgment. Further clarification of the paper's now highly questionable retraction status awaits *The Lancet* editor's decision. A Facebook site is now available for the public to register their disquiet with *The Lancet* over the paper's status [here]. If the ethical questions that have hung over the paper since publication are now resolved, then the paper should be restored to its original position as a peer reviewed paper reporting legitimate research.

An entirely different matter concerns *The Lancet's* role as an archive of past scientific papers and its duty to maintain an intact history of advances in medical science, whether or not these publications were subsequently proved wrong and superseded by new scientific findings. Some *Lancet* readers may continue to argue that the paper's findings – on bowel disease in autistic children and the temporal association between MMR and the onset of behavioural symptoms – remain invalid and that this is sufficient reason for it to remain retracted. However, whatever the validity of these findings, it would clearly undermine *The Lancet's* scientific role if it allowed a paper to remain retracted which had played an important role in the development of medical knowledge

of autism and bowel disease and which remains a significant point of focus and debate for subsequent studies. Not only would it introduce new grounds for retracting the paper – initially retracted for ethical and not scientific reasons – but it would detract from the *Lancet's* longstanding status, since it was founded in 1823, as a guardian of scientific development and a record of the different turnings medical science has taken in advancing knowledge and treatment.