SERIES

Research misconduct: the poisoning of the well

Richard Smith

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Richard Smith was editor of the BMJ *and chief executive of the BMJ Publishing Group for 13 years. In his last year at the journal he retreated to a 15th century palazzo in Venice to write a book. This is a much shortened chapter from the author's book provisionally entitled* The Trouble With Medical Journals *that the RSM Press will publish in the autumn [www.rsmpress.co.uk], and this is the fourth in a series of extracts that will be published in the* JRSM.

On Wednesday 11 January 2006 Seoul National University concluded that Hwang Woo-suk, a pioneer in stem cell research and a national hero in Korea, had fabricated much of his research. His claim in 2005 to have produced stem cells from adult cells had reverberated around the world because it opened up new ways to treat Parkinson's disease and other degenerative diseases. His disgrace was equally high profile, providing one of the most dramatic cases ever of scientific fraud.

Sadly history includes many egregious examples of fraudulent scientists, but they were, until recently, regarded as isolated oddballs who did little damage to science, a self-correcting enterprise. But in the past 20 years country after country has recognized increasing examples of fraud and have come to think that it cannot be ignored, but needs to be recognized and managed. It is a painful transition, which is why few countries have developed an effective, comprehensive, national process for responding to research fraud. The Nordic countries have done so, but none of the large countries of the European Union have yet succeeded.

Responses to fraud are driven by scandals. They accumulate to a point where the scientific community can no longer ignore them and 'something has to be done'. Usually this process is excruciatingly slow.

AN 'IMPERFECT HISTORY' OF RESEARCH MISCONDUCT IN MEDICINE

Stephen Lock in his 'imperfect history' of research misconduct in medicine dates the beginning of the modern story to 1974.[1] William Summerlin from the Sloan-Kettering Institute in New York, one of the world's leading biomedical research centres, claimed to have transplanted human corneas into rabbits. He also faked transplantation experiments in white mice by blackening patches of their skin with a pen; an extraordinarily crude form of forgery. Eventually, Summerlin's misconduct could no longer be ignored, but his behaviour was attributed to a mental health problem. This is a response that is seen repeatedly. It is a form of scientific denial.

John Darsee worked in the department of cardiology at Harvard and was observed falsifying data. His boss, Eugene Braunwald, an eminent cardiologist, decided that this misconduct was an isolated incident and so did not fire him. A few months later, however, it became clear that results he had obtained in a study being conducted in several places were very different from those of the others. An investigation was started and went back to when he was an undergraduate. Many of his more than a 100 studies proved to be fraudulent and had to be retracted.

Case after case followed, but scientists were slow to respond. Eventually politicians became involved—because much of the fraudulent research had been funded with public money—and after many bitter battles between scientists and politicians the Federal Office of Research Integrity was founded.[2]

MALCOLM PEARCE: BRITAIN'S HIGHEST PROFILE CASE

Many British scientists watched the American battles and scandals with smugness, believing that such things could not happen in the less cutthroat and more gentlemanly scientific culture in Britain. Then came the case of Malcolm Pearce, which made it into the front pages of the British newspapers.[3,4]

I first heard of this case when I had breakfast in 1994 with Geoffrey Chamberlain, editor of the *British Journal of Obstetrics and Gynaecology* and president of the Royal College of Obstetricians and Gynaecologists, the owners of the journal. Chamberlain, known to all as 'Bodger', was a kind of obstetric Falstaff, not only in his manner but also in looks. He was much liked, which is one reason why he was filling two prestigious positions in the college that many might have seen as providing a conflict of interest. He told me that there had been 'a bit of trouble'. Malcolm Pearce—an assistant editor on the journal and a senior lecturer in the department at St George's Hospital Medical School where Chamberlain was the professor—had published two papers in the August issue of the journal that were fraudulent. One was a case report of the embryo of an ectopic pregnancy being re-implanted and leading to a

baby being born.[5] Obstetricians had been trying to do this for years, and the report when published received worldwide media attention. The second paper was a trial of treating recurrent miscarriage in nearly 200 women with polycystic ovary syndrome.[6] A whistleblower at the hospital had pointed out that the patient with the re-implanted pregnancy did not exist, and had also questioned whether Pearce could have found 200 patients with polycystic ovary syndrome. There had been an investigation at the medical school, and Pearce had been both fired and reported to the General Medical Council.

A day or two after our breakfast there was a large picture of Chamberlain on the front of the *Daily Mail* together with the full story. Chamberlain, it emerged, had been an author on the fraudulent case report.[5] He was reported as not knowing until after publication that the case did not exist and that it was normal for senior people to put their names on papers even when they had not really contributed anything. He was, ironically, correct, but it was a strange idea to readers of the *Daily Mail* that you would put your name on a scientific paper when you had had little or nothing to do with it. That sounded to them like fraud.

I was subsequently a member of a working party set up by the college to consider the implications of the case for the college, the journal, and the relationship between them.[3] Pearce had by this time been found guilty of serious professional misconduct by the General Medical Council and struck off; Chamberlain had resigned both as editor and president. Both were disgraced. The medical school investigated other studies by Pearce, and another four were retracted, including two that had been published in the *BMJ*. The working party, which was chaired by a senior lawyer, interviewed all the protagonists, including Pearce and Chamberlain, and offered a remarkable insight into what is still Britain's major case of research fraud.

The well-written report we produced (which was not written by me) reads somewhat like a whodunit. It made a great many recommendations which argued that the time had come to move from the long amateur tradition of editing specialist journals to something more professional.[3,4] The appointment, training, support, records, and accountability of editors all needed to be modernized. These recommendations apply to all journals. What happened at the *British Journal of Obstetrics and Gynaecology* could easily have happened at other journals—and probably still could. Indeed, it probably will.

The Pearce case sent a shock though the British academic medical community. It was soon followed by the case of John Anderton, an Edinburgh physician who had been an official of the Royal College of Physicians of Edinburgh. He had faked results in a drug trial. He was found guilty of serious professional misconduct by the General Medical Council. So, too, was Robert Davies, a professor of respiratory medicine in London, who tried to cover up for blunders made in a trial funded by a drug company. These were prominent figures in British medicine. Other cases have since followed.[7]

DEFINING RESEARCH MISCONDUCT?

One of the many unanswered questions on scientific fraud or research misconduct is how commonly it occurs. The answer obviously depends on how it is defined, which is another difficult question.[8]

The Americans have argued long and hard about the definition of research misconduct.[2] Researchers wanted a tight definition that would allow them to know clearly what was and what was not misconduct. They were also anxious that 'honest error' might be mixed up with misconduct, and that a loose definition might allow academic disputes, which are distressingly common, to become accusations of misconduct. In 1995 the United States Commission on Research Integrity produced a definition some 400 words long.[9] Then, at the end of 2000, the federal government produced a slightly shorter definition (but with long footnotes) together with requirements for a finding of misconduct.[10] The definition states:

> Research misconduct is defined as fabrification, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results.
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> Fabrification is making up data or results and recording or reporting them.
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> Falsification is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record.
>
> Plagiarism is the appropriation of another person's ideas, processes, results or words without giving appropriate credit.

The definition continues by making clear that 'research misconduct does not include honest error or differences of opinion'.

A finding of research misconduct depends on three requirements. First, there must be 'a significant departure from accepted practices of the relevant research community'. Secondly, the misconduct must be 'committed intentionally or knowingly, or recklessly'. Thirdly, the allegations must be proved 'by a preponderance of evidence'.

The Nordic countries and Britain have taken a different line from the Americans and opted for broad definitions.[11]

The Norwegian Committee on Scientific Dishonesty defines research misconduct as 'all serious deviation from accepted ethical research practice in proposing, performing, and reporting research'.[11] A British consensus conference held in Edinburgh in 2000 went for something still broader: 'Behaviour by a researcher, intentional or not, that falls short of good ethical and scientific standards'.[12] This definition includes nothing about falling 'seriously' or 'significantly' short of good standards and does not depend on intention.

HOW COMMON IS RESEARCH MISCONDUCT?

The debates on how best to define research misconduct continue, and so there can be no definitive answer on how commonly it occurs. Minor forms of misconduct are common, but we have less good information on the prevalence of serious misconduct. The USA, which has far more biomedical research than any other country and where the problem has been taken seriously for two decades, has seen hundreds of cases, many of them serious. It has also recently had a series of high profile cases in the physical sciences. The committees of scientific integrity in the Nordic countries have seen dozens of cases, few of them serious. Britain has had about two dozen general practitioners participating in trials conducted by pharmaceutical companies found guilty of serious professional misconduct for research fraud. There have also been about a dozen cases among medical academics. Germany has had a very high profile case in molecular biology, which sent shockwaves through the German academic system. The Dutch have also had a prominent professor found guilty of serious research misconduct, but many countries have had few cases.

Mike Farthing, the chairman of the Committee on Publication Ethics who has been the dean of three medical schools, estimates that major institutions in Britain have roughly one serious case a year. That means about 50 cases a year.

Most cases are probably not publicized. They are simply not recognized, covered up altogether; or the guilty researcher is urged to retrain, move to another institution, or retire from research. I have spoken perhaps a dozen times on research misconduct in several countries and often to audiences where people come from many countries. I usually ask the members of these audiences how many know of a case of misconduct. (I consciously do not offer a definition.) Usually half to two-thirds of the audience put up their hands. I then ask whether those cases were fully investigated, people punished if necessary, lessons learnt, and the published record corrected. Hardly any hands go up. Stephen Lock got a similar result from a postal survey he did of friends who were professors of medicine. [13] These 'cover ups' explain why it is so hard to get good data on the prevalence of serious research misconduct; but some countries and disciplines have more cases not, I suspect, because misconduct is more common but because they have actually begun to face up to the problem.

WHY DOES RESEARCH MISCONDUCT HAPPEN?

Why does research misconduct happen? The answer that researchers love is 'pressure to publish', but my preferred answer is 'Why wouldn't it happen?' All human activity is associated with misconduct. Indeed, misconduct may be easier for scientists because the system operates on trust. Plus scientists may have been victims of their own rhetoric: they have fooled themselves that science is a wholly objective enterprise unsullied by the usual human subjectivity and imperfections. It is not. It is a human activity.

HOW SHOULD WE RESPOND TO RESEARCH MISCONDUCT?

A full response to the problem of research misconduct requires, I believe, a national body to provide leadership. It needs to raise consciousness about the problem, provide guidelines on good practice, encourage research and teaching, offer help with investigations of misconduct, and probably provide a place for whistleblowers to report anxieties and for the hearing of major cases or appeals against local judgements. One problem with local bodies—universities or hospitals—dealing with cases is that they often lack competence and sometimes commitment. They also face a deep conflict of interest in that they fear that openly investigating and reporting a case will damage the institution.

The main emphasis in responding to the problem of misconduct should be on raising the overall level of scientific integrity rather than on investigating suspected cases—although there have to be good systems for investigating, judging, and reporting cases. We need codes of good practice rather than simply lists of bad practices to be avoided, and we need to teach integrity rather warn against dishonesty. Once their consciousness is raised, researchers will realize that they are constantly presented with ethically difficult questions around analysis of data, authorship, conflict of interest, informed consent, and a dozen other issues. There are usually not 'right' answers that can be read from a rulebook. Rather, researchers need to be able to think their way through the complexities to reach an ethically defensible answer. They may often need help and should not be afraid to ask for it.

THE ROLE OF JOURNALS IN RESPONDING TO MISCONDUCT

Editors and journals have an important part to play in the response to research misconduct. Editors are often the first people to encounter the results of research, and journals are the conduit through which fraudulent research reaches the world. Editors have only comparatively recently recognized the important role they have to play. In my first 18 years as an editor I certainly encountered misconduct; but the cases seemed to be rare and I often did nothing. Problems usually arose with papers we planned to reject, and we did not think that we had a duty to act. Indeed, the traditional 'confidentiality' of our relationship with authors almost made us think that we should not act.

Between 1997 and when I left the *BMJ* in 2004 I dealt with about 20 cases a year and came to think that it would be misconduct on our part to turn a blind eye to misconduct in authors. This was the effect of the Committee on Publication Ethics (COPE), which was founded in 1997 primarily as a self-help group for editors of medical journals wondering what to do with cases of misconduct they encountered. Its biggest achievement may have been to sensitize editors to recognize misconduct and oblige them to take action.

Although a small group of editors—from *Gut, Lancet, BMJ, Journal of Bone and Joint Surgery*, and other journals—began COPE to help each other: it was also prompted by the series of high profile cases of research misconduct in Britain. Around 200 journals now belong to COPE, most of them British.

The first aim of COPE was to advise editors on cases. The advice has had to be offered anonymously—for fear of libel and to avoid creating a kangaroo court—and the onus remains on the editor to take action. As well as helping editors, COPE wanted to begin to establish what forms misconduct took and how common they might be. So far COPE has dealt with around 250 cases, all of which are described anonymously in the committee's annual reports and are available in full text on the committee's website [http://www.publicationethics.org.uk].

Experience gathered with these cases has been used by COPE to draft guidelines on good publication practice, so achieving its second aim. The guidelines are available in full on the COPE website. It has been keen to emphasize good practice, not just map poor practice. The guidelines cover study design and ethical approval, data analysis, authorship, conflicts of interest, peer review, redundant publication, plagiarism, duties of editors, media relations, advertising, and how to deal with suspected misconduct. The guidelines are regularly revised in the light of new cases and experience.

COPE is ultimately advisory. It remains for individual editors to act, and, although editors may be the first to encounter research misconduct, they are restricted in what they can do. They are in many ways simply privileged 'whistleblowers', privileged in that it is hard for researchers, universities, or even national or international bodies to bully them. Conventional whistleblowers, who are usually junior researchers, are often the people who expose research misconduct. Unfortunately, they often encounter more problems than those on whom they blow the whistle—even when they are thoroughly vindicated.

Those accused of research misconduct have a right to due process—just like anybody against whom a serious accusation is made. Journals cannot provide due process. Furthermore, they do not usually have any legal legitimacy to hear a case and impose punishment. It is employers who do. Unfortunately, many editors do not understand their restricted powers and may take illegitimate actions.

The role of editors is to pass on accusations to the relevant authority, usually an employer but sometimes a regulatory authority. A difficult question is to know how much evidence you need to have. There is an understandable tendency to think that you need a great deal of evidence to make such a dramatic allegation, but gathering it is often difficult, expensive, and time consuming, and can create many problems. I made this mistake with one of the first cases I encountered.

HOW MUCH EVIDENCE DOES AN EDITOR NEED TO BLOW THE WHISTLE?

We were about to publish a paper that suggested that cimetidine, a drug used to treat stomach and duodenal ulcers, might help people lose weight.[14] It was an unlikely and unexpected finding. We had never heard or even thought of cimetidine being used in this way. Nevertheless, the paper had made it through our peer review process. But then we received a similar study that found no evidence that cimetidine helped with weight loss.[15] This made us re-examine the first paper. We noted that it came from a single author, a general practitioner from a rural area. A statistician with an interest in fraud looked at the paper and was worried. A clinical reviewer was also anxious now that the possibility of misconduct had been considered.

In retrospect this was enough evidence to ask the researcher's employer to investigate. At the time I thought I needed more evidence. I rang a friend from the country where the author lived. He made some inquiries, and the result was that many people in the country, including the researcher, knew about my anxieties. The researcher flew to London to see me, telling me stories of being abused by other academics. I was simultaneously accuser and comforter. The whole thing was a mess.

I did eventually ask her employers to investigate. They did and concluded that there was not a problem with the

work. We published the study with a highly sceptical commentary.[14,16] This was years ago, and the idea that cimetidine might help with weight loss is dead. I am not sure if the work was fraudulent, but I am left with severe doubts.

That episode taught me not only that I do not have to assemble a watertight case before asking an employer to investigate, but also that it may be risky to try and do so. When I contacted an employer or regulatory authority to say that I was worried about a paper, I was not saying that the person was guilty of research misconduct. I was simply doing my duty in raising anxieties. The difference is crucial, and a lot less evidence is needed to raise anxieties than conclude that an author has been guilty of misconduct. This is not, however, to say that anxieties can be raised lightly.

WHAT CAN JOURNALS DO WHEN NOBODY WILL INVESTIGATE POSSIBLE CASES OF FRAUD?

Although editors cannot undertake investigations, they do have a duty, I believe, to persist in making sure that justice is done. As I have said repeatedly, institutions are inclined to let accusations fade away. Every time I wrote making an accusation I made a note in my diary to follow it up a month later. Often I had to write again a month later after hearing nothing. Another major advantage that editors have over lone whistleblowers is that the institutions know that journals can publish. They have a means to expose laggard institutions.

Despite the power of journals many institutions still do nothing when anxieties are raised. It is difficult for institutions in Britain not to respond because the *BMJ* knows how to oblige institutions to respond—resorting to the General Medical Council, the Department of Health, or a similar national body if all else fails.

Over the years I made complaints to employers and authorities in Australia, Canada, Egypt, Germany, Greece, India, Jordan, Russia, the UK, the USA, and often I received no response. I usually wrote again at least once, but often I then gave up, thinking that I had discharged my duty in alerting the authorities.

THE CASES OF R B SINGH AND R K CHANDRA

But sometimes the case was so serious that I persisted. I pursued for over 10 years one case of an Indian researcher, R B Singh, who had published dozens of what I thought to be fraudulent studies. The case started in the days when I thought that I needed to assemble a convincing case before I approached an authority to investigate. Assembling the case took years. Then I spent years trying to find an institution to investigate the case. The researcher owned his own institution. Nobody would investigate, so I decided that we ought to publish the whole story in the *BMJ*. The *BMJ* Ethics Committee agreed, and, a year after I left, the story was published.[17]

At the same time that the story was published the *BMJ* published further information on a case of a Canadian researcher, R K Chandra, whom the journal had also been pursuing for years.[18] We had severe doubts about the authenticity of a trial submitted to us. We thought that the data had been fabricated or falsified. Three reviewers, each from different disciplines, agreed with us. I wrote to the Memorial University, Newfoundland, asking it to investigate. One immediate response was a letter from the author's lawyers demanding to know the name of the reviewers. I declined.

The university investigated and found no problem. We were unconvinced by the thoroughness of the investigation, and asked it to look again and provide answers to specific questions. The next letter from the university said that it would not be able to investigate because Chandra had left its employment and the country, leaving only a *poste restante* address in Switzerland. We took this as an admission of guilt.

We then discovered that the author had published the paper we were querying in the journal *Nutrition*.[19] The study that concerned us was closely related to a study published by Chandra in the in the *Lancet* more than 10 years previously.[20] Our ethics committee agreed that we had a responsibility to notify these other journals about our doubts. We discovered as well that the researcher had published a great many randomized trials undertaken on his own in major journals over the past 10 years. There are always doubts about such studies because a randomized trial is a major undertaking and difficult—if not impossible—to do on your own.

Nutrition eventually retracted the study,[21] and the *Lancet* published a letter raising severe doubts about its study.[22] In 2006, Canadian television broadcast programmes showing that Chandra had a long history of misconduct and that the university had investigated him for fraud in the mid-1990s and found severe problems.[23] Chandra had, however, gone on working and publishing.

Both Singh and Chandra have published dozens of studies in major journals, and I and others have severe doubts about all of them. Hardly any of the studies have, however, been retracted. There is simply nobody willing to take on the responsibility of investigating all those past studies. Surely they should be marked in some way as suspect in Medline and other databases.

The Chandra and Singh cases have led to an article on the front page of the *Wall Street Journal*[24] and Canadian television programmes, but very little reaction from the scientific community. It could be that the *BMJ* is utterly unique in coming across two such cases of repeated fraud; but it seem more likely to me that such fraud is happening

equally commonly in the other 30 000 or so scientific journals.

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