Fraud in medical research

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In all types of scientific research there has always been an element of fraud. In history we have figures as various as Newton, Pasteur, Mendel and Sir Cyril Burt as possible fraudsters [1], and research fraud has also played an important part in several novels, pre-war such as Dorothy Sayers's *Gaudy Night* and post-war such as Angus Wilson's *Anglo-Saxon Attitudes* [2]. But our current concerns are in medicine and they fall within the past 20 years. They date back only to 1974, when William Summerlin demonstrated at the Sloan-Kettering Institute in New York what he claimed to be a graft of skin from a black mouse into a white mouse [3]. After this demonstration a laboratory technician noticed that black dye was running from the transplanted patch, and that all of the dye could be removed with a damp swab. Summerlin admitted that he had used a black felt-tip pen to darken a transplant of white skin. In today's terms the reaction to his fraudulence was extraordinary: it was concluded that he had been overworking, and he was given a year's sick leave on full pay.

Five years after this, we had the *'anni horribiles'*—two or three years when several major instances of fraud in medical research were reported not only from the USA but also from Australia and the UK. After this, things were never quite the same again. We had a definition [4] which, though it is still being argued about [5], is a useful beginning. We began to recognise that there were three major types of fraud (or dishonesty or misconduct—these are synonyms for a term on which there is still no international agreement): piracy, plagiarism and forgery. Nevertheless, there was also a spectrum of shady practices, including salami and duplicate publication, gift authorship, and undeclared interest. We had continual reports of new cases all over the world. We had inquiries and reports, both specific to individual cases and about the problem as a whole [6]. We had books about the subject [6–11]. We had debates by some governments (including, in the USA, Congressional hearings) leading to the establishment of official bodies, such as the Office of Research Integrity (ORI) and the Danish Committee. And we had a continual trickle of new cases which persists until this day.

So let us ask some questions about fraud in medical research, even though they cannot all be answered. What is its prevalence? What are its causes? Why does it seem to be largely confined to medicine? What are its major features and how has it been, and should it be, dealt with or, preferably, prevented? Finally, and crucially, why, almost uniquely, has the medical establishment in Britain put its head in the sand and ignored the signs. The problem of research fraud exists everywhere. It has to be taken seriously, and it has to be tackled with courage, whatever the difficulties; we can learn a lot from other countries.

This article is based on a lecture given at the College Day on 30 July 1996 by **STEPHEN LOCK,** CBE, MD, FRCP, FACP, Research Associate, Wellcome Institute for the History of Medicine, London.

Prevalence

The difficult problem of prevalence can be approached in two ways: by looking at the reported cases, and at the results of surveys and audits. Internationally, over the past 15 years there have probably been no more than 600 cases in the public domain—and many of these are violations of Food and Drug Administration (FDA) practices rather than egregious fraud—fairly evenly distributed among academia, hospital practice and family medicine [6]. If we break down one set of US figures—those produced by the ORI [11]—most of the cases concern the invention of data, with plagiarism taking a lesser, but important, part and piracy being nowhere.

Another feature of research dishonesty—one that many of the medical gliterati in the UK who want to ignore the problem seize on to justify their inaction—is that the number of fraudsters seems to be very small. What is more, in Britain, on the basis of fraudsters coming to the General Medical Council (GMC), the gliterati can say (and do say) that the problem is largely confined to general practitioners —and poor general practitioners at that, given that most of them have been single-handed, qualified overseas, and engaged in low-brow multicentre drug trials [6]. Even so, to consider my second piece of evidence, the picture is very different. In several countries the results of surveys (all of which, admittedly, have flaws) show a consistent finding: reported research fraud is an iceberg, of which only the tip comes into the public domain. So in 1988, in a confidential survey of 80 academics and editors of specialty journals in the UK, with a 100% response rate, I found that over half of them knew of 73 cases, only one of which was in the public domain and resulted in any disciplinary action [12]. A US survey of 4,000 students and faculty in non-

medical sciences in 1994 found that between 6% and 9% knew of plagiarised or falsified data [13].

Two years ago, a Norwegian survey of 152 medical investigators found that over a quarter of the 119 replying knew of one or more cases of fraud [14]. This hidden prevalence is supported by the results of audits. In the USA, Shapiro found, under the Freedom of Information Act, that 400 physicians had been penalised by the FDA for a variety of unprofessional practices [15]; interestingly, the list of names includes several doctors from the UK. Another survey found that 27% of scientists had encountered an average of 2.5 cases over 10 years [16]. Two audits in the USA have shown prevalences of 0.1% and 0.25–0.5% [6]. A British audit of 1,000 sets of data in drug trials found four to be fraudulent. So the best estimate today is perhaps that the prevalence of fraud is between 0.25% and 0.5% of research projects.

Causes

We owe a lot to Sir Peter Medawar for elucidating the causes of fraud in medical research [3]. The first is the way in which doctors are evaluated, by the *amount* they have published. It would be trite to emphasise the pivotal role that volume of publication now has in obtaining tenure, promotion, and research funds, but it has long been a fact of life and explains the consistent link of gift authorship with so many cases, particularly when seniors put their names on papers reporting work they have had nothing to do with—indeed, could not have had, given that the work has never been done. The second cause of fraud is vanity—wanting to keep up with one's peers even though one has no proven results which allow one to do so. The third is greed: doctors can make a sizeable amount of money out of drug companies. Even in the late 1980s, Dr Siddiqui, a Teesside psychiatrist who was struck off by the GMC, was being paid £700 for every patient entered into a trial of antidepressants [6]. I suspect that greed accounts for the seemingly high frequency of fraud in medicine as opposed to other disciplines (physicists presumably are not paid for getting their results). Fourth, a few of the fraudulent doctors have had frank mental illness and any inquiry into the fraud has diverted the management of the case into getting this illness treated.

Perhaps the most important cause is what Medawar called the 'Messianic complex'—a scientist becomes so convinced of the rightness of his convictions that he (and it usually is a he; whether women scientists do not commit fraud, or are better at concealing it, we do not know) invents data rather than doing the research to produce them. A good example was Dr William McBride, probably among the first to describe the teratogenic effects of thalidomide, who became obsessed with the harmful effects of all drugs to the fetus and invented results to show this for antiemetics [20]. Lastly, Medawar pointed out that every group has its quota of crooks, and he saw no reason why medicine should be considered an exception.

Reactions—initial and subsequent

All over the world, reactions to scientific fraud have followed a consistent pattern, in three main phases. First come the reactions of colleagues, there is the shock and horror of finding that a colleague or a fellow researcher has actually invented the data. This is perhaps no better expressed than in this passage in a letter to me from a professor in another country:

> 'I still feel considerable bitterness and pain when I recall the incident which occurred in our own department. No one involved has ever completely recovered; for a year or so our morale was absolutely shattered. I believe the way we dealt with this matter was correct in the moral sense but it has in some way affected all our careers and also ourselves as individuals. Since this particular episode I have little doubt that scientific fraud is much more common than is realised and certainly far more common than is revealed openly.'

The next reaction is denial—to say that this is a one-off occurrence, with particular causes, but that otherwise fraud is not a feature of research. The next is to penalise the whistle blowers—to threaten their jobs or to see that they are ostracised in the department. Then the matter has to be brushed under the carpet, so that it never gets into the public domain—a tendency nowhere better expressed than in C P Snow's novel *The Affair:* 'A piece of scientific fraud is of course unthinkable', Snow's Master reflects 'but any unnecessary publicity about it . . . is [also] as near unforgivable as makes no matter'. Publicity would achieve nothing 'except harm for the College' [21].

A feature consistent in many cases (and certainly at the beginning of the story), the actual fraudster gets off scot-free, stays in the department, and even gets promoted. Also, nothing is done about informing the body that provided the research grant or about retracting the fraudulent publication based on the research.

The second phase occurs when the idea that there is a certain amount of research fraud around is taken up by the media, and there is pressure for official statements about guidelines and codes. So we have the reports from universities and official bodies in many countries—the USA, Australia, Canada, the Nordic countries and, commendably, the Royal College of Physicians in Britain [22]. By and large their recommendations for management have followed a similar pattern—a three-stage procedure of receipt, inquiry and investigation, which is characterised by 'due process', the American term that covers fairness to all parties, confidentiality, and speed.

Nevertheless, the third phase—action—is crucial, and it is here that our society has been short-changed in Britain. It is difficult to get all these proposed mechanisms enforced in practice, and one of two things is needed: either pressure from the politicians, as in the

USA, or strong community and professional feelings about good and evil, as in the Nordic countries.

Prevention

Just as important as ensuring that all miscreants are brought to book is prevention. Recent American concepts focus on two main types of actor in the drama: the jerks and the crooks [6]. Clearly the crooks need dealing with through a legalistic mechanism, while the jerks need education about good research practice and research ethics. Using the latter, you can achieve the important aspect of prevention. Both the American ORI and the Nordic central committees on scientific dishonesty address management and prevention. Thus they not only investigate and adjudicate on suspected cases of fraud but also run regular courses on good research practice. Here in Britain we have done virtually nothing about either. How many courses on research ethics have been held in this country? I suspect that the answer is none at all. In Britain, where do whistle blowers (who are often juniors in a small specialty) go for disinterested advice that will not penalise their careers? For that matter, why has there not been a single professional conference in the United Kingdom on the whole issue, compared with scores in the USA, and several in Europe? After the Pearce case in 1995 [6], this College took the initiative and recalled a group of interested physicians and scientists to re-examine the case for a central committee in Britain. The clamour of objections, from those whom Nietzsche would have called the 'nay-sayers' was deafening. There were legal problems; there were financial problems; there were administrative problems; there were personal problems.

As a result, a year after the Pearce case, nothing at all has been done. I feel professionally ashamed and diminished by this sequence of events. The profession here has failed its responsibilities to the community for ensuring probity and that the money the public gives to medical research (through its taxes or through charities) is well spent. Pragmatically, too, I do not believe that our media or our politicians will allow this state of affairs to continue. In the USA, Congressman John Dingell was largely responsible for ensuring that effective action was taken. In this country, Mrs Gwyneth Dunwoody MP has recently been asking a series of probing Parliamentary Questions about research fraud. Media interest was shown by the *Horizon* television programme in 1995; a Radio 4 programme was broadcast in September 1996 (with scores of enquiries to a telephone hot-line afterwards), and another television feature is planned for 1997. We have to remember, moreover, that recently standards were imposed on the teachers; in effect, the government was ordering them how to teach as well as what to teach. However remote the possibility might seem, there is no reason why this should not happen to doctors as well.

Perhaps all this is part and parcel of what some have seen as a decline in British medicine, as evidenced, for instance, by a recent fall in the citation rate of papers coming from British centres. Of course, there is a totally different possible interpretation: there is no problem, and this idea of hidden research fraud in Britain is a distortion by me—one former editor who happens to have got overexcited about several unaddressed cases, but cannot mention these for others to judge because of our stringent libel laws. One of the difficult aspects of considering this subject is having to rely on cases in the public domain. Over the past three years, for instance, I must have been consulted about at least two dozen cases or heard strong rumours about really undesirable practices. I do not know how many of these were securely based, but the ORI experience is that about half of the cases coming to them end in disciplinary action. If this is also the case in Britain then clearly something is wrong, and I wish I could illustrate the problem that has to be faced.

Parallels with human experimentation

Perhaps editors are in a privileged position to encounter fraud. Recent editorials in our two weekly medical journals, the *British Medical Journal* and the *Lancet,* would support this, both concluding that our much vaunted self-regulation is on the point of failing [23,24]. There are good reasons why any establishment is reluctant to have the courage to tackle fraud. It involves a lot of hard work; the accusations may involve our friends and colleagues, some of whom misguidedly may have put their names on papers when they should have known better; and the threat of the law puts many people off. So, perhaps in Western society's sleaze-ridden *fin de siècle* (when lawyers and accountants are also reporting the same sort of fraudulent behaviour) we might take the view that it is not cost-effective for doctors in Britain to address this issue. I happen to believe that this is wrong. Whatever the political niceties and the practical difficulties, evil at any level is a moral issue and it will not go away. Fraud is fraud, wherever it occurs, and a society that does not tackle this issue is seriously flawed. But I may be wrong, so let us look at history, remembering George Santayana's much quoted words, 'Those who forget the mistakes of history are doomed to repeat them'. Are there other examples in history of a similar neglect by the British profession of an important medical issue, with a imminent failure of self-regulation, when society had to step in and compel medicine to put its house in order?

A good example, I believe, concerns the ethics of human experimentation. Such concerns have been around for over a century; it was, after all, the Norwegian Hansen who lost his post at a Bergen hospital for his failure to obtain informed consent before instilling leprous material into a patient's eye, and there was concern over experiments on children in US public

hospitals before the First World War and in Germany over the activities of the pharmaceutical industry in the 1920s. After the Second World War such concerns were rekindled by the accounts of the Nazi concentration camps, and the Nuremberg Code was introduced. Clearly, though, such a code was aimed at barbarians, and the ordinary clinical research worker took little heed of any restrictions. All this culminated in the late 1950s with two senior doctors blowing the whistle, showing how much potentially dangerous clinical research was then going on in both American and British medical institutions without any informed consent by the patients. They had concluded that, without community pressure, the profession was not going to police itself and so went public. In the USA, Henry Beecher, an anaesthesiologist at Harvard, produced a book on human experimentation [25], followed by an article in the *New England Journal of Medicine* [26] a selection of 22 cases from recent literature. In Britain, Maurice Pappworth wrote first an article in a monthly magazine and then a book, *Human guinea pigs*, documenting 60 cases [27].

On both sides of the Atlantic, the initial reaction was the same. Beecher's colleagues at Harvard called a press conference to disassociate themselves from his views, and in this country Pappworth was derided by the (then) medical establishment (though 25 years later this College was to make amends by electing him FRCP, over 50 years after he had obtained the Membership). Nevertheless, on both sides of the Atlantic there was public furore about human experimentation, but there the similarities between the USA and Britain end. After a lot of informed discussion in the USA, the government there created statutory research ethics committees (institutional review boards) in 1966. In the UK this College set up a committee the same year, and it reported in 1967. Nevertheless, its recommendations were not made public for seven years, and even then the formation of research ethics committees was piecemeal. Although they are now at last widely distributed, there is no statutory requirement to have one in place (Kennedy, personal communication, 1996). To be presentist and snide, let us look at a few of the fatuous comments on the ethics of human experimentaion made by the British medical establishment of the time. At a meeting of the 1942 Club (an association of professors of clinical medicine) Sir John McMichael insisted that 'the moral decision must be made by the experimenter', a view echoed by Sir Harold Himsworth that 'the only safeguard is the conscience of the experimenter'. Even the *Lancet* was to rebuke Pappworth for his hauteur; in an editorial reviewing his book, this normally liberal journal stated: 'It is in the instant self-criticism by the profession that the patient obtains the best protection'.

We have, then, to remember that, apart from Pappworth and Hugh Clegg (the *British Medical Journal* editor who, with his Finnish counterpart, was responsible for the Declaration of Helsinki), we owe any action on ethical matters not to the medical profession but to public pressure, especially from some politicians and particularly the Labour MP Stephen Swingler. So let me finally counterpoint a few of the replies to Swingler's persistent Parliamentary Questions on research ethics with the recent ones to Mrs Dunwoody's questions on research fraud. Thus we have in 1967 the Minister stating that allegations that UK doctors had carried out unauthorised experiments on NHS patients were not based on facts, and in 1996 that information on the number of cases of government sponsored research shown to be fraudulent was not available centrally. There is a similar sense of self-satisfaction in the same two years: in 1967 Swingler was told that 'the medical profession for generations has been guided by strict codes', while in 1996 Dunwoody was told that 'good research practice operates largely on a self-regulating basis through peer review and guidelines issued by a number of bodies'. We can, I think, see from this sequence of events that the public, if it thinks that a topic is of sufficient importance but is not being handled well by the profession that has the responsibilty for doing so, will step in and insist that self-regulation is not working. The ethical policing of human experimentaion was one such example, and I believe that fraud in medical research will turn out to be another.

Conclusion

To conclude, I would contend that some element of research fraud has always been around. Nevertheless, probably in the past 15 years it has become more frequent and more visible, possibly associated with the general sleaze in Western societies and linked to the need to publish papers in quantity rather than quality. Peer review is inadequate for detecting it, and it is almost always revealed by whistle blowers, who therefore need not only to be encouraged to report any legitimate suspicions but also to be protected. Prevention is as important as the efficient management of every suspected case, and every civilised society needs to devise mechanisms for both.

In all this, Britain has seriously lagged behind many other advanced societies. One reason for this may be what the Italians call *dolce far niente,* in other words our increasing laziness or refusal to do anything about serious facts staring us in the face. Another reason may be our increasing preference for talk over action, a cheaper alternative that gives the semblance of activity. We can see both features operating in the deliberations over BSE or a national transport policy. For our inaction over research misconduct, how true it is to echo another statement by a German observer of the scene: 'The only aspect that Britain excels in is talk. In all other aspects it is ten years behind the rest of Europe' [28].

This paper is, of course, yet another contribution to

the talk that the German MEP said was so characteristically British. Even so, I hope that, perhaps after a shorter gap than that between the revelations of unethical research and the establishment of research ethics committees, another person might come to this lectern and announce that Britain has after all, if belatedly, addressed the problem of research misconduct.

References

1 Kohn A. *False prophets.* Oxford: Blackwell, 1986.
2 LaFollette MC. *Stealing into print.* Berkeley: University of California Press, 1992.
3 Medawar P. *Advice to a young scientist.* Cambridge: Harper and Row, 1979.
4 Chubin DE. *Research misconduct: an issue of science policy and practice.* Washington: National Science Foundation, 1984.
5 Commission on Research Integrity. *Integrity and misconduct in research.* Washington: DHHS, 1996.
6 Lock S, Wells F (eds). *Fraud and misconduct in medical research.* London: BMJ Publications, 1996.
7 Broad W, Wade N. *Betrayers of the truth.* New York: Simon and Schuster, 1982.
8 Miller DJ, Hersen M (eds). *Research fraud in the behavioral and biomedical sciences.* New York: Wiley, 1992.
9 Bell R. *Impure science.* New York: Wiley, 1992.
10 Grayson L. *Scientific deception.* London: British Library, 1995.
11 Office of Research Integrity. *ORI Newsletters 1993–6.* Rockville: ORI, 1993–6.
12 Lock S. Misconduct in medical research. *Br Med J* 1988; **297**:1531–5.
13 Swazey JP, Anderson MS, Lewis KS. Ethical problems in academic research. *American Scientist* Nov/Dec 1993.
14 Jacobsen G, Hals A. Medical investigators' views about ethics and fraud in medical research. *J R Coll Physicians Lond* 1995;**29**:405–9.
15 Shapiro MF. Data audits in investigational drug trials and their implications for misconduct in science. In: Lock S, Wells F (eds). *Fraud and misconduct in medical research.* London: BMJ Publications, 1996.
16 Hamilton DP. In the trenches doubts about scientific integrity. *Science* 1994;**255**:1636.
17 Cancer and Leukaemia Group B. A successful system of scientific data audit for clinical trials. *JAMA* 1993;**270**:459–64.
18 Rowe PM. Encouraging good scientific conduct. *Lancet* 1994; **343**:1627.
19 Hone J. Combating fraud and misconduct in medical research. *Scrip Magazine* 1993;Mar:14–15.
20 Swann N. Baron Munchausen at the lab bench? In: Lock S, Wells F (eds). *Fraud and misconduct in medical research.* London: BMJ Publications, 1996.
21 Snow CP. *The Affair.* London: Macmillan, 1950.
22 Royal College of Physicians of London. *Fraud and misconduct in medical research.* London: RCP, 1991.
23 Smith R. Time to face up to research misconduct. *Br Med J* 1996; **312**:789–90.
24 Anonymous. Dealing with deception. *Lancet* 1996;**347**:843.
25 Beecher HK. *Experimentation in man.* Springfield, Illinois: Thomas, 1959.
26 Beecher HK. Ethics and clinical research. *N Engl J Med* 1965;**274**:1354–61.
27 Pappworth MH. *Human guinea pigs.* London: Routledge, 1967.
28 Anonymous. A mighty jam. *Economist* 1996;30 March:31.

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