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Medical Fraud - Causes and Consequences

Some personal reflections

Presented to the Bristol Medico-Historical Society, September 2012

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INTRODUCTION

The serious problem of scientific misconduct in medical research and practice has received considerable publicity in the medical, national and international press particularly in recent years [1-9]. Scientific misconduct is defined as "behaviour by a researcher, intentional or not, that falls short of good ethical and scientific standards" [10]. The National Committees on Scientific Dishonesty in the Nordic Countries have defined the more serious scientific fraud as "intentional distortion of the research process by fabrication of data, text, hypothesis, or methods from another researcher's manuscript form or publication; or distortion of the research process in other ways." [11]

How does fraud occur in medical science?

Among the ways that research fraud can arise are:

- Fabrication in which results are made up, then recorded or reported.
- Falsification in which research materials, equipment, or processes are manipulated and/or data or results are changed or omitted such that the research is not accurately represented in the research record.
- Plagiarism in which another person's ideas, processes, results, or words are appropriated without giving due credit
- Suppression in which dissemination and publication of findings contrary to the interests of some parties (e.g. drug companies) are inhibited.

Research fraud may be perpetrated by an individual (with or without collaborators) or an institution [3]. This paper focuses on the former.

In a Sunday Times article of 12 August 2012 [8], Brian Deer names 8 medical or biological scientists and 2 others who, he alleges, have been guilty of serious scientific fraud between 2002 and 2012. A 2009 systematic review [12] reported that around 2% of scientists confessed to committing fraud and 14% were aware of colleagues who had done so. Tavaré [4] quotes Malcolm Green, former vice-principal of the Faculty of Medicine, Imperial College, London as saying that "it is highly likely that for every case of fraud that is detected there are a dozen or more that go undetected".

What drives people to indulge in such fraud?

From personal experience and reading of the literature I wish to suggest that among the reasons, singly or in combination, are the following:

- A desperate need to succeed because of personal ambition or pressure from more senior staff or sponsors.
- An inability to accept that one may be in error because of 'confirmation bias'*, fear of failure or hubris.
- An overweening need for fame and fortune.
- Personality disorders or psychiatric illness (though this is more frequently claimed post hoc than propter hoc).
- Ineptitude or folly

In this paper I wish to provide a personal reflection on some of the above causes focussing on two major cases that have impinged on me particularly during my career as a clinical academic.

Personal Reflection

In the late 1960s, during my training as an obstetrician, I became aware of a problem that no one seemed to be able to resolve. This is that, having a genetic input from both mother and father, the fetus is at least partly 'foreign' i.e. it is an allograft. Why, therefore, is it not detected by the maternal immune system and rejected? Furthermore, could some pregnancy pathologies (e.g. miscarriage or pre-eclampsia?) have an immunological basis? In November 1969 Hellström et al, cancer immunologists working in Seattle, published a paper in Nature [14] suggesting that not only did the maternal immune system recognise the antigenically foreign embryo but that this immune response was blocked by a serum factor presumed to be 'blocking antibodies'. This was a very significant finding not only for feto-maternal relations but it could also have had important implications for tumour immunology. I began to pursue this line of research and was able to obtain an MRC grant to do so (those were the days!). In 1971 I was also fortunate enough to obtain a scholarship from the Royal College of Obstetricians and Gynaecologists to visit the Hellströms in the University of Washington in Seattle. On my arrival in Seattle it was disconcerting to discover that they had replaced the technique reported in the Nature article [14] by another.

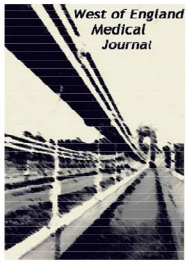
* Confirmation bias is "the tendency to look at evidence and then try to interpret it to suit our original views" [13].

On my return to St Mary's Hospital in London I began to carry out research in the laboratory while still working as a lecturer in Obstetrics and Gynaecology. I could not get their technique to work so developed my own variant of it [15] on which I worked for the next two years. I still could not reproduce their results. Was this a problem with the method or me; or was this the real situation? Negative findings are always more difficult to sell to the scientific community and examiners of theses! Whatever the cause this was a stressful time and I began to think what I might need to do to come up with some more positive results. Exactly at that moment in 1974 what became a cause celebre hit the headlines.

The Sloan-Kettering Affair [16]

This was named after the famous cancer research institute in New York in which it occurred. The primary player was William Summerlin, a young dermatologist from Minneapolis. He was carrying out research on skin transplantation in mice and reported that he could transplant tissue from genetically unrelated animals without rejection by the recipient animal if he kept the tissue from the donor in organ culture for four to six weeks. Given that he was working during the time of the Vietnam War, this had tremendous implications for skin grafting of burn victims from that war as well as from other causes. This work came to the attention of Robert A. Good, the famous cancer immunologist, in the Sloan-Kettering Institute. Summerlin went to work with Good in the early 1970's. Initially Summerlin could not reproduce the results and he claims that Good put him under pressure. The results seemed to improve and on 26 March 1974 he was due to report to Good on the results of the latest experiments. This was a fateful day! A technician noticed that the transplanted patches were actually painted or touched up on the skin of the mice with a felt-tipped marker. When confronted, Summerlin admitted the fraud and other issues emerged later relating to corneal grafts in rabbits.

Summerlin pleaded stress and mental illness and he left to work in obscurity in Louisiana. Robert Good was accused of manipulating national attention and attracting an enormous amount of money for the Institute. Soon afterward he stepped down as director of Sloan-Kettering. This whole episode was described in the New



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York Times [17] as “a medical Watergate” that reflected “dangerous trends in current efforts to gain scientific acclaim and funds for research. ”

There is an interesting codicil to this story. One of the mice in the original experiments in which the skin graft had survived was still alive. When tested it was found not to be pure bred but a hybrid. At the time I recall being told anecdotally that a lab technician in the original laboratory had allowed some of the pure bred mice to escape and had hastily tried to put them back in their cages without confessing this at the time. This cannot now be confirmed but if mice of different strains had been mixed they would interbreed and produce hybrid offspring. The original success may have been due to the actions of the lab technician rather than any intent to commit fraud by Dr Summerlin. Unfortunately he became trapped by this pseudo success. For me this was a wake up call and, in 1975, I reported my findings, ‘warts and all’, in my MD thesis.

On moving to Oxford University in 1975, I was subsequently part of a research team that was among the first to demonstrate that the fetus was protected against rejection by very special properties of the placenta and not by ‘blocking antibodies’ at all [18]. Interestingly it is the placenta that provides the link to the second story I wish to tell.

The Fraud of Abderhalden’s Enzymes [19]



Figure 1: Emil Abderhalden (1877-1950) as a young man (Wikipedia)

Emil Abderhalden, born in Switzerland in 1877, has been called the founder of scientific biochemistry. He was Professor of Physiology and Physiological Chemistry in Halle University, Germany, from 1911 to his death in 1950. Interestingly, in light of subsequent events, he edited the journal ‘Ethik’ from 1922 to 1935 and was president of the Leopoldina, Germany’s oldest Academy of Science, between 1931 and 1946. He was author of more than 1000 research papers though his scientific approach was interesting - he once told an eminent immunologist “if an experiment worked well once why should it be repeated?” [19] Actively anti-semitic, he was also a convinced eugenicist [19].

In 1909 he reported a discovery that he considered to be the most important of his long career. This was of ‘abwehrfermente’ (defence or protection enzymes) that were produced by a process that started with boiling a placenta. Among the suggested uses of their detection were the diagnosis of pregnancy, cancers, infectious diseases such as syphilis and psychiatric diseases such as schizophrenia.

By 1914 there were 451 papers enthusiastically describing various uses of the test for abwehrfermente and Abderhalden suggested that “cancer treatment using abwehrfermente is just around the corner” without giving any information as to the mechanism for this. However, also in 1914 Michaelis and Lagermark [20] published a paper stating that they could not repeat Abderhalden’s experiments. This was the end of Michaelis’s career in Germany. Belief in the value of testing for abwehrfermente persisted. In 1942 the test was used to demonstrate supposed racial differences in responses to infectious diseases and in 1943 Verschuer and Mengele obtained a grant from Deutsche Forschungsgemeinschaft to test the production of these enzymes in response to deliberate infections of over 200 individuals of various races [19]. These tests took place in Auschwitz.

Emil Abderhalden died in 1950 but his son Rudolf continued with his father’s work. He declared that abwehrfermente were “the perfect diagnostic tools to determine the optimal cell type for ‘fresh cell therapy’” [19] (another medical fraud!) Despite their non-existence papers on the subject did not disappear from the literature until the 1960s and fresh cell therapy was outlawed in Germany only in 1997. Deichmann & Muller-Hill [19] ask “How could Abderhalden continue with the deception from 1915 until his death in 1950? His strategy was simple and straightforward. He must have had collaborators who

found what he wanted them to find. In medical biochemistry, ideas or hope may be stronger than experimentally proven reality”.

Recent literature already referred to [1-9] suggests that this chilling tale has counterparts in modern science and medicine.

What are the Consequences of Medical Fraud?

In the above stories some of the consequences of medical fraud have been explicit and others implicit. Among them are that it:

- Directly or indirectly harms patients [2,5]. False hopes or unwarranted alarm may be generated.
- Distorts the evidence base
- Misdirects research efforts
- Wastes funds
- Destroys careers both of the perpetrators, their associates and, sometimes, ‘whistle blowers’.
- Damages public trust in Science

It is, therefore, important that effective action be taken to prevent scientific misconduct and fraud. In 1989 the National Institute of Health in the USA established the Office of Scientific Integrity though it has been described as ‘Orwellian’ [21].

The independent UK Research Integrity Office, established in 2006, aims to promote the good governance, management and conduct of academic, scientific and medical research; share good practice on how to address poor practice, misconduct and unethical behaviour; and give confidential, independent and expert advice on specific research projects, cases, problems and issues [22]. In 2009 it published a Code of Practice for Research [23]. In addition, on 11 July 2012, Universities UK launched a concordat to strengthen research integrity of government departments. It remains to be seen how effective these measures really are but further consideration is beyond the scope of this paper.

REFERENCES

1. Evered D, Lazar P. Misconduct in medical research. *Lancet* 1995; 345: 1161-2
2. Godlee F. The fraud behind the MMR scare. *BMJ* 2011; 342:d22
3. Godlee F. Institutional research misconduct *BMJ* 2011; 343: d7284
4. Tavaré A. Managing research misconduct. Is anyone getting it right? *BMJ* 2011; 343:d8212
5. Godlee F. Research misconduct harms patients. *BMJ* 2012; 344: e-14



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References (continued)

6. Godlee F, Wager E. Research misconduct in the UK BMJ 2012; 344: d8357.
7. Tavaré A, Godless F. Tackling research misconduct BMJ 2012; 345 :e5402
8. Deer B Doctoring the evidence: What the science establishment doesn't want you to know. Sunday Times 12 August 2012.
9. Riis P Scientific dishonesty: European reflections. J Clin Pathol 2001; 54: 4-6
10. Nimmo WS, ed. Misconduct in biomedical research: final consensus statement. In: Joint consensus conference on misconduct in biomedical research. Proc R Coll Physicians Edinb; 2000; 30(suppl 7):2.
11. Nylenna, M et al. Handling of scientific dishonesty in the Nordic countries. National Committees on Scientific Dishonesty in the Nordic Countries. Lancet 1999; 354: 57-61
12. Fanelli D. How many scientists fabricate and falsify research? A systematic review and meta-analysis of survey data. PloS One 2009;4: e5738
13. Aaronovitch D. The Stalinists of the mind are alive and well. Sunday Times 23 August 2012 p.21.
14. Hellstrom KE, Hellstrom I, Brawn J Abrogation of cellular immunity to antigenically foreign mouse embryonic cells by a serum factor. Nature 1969; 224:914-5
15. Stirrat GM. A terminal-labelling microcytotoxicity assay with ¹²⁵I-iododeoxyuridine as a label for target cells. J. Immunol. Methods 1976; 12:201-8.
16. Culliton BJ. The Sloan-Kettering Affair Science 1974; 184; 1154-7.
17. Brody JE. Charge of False Research Data Stirs Cancer Scientists at Sloan-Kettering New York Times April 18 1974
18. Sunderland CA, Naim M et al The expression of MHC antigens by human chorionic villi. J. Reprod Immunol 1981; 3: 323.
19. Deichmann U, Muller-Hill B. The Fraud of Abderhalden's Enzymes Nature 1998; 393: 109-111
20. Michaelis, L. & Lagermark, Lv. Bedeutung der Abderhalden'schen Untersuchungsmethode. Deutsche Med. Wochenschr. 1914; 7: 316-319
21. Klein DF. Should the government assure scientific integrity? Academic Medicine 1993; 68 (9 suppl.) S56-9
22. UK Research Integrity Office <http://www.ukrio.org/> accessed 13 September 2012.
23. Code of Practice for Research: Promoting good practice and preventing misconduct. UKRIO 2009 <http://www.ukrio.org/what-we-do/code-of-practice-for-research/> accessed 13 September 2012.