

ISSUES IN DENTAL ETHICS

American Society
for Dental Ethics

ASSOCIATE EDITORS

James T. Rule, DDS, MS
David T. Ozar, PhD

EDITORIAL BOARD

Muriel J. Bebeau, PhD
Phyllis L. Beemsterboer, RDH, EdD
Larry Jenson, DDS
Anne Koerber, DDS, PhD
Donald E. Patthoff, Jr., DDS
Bruce N. Peltier, PhD, MBA
Gary H. Westerman, DDS, MS
Gerald R. Winslow, PhD
Pamela Zarkowski, RDH, JD

Correspondence relating to the
Issues in Dental Ethics section of the
*Journal of the American College of
Dentists* should be addressed to:
James Rule
8842 High Banks Drive
Easton, MD 21601
jimrule@goecw.net

VIOLATION OF TRUST

ETHICAL AND LEGAL CONSIDERATIONS IN A CASE OF RESEARCH FRAUD

Sigrid I. Kvaal, BDS, Dr Odont

ABSTRACT

In 2006 a researcher at the main hospital in Norway admitted that he had forged data in a study published in the medical journal *The Lancet* that was co-authored by 13 others from both Europe and America. The researcher, dually qualified in dentistry and medicine, immediately admitted fabricating the results. A Commission of Enquiry reported that most of his publications were fabricated or manipulated and that he was alone in the fraud. As a result, the researcher lost his authorization to practice medicine and dentistry. His action has shaken the trustworthiness of science and the trust for the scientific community, both in the institutions that support the research and in the review process in science publications.

Following this revelation, the management of scientific fraud has been widely discussed, including concerns about the dual role of a Commission of Enquiry as both investigator and judge, and also the legal rights of fraudulent scientists. Other issues concern the responsibilities of supervisors and institutions in the guidance of candidates in research procedures and ethics. In addition, commentaries have appeared in national newspapers as well as in medical and dental scientific journals. Various issues have been discussed, including the fact that editors and referees in scientific publications rarely have the opportunity to check raw data, which emphasizes the need for data confirmation by independent groups. These reflections have been fruitful for the community, although it will not, nor can it, prevent fraud in the future.

A press release on January 16, 2006 from the Rikshospitalet-Radiumhospitalet Medical Center in Norway stated that a hospital scientist had fabricated data in cancer research. He had written, together with 13 co-authors from both Europe and America, an article that was published in the prestigious scientific medical journal *The Lancet* in October 2005 (Sudbø et al, 2005). The article, which was based on the author's doctoral dissertation research, reported that non-steroidal anti-inflammatory drugs (NSAID) might reduce the risk of oral cancers but increase the risk of cardiac problems.

The division director of the newly established national health register discovered that the study's data were claimed to have been received from a drug registry before it was actually operational. She warned other colleagues and health institutions about this discrepancy. When a search was made in the raw data, it was obvious that all 908 patients had been invented. A couple of years earlier the American National Cancer Institute had awarded a \$10 million research grant to a prestigious international research group, and a



Dr. Kvaal is a member of the Faculty of Dentistry, Institute of Clinical Dentistry, University of Oslo, Norway; skvaal@odont.uio.no.

substantial amount of that sum had been allocated to a clinical study at the Radiumhospital in Norway. The fraud, with its international involvement, was picked up by news agencies and became a worldwide research scandal.

The lead researcher, who was also employed as a consultant at the hospital, was dually qualified in odontology and medicine and had obtained a doctorate in medicine in 2001 at the University of Oslo, Norway. He had 38 publications listed in *PubMed*. It soon became clear that it was not only *The Lancet* article that was based on fraud, for he admitted a partial manipulation of data in earlier articles in the *Journal of Clinical Oncology* and *The New England Journal of Medicine*. In addition, several other of his publications were suspected of containing fictional or incorrect data. Both *The Lancet* and *The New England Journal of Medicine* have issued expressions of concern (Curfman et al, 2006; Horton, 2006).

A Commission of Enquiry was appointed in the middle of January 2006. Although the researcher had confessed to inventing and manipulating the data in three publications that derived from his doctoral thesis, the commission concentrated on the research work which made up most of his doctoral thesis and the articles that resulted from it. The investigation turned out to be more extensive than first anticipated, and at the end of June 2006 the Commission published a 144-page report. This report is the major source of background material for this article and is available in English at www.rikshospitalet.no/portal/page/portal/no/forsiden/globale/oss/article_doc?p_doc=411236&p_dim_id=44887. (Although this paper contains

only references in English, much of the source material is available in Norwegian, and scholars who are interested may contact the author.)

Thirty-eight articles were reviewed and almost 60 co-authors in five different countries were contacted by the commission in its investigation. In the initial phase, the co-authors were asked to make a written statement of their involvement and answer questions. All the co-authors responded to the initial contact, which demonstrated their willingness to co-operate and may indicate that they did not have anything to hide. Some of the co-authors were also called for one or more interviews with the commission, during which they were questioned on their statements and asked to clarify inconsistencies. In addition to these statements, the commission obtained copies of correspondence and documentation from co-workers and compared these with the published results.

The commission found that most of the published research was based on manipulated or incorrect data, and they recommended that 13 of the articles be withdrawn. As early as 2001, an article in *The New England Journal of Medicine* contained examples of manipulations such as double registration of patients and fictitious interviews. In addition, various other inconsistencies were noted. For example, patients who already had been diagnosed with cancer were included in a study of patients with a risk of developing cancer. Altogether, 69 out of 141 patients should have been excluded for various reasons. The results presented in the article were therefore not representative.

An article in the *Journal of Clinical Oncology* from 2005 contained inconsistencies and incorrect registration of data, and the commission also questioned whether the patient material presented in the paper existed at all. *The Lancet* article from 2005 was based on 454 fictitious patients and an equal number

of controls, and was thus founded entirely on fabricated material.

The report concluded that the researcher had acted independently in manipulating the data. This he could do because he had full control over the material and all communication. There was no evidence that any of the co-workers were involved in the fraud. None of the co-authors were given opportunity to check the results, and, when they made enquiries, they were given different explanations. In one of the articles it was stated that the diagnosis of the material was checked by one of three oral pathologists, but it did not specify who. When questions were raised, inquirers were given the impression that it had been done by one of the other two, which as it turned out, was not the case. This was an example of collective and cumulative mistakes.

As a consequence of a recommendation from the commission, the University of Oslo retracted the researcher's doctoral degree. The Norwegian Board of Health Supervision has also withdrawn his authorization to practice as a medical doctor and dentist.

This paper looks at some ethical issues related to the report of the Commission of Enquiry. Some ethical aspects related to co-workers, co-authors, and institutions to which they belong will also be discussed. Included are some reflections on the process of peer review in scientific journals and on the responsibility of editors, both in scientific publications and in the national press.

ETHICAL CONSIDERATIONS

Fraud in science may be defined as the intention to deceive, in contrast to error or carelessness. It includes fabrication, falsification, and plagiarism. The term dishonesty may be used to separate all

forms of misconduct from carelessness and honest mistakes (Franzen et al, 2007).

DETERMINATION OF FRAUD

The Commission of Enquiry that was appointed in this case was headed by a highly respected non-Norwegian professor of epidemiology at the Karolinska University Hospital in Stockholm. The other four members were from the Faculty of Law and the Faculty of Medicine at the University of Bergen, from the Institute of Public Health, and from the Research Council of Norway. The secretary, a law graduate, was from the Department of Public Health and General Practice at the University in Trondheim, Norway. All members represented institutions not connected to the Radiumhospital or the University of Oslo, and nobody has questioned the impartiality of the commission.

The task of the Commission of Enquiry was to conduct an independent investigation in accordance with the detailed terms of reference. As explained in its paper, the commission has applied “a standard of evidence entailing a qualified preponderance of probability as a condition for accepting a particular fact as grounds for the report.”

One of the differences between a court of law and a commission of enquiry is that in the latter case, the same group of people performs the investigation, presents findings, draws a conclusion, and in most cases gives recommendations for action in such a way that it acts both as the investigator and judge. The conclusion has no official judicial status, but such a commission's recommendations have serious and wide-reaching implications. The hearings are private, and although the defendant and some of the co-authors in this case were given drafts that included the opportunity to challenge their findings, the commission's findings are regarded as facts with no opportunity to appeal. It is essential that such a

commission has members that can understand both scientific and legal implications of the case. In addition, members must be independent and preferably from outside the institution, since administrators at research institutions and universities often do not have such expertise and may not appear to be impartial. Furthermore, some universities are reluctant to initiate investigation in alleged fraud cases because they may fear that a guilty verdict will stain their reputation (Brumfield, 2007). Such concerns are magnified when, as in this case, the researcher has legal representation.

SUPERVISORY RESPONSIBILITY

Another ethical concern in this case pertains to the responsibility of the supervisor of a doctoral thesis to guide and advise the candidate. A doctoral thesis must be original and independent research, and it is the supervisor's responsibility to ensure that quality assurance control of the work is performed. However, the candidate might easily get a feeling of distrust if the supervisor repeats all the tests in order to verify the candidate's data entries. Some candidates work more independently than others, and in this case there was no reason to question whether anything untoward had been done when the researcher said that he had done it. Another responsibility of a supervisor is to help with the applications to the various legal and ethical committees. In Norway there are several examples—including this case—of compromised follow-up.

The working relationship between a supervisor and a PhD candidate is now more formalized than it was 15 years ago. The present regulations for the degree of Philosophiae Doctor (PhD) state that supervisors and PhD candidates must maintain regular contact and that

The Lancet article from 2005 was based on 454 fictitious patients and an equal number of controls, and was thus founded entirely on fabricated material.

the supervisor is responsible for ensuring that the PhD candidate participates regularly in an active research group. Both parties have to sign ethical regulations. The examples set by senior researchers and department heads who show positive leadership appear to be important in fostering good ethical conduct (Giles, 2007).

RESPONSIBILITIES OF AUTHORSHIP

Co-authors' and institutions' responsibilities have been widely discussed in the medical community and in the press. The International Committee of Medical Journal Editors, Uniform Requirement (Vancouver Regulations) states that the authorship credit should be based on "substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; drafting the article or revising it critically for important intellectual content; and final approval of the version to be published." Authors must meet all requirements. These requirements are available at www.icmje.org.

The requirements state quite clearly that co-authors should contribute substantially to the article. Even so, the requirement that all co-authors should be involved in all three processes has been criticized for its strictness (Kwok, 2005). Current research is often so specialized that there are few others who can do the job. However, all authors have to take part in discussions, critical reviews, and the granting of final approval of the manuscript.

In addition, the granting of authorship requires justification. Collection of data alone no longer is considered as meeting that requirement. Along a

different line, in at least one of the articles investigated in the fraud case, the suppliers of research material were co-authors. According to the Vancouver instructions, they should only have been included in the acknowledgments.

The tradition of gift authorship was once an accepted procedure, but no longer meets the requirements of the International Committee of Medical Journal Editors. An example is that in some countries there has been a tradition that the head of department is always included as an author. Such traditions also exist in some departments in Norway, but not in the fraud case presented here.

ISSUES IN THE EDITORIAL PROCESS

The editors of scientific journals have authority over the editorial content as well as the quality and scientific relevance for their readers. They seek advice from referees, but they make the final decision themselves, which means that they have the responsibility to see that what they publish is of the required quality and scientific standard. However, each country has its own national regulations and medical systems, and it is unreasonable that overseas editors will know about them.

Another issue is the duty of the editors to retract already published articles where it turns out that the research is based on false and incorrect data. Equally, the co-authors should check their references to ensure that retracted articles are not included (Sox & Drummond, 2006). (One exception might be that the retracted paper contains detailed description of methods unavailable elsewhere.) Then comments and retractions should be included (Odell, 2007).

The responsibility of referees in scientific journals is considerable, but

also limited. They can comment on the scientific content and presentation. They should check that the relevant statistical methods are applied, but they have to trust the authors' statement on how the raw material was collected and entered into the analyses. Articles must present new discoveries or methods to the scientific community to reach the high-ranking medical journals. This fraud case, as well as several others, shows how important it is that all new discoveries are confirmed by other independent groups before they can be accepted in the scientific community.

OTHER ETHICAL ISSUES

Plagiarism has long been a difficult issue for editors and the scientific community to deal with. In today's world, the risk of plagiarism is significantly increased by access to the Internet and is not easy to demonstrate unless the entire work is copied. Plagiarism was not an issue in the current case.

Another issue pertains to the education of researchers. All research institutions—hospitals, universities, or national organizations—together with the supervisors and co-worker have the responsibility to educate the fresh researcher in the ethical principles of research. This not only implies attending courses but also the daily application of principles by supervisors and senior researchers who inevitably must be regarded as role models. It is also important that the institutional recommendations for the conduct of research be known and followed by all researchers. In addition, a procedure for making complaints should be available and known by all.

Commercialism in science and publications may also encourage misconduct. For example, some scientific journals are dependent on "revealing" discoveries in order to sell their product. Research groups are dependent on

grants that are awarded to innovative groups who produce many publications in journals with a high impact factor. Such competition may lead to rushed results rather than well-controlled studies.

RESPONSE FROM THE SCIENTIFIC COMMUNITY AND THE PUBLIC

A book describing a case of whistleblowing in medical research was published in Norway shortly before this research fraud was discovered. The *Journal of the Norwegian Medical Association* received letters to the editor related to the content of the book and to ethics in research in general; misconduct reported earlier in this paper was a case in question.

The first issue of the *Norwegian Dental Journal* in 2006 contained an editorial on ethics in research which was in print before the fraud case described in this paper was made public, and the journal closed the year with another editorial summing up what had happened during the year. Both the aforementioned journals published separate expressions of concern related to a single article that was published in both journals. Based on the statements in the commission's report in the current case, the article has been retracted without the researcher's consent. In addition, all the co-authors have taken the initiative to write to the two journals and to ask for retraction of the relevant articles.

The research fraud described in this paper was also a popular topic in the national press in Norway. The researcher was regarded as guilty from the start, and since he had admitted fraud, this assumption was to some extent correct. The co-authors, on the other hand, were found neither responsible nor negligent by the commission. They were, however, heavily criticized in the press before the commission's report was published. It

was repeatedly maintained that there was no way they could be co-authors and not know of the fraud. A letter to the editor from a medical professor published by a national paper led to a complaint to the Ethics Council of the Norwegian Medical Association. The council considered it "important, timely, and commendable" that the responsibilities of the research institutions with regard to publications are discussed in public, but in this case "unnecessary condemnatory phrases had been used to characterize co-authors."

There are many stories of how whistleblowers have been treated badly by the research community and institutions. This case was different. The division director of the national register, who first alerted colleagues to the fact that the cancer research may contain irregularities, has today more fame than she feels she deserves. She maintains that she is no hero but did what she felt was her duty as a newly appointed administrator. This duty is to notify the appropriate authorities when irregularities are discovered in research, provided that the irregularities are based on well-founded facts.

IMPLICATIONS AND REVERBERATIONS

As mentioned previously, the researcher was found guilty of fraud, lost his job, his PhD, and his authorization to practice both as a physician and dentist. In addition, his scientific work is regarded as invalid. More than that, his fraudulent scientific work could have serious consequences for patients and is not in conformity with good medical or dental practice. Based on these arguments there was no other choice but to withdraw his authorization to practice. Furthermore, his doctoral thesis contained so many errors in the data that it should not have qualified for a degree. Each of these decisions is well founded, and when such fraud is uncovered it must have

The researcher was found guilty of fraud, lost his job, his PhD, and his authorization to practice both as a physician and dentist.

The examples set by senior researchers and department heads who show positive leadership appear to be important in the fostering of good ethical conduct.

serious consequences. It is a truly serious and tragic end for a good clinician and a highly intelligent scientist.

When the fraud was made public, a PhD candidate from the Faculty of Dentistry had just submitted her thesis. Some of her research had been based on material received from the fraudulent researcher. Her thesis had to be withdrawn and she had to start again from scratch.

Anxious telephone calls have been received from patients who wondered what was going on. Fortunately, even though some patients had been allocated to the research program, none of them had been included. Therefore these anxious callers could be reassured. This program is now discontinued.

The commission had recommended that institutions and universities strengthen their controls to prevent fraud. On June 1, 2007 a new act on ethics and integrity in research was introduced in Norway. This act reinforces the previous regulations and makes them more formalized. The preparation work for this act was started before the fraud presented here was discovered, but this case reinforced the need for ethical approval and complaint procedures in research. Both national and regional ethical committees will be established, and prior approval has to be obtained if the research involves human subjects. The National Committees for Research Ethics in Norway were established as independent institutions as long ago as 1990. Having been initially disbanded, the new act has called for the reinstatement of such national and regional committees.

The Faculty of Medicine, University of Oslo, already has a Web site with good information regarding ethical issues which is both relevant for undergraduates as well as established researchers, and

both the Faculty of Medicine and the Faculty of Odontology now cooperate on education regarding research ethics and procedures.

Several questions remain unanswered, among them the fraudulent researcher's motives for acting as he did and choosing to violate the trust given to him by his supervisor, his co-workers, and his research institution. It is quite clear that the article in *The Lancet* was written with the intention of deceiving, and in some of the other publications there is certainly a strong suspicion of intent to defraud. His earlier work could at best be attributed to ignorance. One can only speculate on the reason why he chose this course of action. It has been shown that some researchers constantly try to prove themselves by publishing papers or behaving unethically if they think managers are treating them unfairly (Giles, 2007). Whether this is a possibility here is unknown.

Science published in July 2006 an article entitled "Fake data, but could the idea still be right" (Couzin, 2006). It states that three groups are trying to follow up the researcher's initial work on DNA abnormalities in cells as a prognostic factor. An article from March 2007 shows that the diagnostic technique using DNA abnormality to predict the development of cancer can have predictive value in oral verrucous leukoplakia, but the background material in this article is very small (Klanrit et al, 2007). It has also been shown that the abnormal DNA in cells from lesions on other sites than the oral cavity can be used to predict the outcome of treatment.

It is possible that the researcher's main conclusion was correct. However, the evidence so far has not been as convincing as his research maintains—not a surprising observation since he had deliberately improved the results. Regarding NSAID in cancer prevention, that is still an open question (Rainsford, 2007).

One other issue that evolved from this case should be noted. In June 2007 the researcher was granted restricted authorization and allowed to practice dentistry under supervision in a community dental clinic. This action has provoked questions about whether lower ethical standards are required to practice dentistry than medicine.

CONCLUSION

Scientific journals make public the results of research work done all over the world. The scientific community has always relied on trust from co-workers and institutions, and that what is submitted for publication is factually correct, but someone will always try to manipulate the truth and betray that trust. When serious fraud comes to light, other minor irregularities are also discovered. Errors, however, are made all the time. They may be unintentional by excluding outlying data, not including patients where data is missing, incorrect statistical handling, etc. (Franzen et al, 2007). Such minor acts of misconduct are much more common and potentially more damaging to the scientific progress and are rarely discovered (Giles, 2007). Preventive measures cannot stop those whose intention it is to commit misconduct. Good record keeping, robust and positive mentoring, and experiments which are run properly rather than rushed are important factors so that professionals and the public can trust biomedical science. New revelations in scientific research are rarely valid before they have been replicated by independent groups. This case is an example of fallibility in many aspects, including the education and training of researchers, the peer review process of journals, and the self-regulation of scientific professionals. ■

REFERENCES

- Brumfield, G. (2007). Misconduct? It's all academic. *Nature*, 445, 240-241.
- Couzin, J. (2006). Fake data, but could the idea still be right. *Science*, 313, 154.
- Curfman, G. D., Morrissey, S., & Drazen, J. M. (2006). Expression of concern: Sudbø, J. et al., DNA content as a prognostic marker in patients with oral leukoplakia and Sudbø, J. et al., The influence of resection and aneuploidy on mortality in oral leukoplakia. *New England Journal of Medicine*, 354, 638.
- Franzen, M., Rödder, S., & Weingart, P. (2007). Fraud: Causes and culprits as perceived by science and the media. *European Molecular Biology Organization Journal*, 8, 3-7.
- Giles, J. (2007). Breeding cheats. *Nature*, 445, 242-243.
- Horton, R. (2006). Expression of concern: Non-steroidal anti-inflammatory drugs and the risk of oral cancer. *The Lancet*, 367, 196.
- Klanrit, P., Sperandio, M., Brown, A. L., Shirlaw, P. J., Challacombe, S. J., et al (2007). DNA ploidy in proliferative verrucous leukoplakia. *Oral Oncology*, 43 (3), 310-6.
- Kwok, L. S. (2005). The White Bull effect: Abusive co-authorship and publication parasitism. *Journal of Medical Ethics*, 31, 551-556.
- Odell, E. (2007). Reply to "Letter to the Editor" from Jan Olofsson. *Oral Oncology*, 43, 622.
- Pincock, S. (2006). Lancet study faked. *The Scientist*, 16 January.
- Rainsford, K. D. (2007). Anti-inflammatory drugs in the 21st century. *Subcellular Biochemistry*, 42, 3-27.
- Sox, H. C., & Drummond, R. (2006). Research misconduct, retraction and cleansing the medical literature: Lessons from the Poehlman case. *Annals of Internal Medicine*, 144, 609-613.
- Sudbø, J., Lee, J. J., Lippman, S. M., Mork, J., Sagen, S., et al (2005). Non-steroidal anti-inflammatory drugs and the risk of oral cancer: A nested case-control study. *The Lancet*, 366, (9494), 1359-1366.

This duty is to notify the appropriate authorities when irregularities are discovered in research, providing the irregularities are based on well-founded facts.