Research misconduct

Peter Wilmshurst
Consultant Cardiologist
Royal Stoke University Hospital
Conflicts of interest

• Investigated research misconduct in UK and abroad
• Reported more than 25 doctors to GMC
• My first involvement with research misconduct was in 1980s
• I have been threatened with legal action several times when I reported misconduct
• 2007-2011 sued for libel 4 times by NMT Medical until they went into liquidation
Name of Respondent Doctor: Dr Andrew John DOWSON

Registered Qualifications: MB BS 1984 Lond

Registration Number: 2953399

Type of Case: New Case
Misconduct

Panel Members: Mr Douglas Gentleman – Chairman (Medical)
Rev John Philpott (Lay)
Mr Andrew Popat (Lay)
Professor Michael Whitehouse (Medical)

Legal Assessor: Mr Gerald Godfrey CBE QC

Secretary to the Panel: Mrs Nilla Varsani

Representation:

GMC: Mrs Sarah Plaschkes, Counsel, instructed by the Mills & Reeve Solicitors represented the General Medical Council.

Doctor: Dr Dowson was present and was represented by Mr Angus McCulloch, Counsel instructed by the Medical Protection Society.
Amrinone: 1980s

- Ineffective and unsafe cardiac drug
- Offered bribe and then made legal threats
- Sterling-Winthrop submitted false data
- Unethical marketing of a drug that increased patient mortality in Africa and Asia
- No prosecution for breaking UK law
- GMC refused to investigate doctors
- BMJ, Lancet & Nature refused to report
Drugs firm ‘made threats’

By James Erlichman

Three doctors at a London teaching hospital say that the Sterling-Winthrop pharmaceuticals company threatened them and tried to discredit their research when they discovered that its new heart drug was dangerous and ineffective.

The company, in a statement, denies these claims. But

Drug tested without DHSS clearance, page 6

...the doctors, all senior cardiologists at St Thomas’ Hospital, believe that their warnings played a key role in keeping the capsule, called amrinone, off the British market and in severely restricting its use elsewhere.

They say the company had allowed them to believe that it had received safety clearance from the Department of Health to begin clinical trials with oral amrinone on seriously ill patients at St Thomas’. In fact, a clinical trials certificate was never issued.

"Sterling-Winthrop's behaviour in this whole matter was quite unbelievable," said Dr Stephen Jenkins, one of the consultants involved in the clinical trial who has since become Lambeth Health Authority's district general manager. "It shattered us here at St Thomas' that a drug company would behave in this way."

The drug company claimed amrinone had a good safety record and unique life-saving properties. But more than half of the heart patients in the trial suffered adverse reactions, including liver failure, serious gastric conditions and disturbance of the immune system. The doctors could find no evidence, as the company had claimed, that amrinone improved the heart's pumping.

Instead of heeding these warnings, the doctors say Sterling-Winthrop accused them of fabricating their results and threatened them with legal action. At one stage Sterling-Winthrop removed supplies of amrinone from the pharmacy at St Thomas’s without the doctors' knowledge.

Dr Michael Webb-Peploe, the senior consultant who supervised the clinical trial, said: "The two things that upset me most are that undue pressure was brought to bear on us by Sterling-Winthrop and supplies of the drug were taken from the hospital without our permission."

The doctors say that the company tried repeatedly to convince them that their fears about amrinone were at variance with eminent medical opinion elsewhere, especially in the United States.

Much was riding on the drug's success. Stock market analysts, still believing that amrinone would prove a genuine breakthrough in the treatment of congestive heart failure, expected its worldwide

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Research misconduct includes:

- Falsification, fabrication and plagiarism
- Duplicate publication (effects meta-analysis)
- Failure to retract fraudulent publications
- Lack of ethics approval / informed consent
- Poor trial design / literature review
- Delay in or failure to publish results
- Failure to disclose conflicts of interest
- Misuse of research grants
Impact of research misconduct

• Harms patients, wastes resources and undermines public trust in science
• But can be beneficial for career advancement of fraudsters and profits of healthcare corporations
Prevalence of research misconduct

• Unknown prevalence because it is concealed

• BMJ 1988 – Half of UK academics knew of research fraud, 8% retracted, 3% dismissed

• Retraction Watch - 200 retraction in 2010 & more than 18,000 by 2018
Number of retractions

- Yoshitaka Fujii, Japan, anaesthetics, 183
- Joachim Boldt, Germany, anaesthetics, 96
- Bob Slutsky, USA, cardiology, 79 *
- John Darsee, USA, cardiology, 60*
- Diederik Stapel, Netherlands, Psychology, 58

* Slutsky & Darsee were not exposed by colleagues who knew of fraud – in Slutsky’s case known for more than 5 years
The code of silence

Peter Wilmshurst

Documentary evidence corroborating Dr Wilmshurst's article was made available to The Lancet.

References
Dr AK Banerjee & Prof Tim Peters

- 1990 Banerjee admitted research frauds to senior officials at King’s College London
- Whistleblowers silenced, evidence destroyed, research grants not repaid
- Banerjee & Peters published fraudulent data
- 1991 Banerjee awarded MS degree
- 1998 I reported to GMC
- 2000 serious professional misconduct
- 2015 MS withdrawn by London University
Institutional corruption in medicine

Peter Wilmshurst

The General Medical Council recently found that Mr Anjan Kumar Banerjee and Professor Timothy John Peters were guilty of serious professional misconduct for research misconduct committed a decade earlier. Peter Wilmshurst argues that this is not just a case of one doctor covering up for another but of corruption at a senior level in academic institutions.

For the triumph of evil it is only necessary for good men to do nothing

Edmund Burke

A decade elapsed between Anjan Kumar Banerjee admitting to senior doctors at King’s College Hospital that he had falsified scientific research and the finding by the Professional Conduct Committee of the General Medical Council on 30 November 2000 that Banerjee was guilty of serious professional conduct because of that dishonesty. Professor Timothy John Peters, Banerjee’s research supervisor from 1988 to 1991, was also found guilty of serious professional misconduct at a separate hearing on 28 February 2001. The GMC found that, after he became aware that Banerjee had falsified research, Peters had failed to prevent Banerjee falsifying further research, failed to retract publications that contained falsified research and which named both of them as authors, failed to bring Banerjee’s misconduct to the attention of the GMC, and supplied a misleading final report on Banerjee’s work to the Medical Research Council, which had funded the work.

This much is well reported, but the greater scandal

Summary points

The finding by the General Medical Council that Anjan K Banerjee and Timothy J Peters were guilty of serious professional misconduct for research misconduct committed a decade earlier is an indictment of the senior management in the academic institutions that helped to conceal the misconduct.

Senior academics (Professors Harold Baum and TJ Peters) and the secretary of King’s College Hospital Medical School (Mr H T Musselwhite) were aware that Banerjee had falsified his research but failed to bring this to the attention of the GMC, the funding bodies, or the journal that had published the falsified research.

The University of London was informed that Banerjee had falsified his master of surgery thesis but did not withdraw the degree.
Dr Clive Handler

- Finding of serious professional misconduct by the PCC in Nov 2002
- Embezzled charitable research funds
- Hospital internal investigation chaired by Professor Peter Richards (Medical Director)
- Prof Richards and Trust Board agree a severance agreement with Handler including that they would not inform police or GMC
Professor Peter Richards

• Professor Richards was GMC member & Chair of Professional Conduct Committee
• Chairman of the Council of Deans of UK Medical Schools & Faculties
• GMC’s lawyers and I complained about conduct of Richards and the GMC refused to act
• GMC allowed Richards to chair PCC hearings after this case
“Science is self correcting”
Professor Don Poldermans

- Erasmus Medical Centre, Rotterdam
- The data from multicentre DECREASE trials suggested use of perioperative betablockers improved survival of high risk patients
- Member of Committee for Practice Guidelines & Chair Task Force of the European Society of Cardiology
- ESC guideline recommended perioperative betablockers for this patient group
DECREASE Trials

• Research misconduct demonstrated in five DECREASE Trials
• Erasmus dismissed Poldermans in 2011
• Trials by other researchers showed perioperative betablockers increase mortality by 27%
• Statistical estimation of 800,000 excess patient deaths as a result of the ESC guidelines based on the fraud (10% in UK)
• ESC guidelines not withdrawn
Clinical transplantation of a tissue-engineered airway

Paolo Macchiarini, Philipp Jungebluth, Tetsuhiko Go, M Adelaide Asnaghi, Louisa E Rees, Tristan A Cogan, Amanda Dodson, Jaume Martorell, Silvia Bellini, Pier Paolo Parmigotto, Sally C Dickinson, Anthony P Hollander, Sara Mantero, Maria Teresa Conconi, Martin A Birchall

Summary

Background The loss of a normal airway is devastating. Attempts to replace large airways have met with serious problems. Prerequisites for a tissue-engineered replacement are a suitable matrix, cells, ideal mechanical properties, and the absence of antigenicity. We aimed to bioengineer tubular tracheal matrices, using a tissue-engineering protocol, and to assess the application of this technology in a patient with end-stage airway disease.

Methods We removed cells and MHC antigens from a human donor trachea, which was then readily colonised by epithelial cells and mesenchymal stem-cell-derived chondrocytes that had been cultured from cells taken from the recipient (a 30-year old woman with end-stage bronchomalacia). This graft was then used to replace the recipient’s left main bronchus.

Findings The graft immediately provided the recipient with a functional airway, improved her quality of life, and had a normal appearance and mechanical properties at 4 months. The patient had no anti-donor antibodies and was not on immunosuppressive drugs.

Interpretation The results show that we can produce a cellular, tissue-engineered airway with mechanical properties that allow normal functioning, and which is free from the risks of rejection. The findings suggest that autologous cells combined with appropriate biomaterials might provide successful treatment for patients with serious clinical disorders.
Claudia Castillo – her left main bronchus was grafted
Findings

• The graft immediately provided the recipient with a functional airway, improved her quality of life, and had a normal appearance and mechanical properties at 4 months.

• The patient had no anti-donor antibodies and was not on immunosuppressive drugs.

• Now know there was no improvement in lung function & transplanted airway collapsed after 3 weeks and required a stent - subsequently she had a left pneumonectomy.
Joint senior authors: Prof Paolo Macchiarini & Prof Martin Birchall

- Macchiarini moved to Karolinska Institute & continued tracheal transplantations with fatal outcomes for patients (also had honorary UCL appointment)
- Birchall moved to UCL & continued tracheal transplantation research with fatal outcomes for Shaun Davison and Keziah Shorten when their tracheas collapsed
Keziah Shorten & Shauna Davison
Karolinska investigation

• Macchiarini’s contract terminated in 2016
• In 2017 investigation found Macchiarini & six co-workers guilty of misconduct
• Requested retraction of 6 publications that were the result of research at the Karolinska, including 2 in the Lancet
• Lancet retracted the two papers in July 2018, but has refused to retract original 2008 paper and a 5 year follow up paper in 2014
The Lancet 2008 paper

- Director of Hospital Clinic Barcelona informed the Lancet that claims in the 2008 paper are false
- Dr Horton, the editor, has refused repeated requests to retract the paper
- 15th January 2019 Chairs of Science and Technology Committee and of Health and Social Care Committee jointly wrote to Horton asking for an explanation
Prof Birchall’s funding for tissue engineered airway research

- Innovate UK for Inspire trial £1.9 million
- MRC for RegenVOX trial £2.8 million
- EU for TETRA trial £5.8 million
- Plus a number of small grants for related research totalling about £4 million
Conclusions

• Research misconduct is common because the rewards are high and risks to fraudsters are low
• It is concealed by institutions and journals
• The guilty often escape serious sanctions