Publication Misconduct and Retraction: Crime and Punishment

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Globalization of Clinical Research

www.clinicaltrials.gov
Globalization of Authorship

Number of papers with co-authors from China and the US (1985-2010)

China and US co-authored publications

Science Citation Index 2000-2010

- 1985-1990
- 1991-1995
- 1996-2000
- 2001-2005
- 2005-2010

Number of papers:
- 0
- 10000
- 20000
- 30000
- 40000
- 50000
- 60000
- 70000
Outline

- Crime
- Punishment
- Characteristics of retracted misconduct publications
- Prevention - what can publication professionals do?
THE CRIME

Altering instrumentation or processes
Non-replicable findings
Dropping data points
Selective reporting
Faking data
Image manipulation

Alteration

Inadequate record keeping
Disputes
Copying ideas
Copying results
Copying words
Duplicate publication

Copying

Falsifying ethics approval / informed consent
"False" study design
Image manipulation
Faking data
Copy results
Copy ideas
Copy

Fabrication
Falsification
Plagiarism
THE PUNISHMENT
National Library of Medicine

- To be retracted from MEDLINE
  - Clear statement of retraction
  - Signed by authors or legal counsel, head of institution, or journal editor
  - Must appear on a numbered page in an issue of the journal
THE PUNISHMENT
Journal practice

Committee on Publication Ethics

http://publicationethics.org/flowcharts
Lack of involvement of medical writers and the pharmaceutical industry in publications retracted for misconduct\textsuperscript{1}

Odds ratio (95\% CI)
Misconduct retraction (n = 213) vs Mistake retraction (n = 220)

Medical writer
Pharmaceutical industry
Single author
First author with at least one other retraction
First author affiliated with a lower-income country

\textsuperscript{1} Woolley K et al. Curr Med Res Opin 2011; In press.
Objectives

- To determine whether the proportion of plagiarism retractions differed between authors affiliated with lower-income and higher-income countries

- To determine other author, journal, and publication factors associated with plagiarism retractions
## Methods

### Search

| MEDLINE: Publications retracted for misconduct |
| Limits: Human, English, Jan 1966 to Feb 2008 |

### Data Extraction

- Original publication and retraction notices
- Data extracted using standard definitions and a standardized data collection tool
- Lower-income countries comprised low and middle income countries, based on World Bank classifications

### Statistical Analysis

- Odds ratio (OR), 95% confidence interval (CI), Chi-square test
- Primary outcome = plagiarism retractions
- Reference group = other misconduct retractions
- Independent academic statistician reviewed and approved the study design, and conducted all analyses

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What were the main reasons for misconduct retractions?

- Plagiarism accounted for almost half of all misconduct retractions

Figure. Type and percentage of misconduct retractions (N = 213)
Have misconduct retractions changed over time?

- Plagiarism retractions have increased over the past decade
Did misconduct retractions differ between countries?

- Significantly higher odds of plagiarism retractions for first authors affiliated with lower-income than higher-income countries (OR, 95% CI: 5.4, 4.5 - 52.9; \( P < 0.001 \))
Should we be concerned?

Other Misconduct retractions per 10,000 MEDLINE publications

Plagiarism retractions per 10,000 MEDLINE publications

- Germany
- South Africa*
- Norway
- Republic of South Korea
- Australia, Canada, Europe, Israel, Japan, Taiwan*, USA, UK
- China*, Iran*, India*, Kuwait, Thailand*, Turkey*, Singapore

* Lower-income country

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Research conclusions

- Almost half of all misconduct retractions were because of plagiarism.
- The number of plagiarism retractions as a proportion of MEDLINE publications has increased in the past decade.
- The type of misconduct retraction differed between authors affiliated with lower- and higher-income countries.
“When a thing has been said well, have no scruple. Take it and copy it.”

- Publication professionals should
  - Challenge perceptions
  - Know the risk factors
  - Inform / educate their authors

Anatole France
(Nobel Prize for Literature 1921)
Publication Misconduct: What Publication Professionals Need to Know

John C. Galland, Ph.D., Director
Division of Education and Integrity
Office of Research Integrity
United States Department of Health and Human Services
Guardians of the Trust

Responsible for:

1. Assessing & adjusting their ethical climates
2. Supporting the individual researcher’s ability to function at the leading edge of professional integrity

NAS - Integrity in Scientific Research: Creating an Environment that Promotes Responsible Conduct (2002)

What are the responsibilities of ISMPP for fostering research integrity?

Partnerships for Success
RCR Instructional Areas

1. Research misconduct
2. Human Subjects
3. Animal Welfare
4. Mentor/Trainee Responsibilities
5. Data Acquisition, Management, Sharing, & Ownership
6. Publication Practices & Responsible Authorship
7. Peer Review
8. Conflict of Interest and Commitment
9. Collaborative Science
RCR Instructional Areas

10. Management
11. Advocacy
12. Leadership
13. Security (Dual Use)
14. Ethics
15. Communication
16. Safety
17. Green (Sustainable) Labs
18. ?
For Whom Does DEI Serve?

Questionable research practices far more common than outright misconduct

Frequency

Research Performance Level

FFP Falsification, Fabrication, Plagiarism
QRP Questionable Research Practices
RCR Responsible Conduct of Research
ERP Exceptional Research Practices
For Whom Does DEI Serve?

![Graph showing frequency distribution across Research Performance Levels: FFP, QRP, RCR, ERP.](image-url)
Scope of RCR Education

- Information about compliance (i.e., rules, regulations, policies, guidelines)
- The ethics of the research itself and of the research process
- Abilities that give rise to ethical behavior
  - ethical sensitivity, reasoning and judgment, identity formation, habits (James Rest, 1983)
- The manner in which the research is conducted (that reduces uncontrolled variability)
- The situation or conditions (location, urgency) under which planning and execution depends
What jeopardizes research integrity?

– Anything that introduces uncontrolled variation into the dataset?

– When self interest replaces truth as the primary goal of research
U.S. Public Funding Agencies

• Health and Human Services (HHS)
  – National Institutes of Health (NIH)
  – Centers for Disease Control (CDC)
  – Food and Drug Administration (FDA)

• National Science Foundation (NSF)

• National Aeronautics and Space Administration (NASA)

• Other Cabinet level funding agencies
Research Integrity
Regulatory Offices in HHS

• Office of the Secretary
  – Office of Research Integrity (ORI)
  – Office of Human Research Participants (OHRP)

• National Institutes of Health
  – Office of Laboratory Animal Welfare (OLAW)
  – Office of Management Assessment
Legal Definition of Research Misconduct

Research misconduct is defined as *fabrication, falsification, or plagiarism* (FFP) in proposing, performing, or reviewing research, or in reporting research results.
Definition of Research Misconduct

- **Fabrication** is making up data or results and recording or reporting them.

- **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.
Definition of Research Misconduct

• **Plagiarism** is the appropriation of another person’s ideas, processes, results, or words without giving appropriate credit

• Research misconduct does not include honest error or differences of opinion (42 CFR Part 93.103)
Proof of Research Misconduct
Requires all the following:

- That there be a significant departure from accepted practices of the relevant research community, and

- The misconduct be committed intentionally, knowingly, or recklessly; and

- The allegation be proven by a preponderance of the evidence. (42 CFR Part 93.104)
Handling Cases of Research Misconduct

Institution
- Allegation
  - Assessment
  - Inquiry
  - Investigation

ORI
- DIO Review
  - Recommendation
  - Settlement or charge letter

Judge
- Hearing
  - Appeal
  - Admin. action
Dr. Poehlman’s changes to total energy expenditure values included many fabrications (blue) and reversals of visit one and visit two values (red). The net effects were to greatly inflate the number of subjects and to reverse the apparent effect of aging.
Can you tell if numbers have been fabricated?

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<th>15</th>
<th>20</th>
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</table>

Graph showing the comparison of cpms for different treatments.
What do you do when you suspect FFP?

- Reject the manuscript?
- Talk to the primary author?
- Talk to all the authors?
- Talk to the primary reviewer?
- Talk to the primary author’s Dean?
- Talk to the RIO at the primary author’s institution?
- Talk to ORI?
## Some ORI Statistics
### 1992 to July 2007

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<th>Category</th>
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<td>Total misconduct findings</td>
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<td>Findings leading to debarment</td>
<td>119</td>
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<tr>
<td>Total cases opened from 1992</td>
<td>501</td>
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<tr>
<td>Total cases closed from 1992</td>
<td>531</td>
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<tr>
<td>Total cases pending</td>
<td>43</td>
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<tr>
<td>Misconduct findings involving clinical research</td>
<td>27%</td>
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<tr>
<td>Total allegations (≈225/year)</td>
<td>3,084</td>
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</table>
Statistics (Journal Articles)

- Retracted papers: 114
- Corrected papers: 31
- Withdrawn papers: 4

Total: 149
PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR ASSURANCE:
I certify that the statements herein are true, complete and accurate to the best of my knowledge. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. I agree to accept responsibility for the scientific conduct of the project and to provide the required progress reports if a grant is awarded as a result of this application.

APPLICANT ORGANIZATION CERTIFICATION AND ACCEPTANCE:
I certify that the statements herein are true, complete and accurate to the knowledge and accept the obligation to comply with Public Service terms and conditions if a grant is awarded as a result of this application and aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties.

398 (Rev. 4/98)
Advancing Values: It’s about character

Shared Values in the Culture of Science

- Honesty
- Accuracy
- Efficiency
- Objectivity
Welcome to….
The 7th Annual Meeting of ISMPP

Anticipating Change in Medical Publications: Leading Now for the Future
Publication Misconduct: What Publication Professionals Need to Know

Cindy W. Hamilton, PharmD
John C. Galland, PhD
Serina Stretton, PhD
Evidence of a Pluripotent Human Embryonic Stem Cell Line Derived from a Cloned Blastocyst

Woo Suk Hwang,1,2* Young June Ryu,1 Jong Hyuk Park,3 Eul Soon Park,1 Eu Gene Lee,1 Ja Min Koo,4 Hyun Yong Jeon,1 Byeong Chun Lee,1 Sung Keun Kang,1 Sun Jong Kim,3 Curie Ahn,5 Jung Hye Hwang,6 Ky Young Park,7 Jose B. Cibelli,8 Shin Yong Moon5*

Somatic cell nuclear transfer (SCNT) technology has recently been used to generate animals with a common genetic composition. In this study, we report the derivation of a pluripotent embryonic stem (ES) cell line (SCNT-hES-1) from a cloned human blastocyst. The SCNT-hES-1 cells displayed typical ES cell morphology and cell surface markers and were capable of differentiating into embryoid bodies in vitro and of forming teratomas in vivo containing cell derivatives from all three embryonic germ layers in severe combined immunodeficient mice. After continuous proliferation for more than 70 passages, SCNT-hES-1 cells maintained normal karyotypes and were genetically identical to the somatic nuclear donor cells. Although we cannot completely exclude the possibility that the cells had a parthenogenetic origin, imprinting analyses support a SCNT origin of the derived human ES cells.

Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children

A J Wakefield, S H Murch, A Anthony, J Linneil, D M Casson, M Malik, M Berelowitz, A P Dhillon, M A Thomson, P Harvey, A Valentine, S E Davies, J A Walker-Smith

Summary

Background We investigated a consecutive series of children with chronic enterocolitis and regressive developmental disorder.

Methods 12 children (mean age 6 years [range 3–10], 11 boys) were referred to a paediatric gastroenterology unit with a history of normal development followed by loss of acquired skills, including language, together with diarrhea and abdominal pain. Children underwent gastroenterological, neurological, and developmental assessment and review of developmental records. Ileocolonoscopy and biopsy sampling, magnetic-resonance imaging (MRI), electroencephalography (EEG), and lumbar puncture were done under sedation. Barium follow-through radiography was done where possible. Biochemical, haematological, and immunological profiles were examined.

Findings Onset of behavioural symptoms was associated by the parents, with measles, mumps, and rubella vaccination in eight of the 12 children, with measles infection in one child, and otitis media in another. All 12 children had intestinal abnormalities, ranging from lymphoid nodular hyperplasia to atresial ulceration. Histology showed patchy chronic inflammation in 11 children and reactive ileal lymphoid hyperplasia in seven, but no granulomas. Behavioural disorders included autism (nine), disintegrative personality disorder (one), and possible postural or occipital encephalitis (two). There were no focal neurological abnormalities and CSF and EEG tests were normal. Abnormal laboratory results were significantly raised urinary ethylmalonic acid compared with age-matched controls (n=5, 0.03), low haemoglobin in four children, and low serum IgA in all children.

Interpretation The identified associated gastrointestinal disease and developmental regression in a group of previously normal children, which was generally associated in time with possible environmental triggers.

See Commentary page

Introduction

We saw several children who, after a period of apparent normality, lost acquired skills, including communication. They all had gastrointestinal symptoms, including abdominal pain, diarrhoea, and constipation, and, in some cases, food intolerance. We describe the clinical findings, and gastrointestinal features of these children.

Patients and methods

12 children, consecutively referred to the department of paediatric gastroenterology with a history of a pervasive developmental disorder with loss of acquired skills and intestinal symptoms (mainly abdominal pain, bloating and food intolerance), were investigated. All children were admitted to the ward for a week, accompanied by their parents.

Clinical investigations

- Each child had a detailed history including details of immunisations and exposure to infectious diseases, and assessed the children. In 11 cases, the history was obtained by the senior clinician (JW-S).
- Neurological and psychiatric assessments were done by consultant staff (PH, MB) with DSM-IV criteria. Developmental assessment included a review of prospective developmental records from parents, health visitors, and general practitioners. Four children did not undergo psychiatric assessment in hospital; all had been assessed professionally elsewhere, so these assessments were used as the basis for their behavioural diagnosis.

After bowel preparation, ileocolonoscopy was performed by SHM or MAJ under sedation with midazolam and pethidine. Paired frozen and formalin-fixed mucosal biopsy samples were taken from the terminal ileum, ascending, transverse, descending, and sigmoid colons, and from the rectum. The procedure was recorded by video or still images, and were compared with images of the previous seven consecutive paediatric colonoscopies (four normal colonoscopies and three on children with ulcerative colitis), in which the physician reported normal appearances in the terminal ileum. Barium follow-through radiography was possible in some cases.

Also under sedation, cerebral magnetic-resonance imaging (MRI), electroencephalography (EEG) including visual, brain stem auditory, and sensory evoked potentials (where compliance made these possible), and lumbar puncture were done.

Laboratory investigations

Thyroid function, serum long-chain fatty acids, and cerebrospinal-fluid lactate were measured to exclude known causes of childhood neurodegenerative disease. Urinary ethylmalonic acid and other organic acids were measured. Results were compared with published control values.

What is publication misconduct?

• Research misconduct
  – Fabrication (making up data or results)
  – Falsification (manipulating research materials, or changing or omitting data or results)
  – Plagiarism (appropriation of another’s ideas)
  – *Not* honest error or differences of opinion

• Other types of publication misconduct (duplicate publication, self-plagiarism, faked author approval, and other ethical violations)

Office of Research Integrity
http://ori.hhs.gov/misconduct/definition_misconduct.shtml
What’s the harm?

- Distraction from truth
- Adoption of ineffective or harmful interventions
- Damaged reputations
- Sensationalism in news media
- Erosion of trust in research

Trikalinos et al. *J Clin Epidemiol* 2008
What can be done?

- Identify every tainted article.¹
- Retract fraudulent articles.¹
  - Time to retraction: >28 months²
  - Awareness of retraction: <5% of citing papers³
- Prevent citation of fraudulent research.¹

Tip of the iceberg?

- 0.3 misconduct retractions per 10,000 MEDLINE publications¹
- 41 highly similar publications per 10,000 MEDLINE publications in 2008²
- 2% of scientists admitted to fabricating, falsifying, or modifying data at least once³
- 34% of scientists admitted to questionable research practice³

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1. Stretton et al. Unpublished data
Déjà vu?