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Retracted Publications: The Hidden World of Biomedical Literature

Merle Rosenzweig, Anna Ercoli Schnitzer, Katy Mahraj, and Irina Zeylikovich
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1

2 The biochemical basis and treatment of autism: Interactions between

3 mercury, transsulfuration, and androgens[☆]

4 David A. Geier^a, Mark R. Geier^{b,*}

5

6 ^a The Institute of Chronic Illnesses, Silver Spring, MD 20905, USA

7 ^b The Genetic Centers of America, 14 Redgate Ct., Silver Spring, MD 20905, USA

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8

9 Abstract

10 Impairments in social relatedness and communication, repetitive behaviors, abnormal movement patterns, and sensory

11 dysfunction characterizes autism spectrum disorder (ASDs). It has long been recognized that there is a genetic component to

12 some ASDs, but recent studies have also suggested that some ASDs are being greatly influenced by environmental factors. Mercury exposure

13 can cause immune, sensory, neurological, motor, and behavioral dysfunction similar to traits defining or associated with ASDs,

14 and recent studies have shown increased body-burdens of mercury in some ASDs. It has also been shown that mercury exposure

15 can trigger a biochemical cyclical pattern of interaction to develop between the transsulfuration and androgen pathways that are

16 directly characteristic with the biochemistry of ASDs in some ASDs, and would be expected to correlate with the behavioral/

17 physical traits associated with or defining ASDs. In light of potential blocks in manipulating the transsulfuration pathway in

18 ASDs, LUPRON[®] therapy has been utilized for the correction of androgen abnormalities in ASDs. The use of LUPRON[®] in a

19 large cohort of ASDs of various ages has been observed to be associated with a significant clinical amelioration in

20 hyperactivity/impulsivity, aggression, self injury, severe sexual behaviors, and irritability behaviors that frequently accompany

21 ASDs.

22 © 2006 Published by Elsevier B.V.

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25 **Keywords:** GnRH; Luteinizing hormone-releasing hormone agonist; Prepubertal puberty; Thimerosal

26

27 **Contents**

28 1. Background on autistic disorders..... 0

29 2. Mercury exposure inducing autistic disorders..... 0

30 3. Biological markers of elevated mercury body-burden/toxicity in autistic disorders..... 0

31 4. Transsulfuration and androgen pathway markers in autistic disorders..... 0

32 5. Transsulfuration and androgen pathway interactions in autistic disorders..... 0

[☆] Potential conflict of interest: Dr. Mark R. Geier has been an expert witness and a consultant in vaccine/biologic cases before the no-fault National Vaccine Injury Compensation Program (NVICP) and in civil litigation. David Geier has been a consultant in vaccine/biologic cases before the no-fault NVICP and in civil litigation. Dr. Mark R. Geier and David Geier jointly have a patent pending for the treatment of autistic disorders.

* Corresponding author. Tel.: +1 301 989 0548; fax: +1 301 989 1543.
E-mail address: mgeier@comcast.net (M.R. Geier).

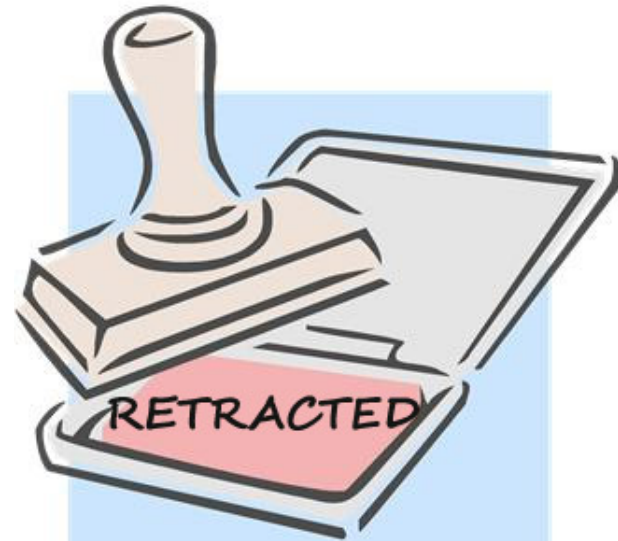
1568-9972/\$ - see front matter © 2006 Published by Elsevier B.V.
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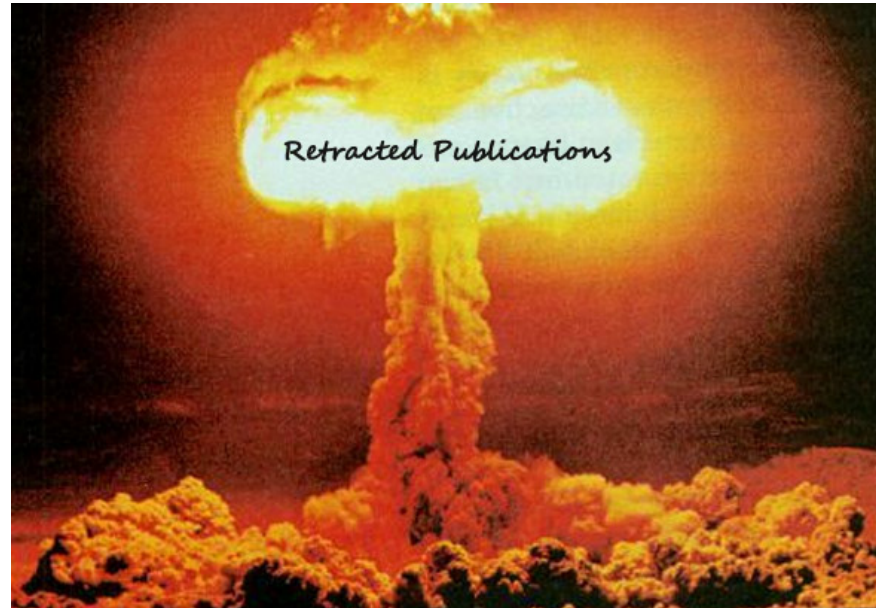


Reasons a publication may be retracted are varied

- Scientific misconduct
- Plagiarism or self-plagiarism
- Author or copyright issues
- Duplication of a publication, either by the author or the fault of the publisher
- Unintentional errors
- Conducting human subject research without IRB approval



Surge in retracted publications



❖ Van Noorden R. Science publishing: The trouble with retractions. *Nature*. 2011

Oct 5;478(7367):26-8. doi: 10.1038/478026a. PubMed PMID: 21979026.

❖ Naik G. Mistakes in Scientific Studies Surge. *The Wall Street Journal*, Wednesday, August 10,

2011. <http://online.wsj.com/article/SB10001424052702303627104576411850666582080.html>.

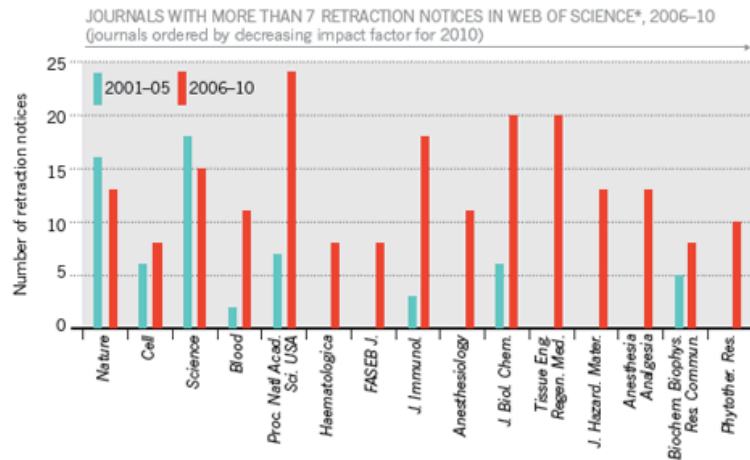
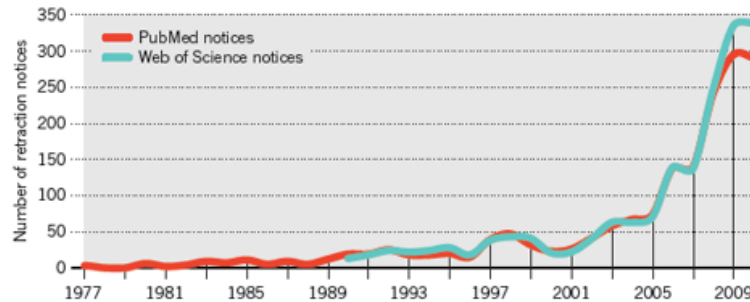
Why the surge & the impact

- The pressure to publish in academia to further a career.
- The stigma of retraction can haunt the author or authors throughout a lengthy career, even if the reason for the retraction is not due to scientific misconduct—plagiarism, false claims or fake data—but is caused simply by embarrassing, unintentional errors.
- Lead to erosion in the public mind of the trustworthiness of the results presented.
- Influence the delivery of health care.

Van Noorden R. Science publishing: The trouble with retractions. Nature. 2011 Oct 5;478(7367):26-8.

RISE OF THE RETRACTIONS

In the past decade, the number of retraction notices has shot up 10-fold (top), even as the literature has expanded by only 44%. It is likely that only about half of all retractions are for researcher misconduct (middle). Higher-impact journals have logged more retraction notices over the past decade, but much of the increase during 2006–10 came from lower-impact journals (bottom).



*Not shown: Acta Crystallographica E saw 81 retractions during 2006–10.

Richard Van Noorden is an assistant news editor for Nature in London.

Naik G. Mistakes in Scientific Studies Surge. The Wall Street Journal, Wednesday, August 10, 2011.

THE WALL STREET JOURNAL. HEALTH

HEALTH INDUSTRY | August 10, 2011

It was the kind of study that made doctors around the world sit up and take notice: Two popular high-blood-pressure drugs were found to be much better in combination than either alone. “There was a ‘wow’ reaction,” recalls Franz Messerli, a New York doctor who, like many others, changed his prescription habits after the 2003 report.

Unfortunately, it wasn’t true. Six and a half years later, the prestigious medical journal The Lancet retracted the paper, citing “serious concerns” about the findings.

The damage was done. Doctors by then had given the drug combination to well over 100,000 patients. Instead of protecting them from kidney problems, as the study said the drug combo could do, it left them more vulnerable to potentially life-threatening side effects, later studies showed.

*Oparil S, Yarows SA, Patel S, Fang H, Zhang J, Satlin A. Efficacy and safety of combined use of aliskiren and valsartan in patients with hypertension: a randomised, double-blind trial. Lancet. 2007 Jul 21;370(9583):221-9.

The Lancet's 1998 Wakefield Retraction

The New York Times

Journal Retracts 1998 Paper Linking Autism to Vaccines

By GARDINER HARRIS

Published: February 2, 2010

"...The Lancet...retracted a 1998 research paper that set off a sharp decline in vaccinations in Britain after the paper's lead author suggested that vaccines could cause autism. The retraction by The Lancet is part of a reassessment that has lasted for years of the scientific methods and financial conflicts of Dr. Andrew Wakefield, who contended that his research showed that the combination measles, mumps and rubella vaccine might be unsafe.

Despite a wealth of scientific studies that have failed to find any link between vaccines and autism, the parents fervently believe that their children's mental problems result from vaccinations. ...the overwhelming body of research by the world's leading scientists...concludes there is no link between M.M.R. vaccine and autism...."

Anil Potti Scandal

The
Economist

Misconduct in science

An array of errors

Investigations into a case of alleged scientific misconduct have revealed numerous holes in the oversight of science and scientific publishing

ANIL POTTI, Joseph Nevins and their colleagues at Duke University in Durham, North Carolina, garnered widespread attention in 2006 when they announced that they could predict ... which chemotherapy drug would be most effective for an individual for the treatment of lung, breast or ovarian cancer using a colorful chart of genes called expression arrays. At the time, their work looked like a great step in advancing personalized medicine. However, when researchers at the MD Anderson Cancer Center in Houston tried to reproduce the results that Potti and Nevins reported in several papers, they were unable to do so, finding serious errors in the research. The MD Anderson researchers concluded that "...patients whose doctors relied on" the model reported by Potti and Nevins "would end up being given a drug they were less likely to benefit from instead of more likely" ...They also concluded that following the procedures proposed by Potti et al. would have "the potential to be very damaging to patients."

Anil Potti in Retraction Watch

Retraction Watch

Feb 14, 2012

The Anil Potti retraction record so far

with 15 comments

A [60 Minutes segment Sunday on Anil Potti](#) has drawn national attention to the case, so we thought this would be a good time to compile all of the retractions and corrections in one place.

Duke has [said](#) that about a third of Potti's 40-some-odd papers would be retracted, and another third would have "a portion retracted with other components remaining intact," so this list will continue to grow. We'll update it as we hear about new changes.



Retractions:

1. "[Gene-expression patterns predict phenotypes of immune-mediated thrombosis](#)," in *Blood*
2. "[Characterizing the Clinical Relevance of an Embryonic Stem Cell Phenotype in Lung Adenocarcinoma](#)," in *Clinical Cancer Research*
3. "[An Integrated Genomic-Based Approach to Individualized Treatment of Patients With Advanced-Stage Ovarian Cancer](#)," in the *Journal of Clinical Oncology (JCO)*
4. "[Pharmacogenomic Strategies Provide a Rational Approach to the Treatment of Cisplatin-Resistant Patients With Advanced Cancer](#)," also in the JCO
5. "[Gene Expression Signatures, Clinicopathological Features, and Individualized Therapy in Breast Cancer](#)," in the *Journal of the American Medical Association (JAMA)*
6. "[Validation of gene signatures that predict the response of breast cancer to neoadjuvant chemotherapy: a substudy of the EORTC 10994/BIG 00-01 clinical trial](#)," in *The Lancet Oncology*
7. "[Genomic signatures to guide the use of chemotherapeutics](#)," in *Nature Medicine*
8. "[A Genomic Strategy to Refine Prognosis in Early-Stage Non-Small-Cell Lung Cancer](#)," in the *New England Journal of Medicine (NEJM)*
9. "[An Integrated Approach to the Prediction of Chemotherapeutic Response in Patients with Breast Cancer](#)," in *PLoS ONE*
10. "[A genomic approach to colon cancer risk stratification yields biologic insights into therapeutic opportunities](#)," in the *Proceedings of the National Academy of Sciences (PNAS)*

Corrections:

1. "[An integration of complementary strategies for gene-expression analysis to reveal novel therapeutic opportunities for breast cancer](#)," in *Breast Cancer Research*
2. "[Gene Expression Profiles of Tumor Biology Provide a Novel Approach to Prognosis and May Guide the Selection of Therapeutic Targets in Multiple Myeloma](#)," in the JCO
3. "[Age-Specific Differences in Oncogenic Pathway Dysregulation and Anthracycline Sensitivity in Patients With Acute Myeloid Leukemia](#)," in the JCO
4. "[Young Age at Diagnosis Correlates With Worse Prognosis and Defines a Subset of Breast Cancers With Shared Patterns of Gene Expression](#)," in the JCO
5. "[Age-Specific Differences in Oncogenic Pathway Deregulation Seen in Human Breast Tumors](#)," in *PLoS ONE*
6. "[A genomic approach to colon cancer risk stratification yields biologic insights into therapeutic opportunities](#)," in *PNAS*

Partial retraction:

1. "[A Genomic Approach to Identify Molecular Pathways Associated with Chemotherapy Resistance](#)," in *Molecular Cancer Therapeutics*



Our ongoing research focuses on:

1. Finding the number of retractions to publications that appear in PubMed, the primary database of biomedical journals created by the National Library of Medicine.
2. Tracking the time from when a retracted article is posted on line to the time that the retraction to said article is posted.
3. Determining the reason(s) that selected articles for our study are retracted.
4. Tracing via a cited-article database to determine whether the retracted article continues to be cited in the literature.

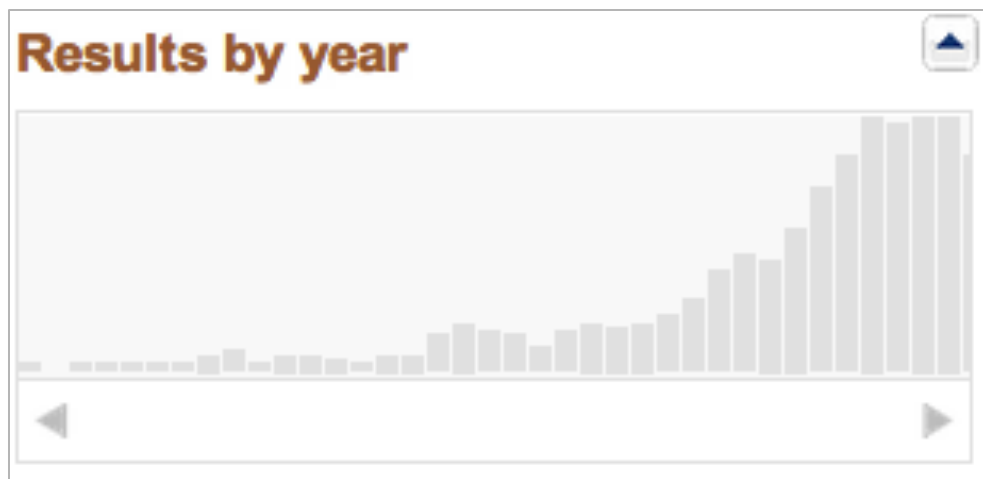
Methods: Locating Retractions & Collecting Data

PubMed:

- Publication Type: Retracted Publication
- Date range: 10 years (from 26 Nov 2011)

Data Points:

- First Author
- PMID
- Publication Date (month/year)
- Retraction Date (month/year)



<http://www.ncbi.nlm.nih.gov/pubmed?term=retracted%20publication%5BPublication%20Type%5D>

Methods: Coding

- Author Issues
- Data Error
- Data Manipulation
- Duplicate Publication
- IRB Approval
- No Reason Given
- Other
- Plagiarism
- Self-Plagiarism
- Unable to Replicate Results

Article Index	PMID	First Author (Last, First)	Publication Date	Retraction Date	Months to Retraction	Retraction Reasc
799	16478859	Mitsuyama H	February-06	October-08	32	Data Manipulation
800	16478645	Akyol A	April-06	October-06	6	Plagiarism
801	16474136	Hui EK	March-06	October-06	7	Data Error
802	16468883	Doughan DI	February-06	August-06	6	Data Manipulation
803	16467873	Liu XY	January-06	August-06	7	Self-Plagiarism
804	16467142	Coldren BA	February-06	December-06	10	Duplicate Publicatio
805	16466641	Kim SY	Jan-06	Apr-10	51	Self-Plagiarism
806	16465358	Meel BL	December-05	November-09	47	Duplicate Publicatio
807	16462106	Li X	December-05	March-07	15	Plagiarism
808	16459994	Piedimonte LR	January-06	July-06	6	No Reason Given
809	16455819	Glaros S	May-06	March-08	22	Data Error
810	16451145	Röhm KD	January-06	August-11	67	IRB Approval
811	16432154	Davies KJ	January-06	December-06	11	Duplicate Publicatio
812	16428550	Reuben SS	February-06	April-09	38	Data Manipulation
813	16428532	Mayer J	February-06	May-11	63	IRB Approval
814	16424524	McGwin G Jr	February-06	April-11	62	No Reason Given
815	16424224	Matsuyama W	February-06	November-08	33	Data Manipulation
816	16421562	Razem FA	January-06	December-08	35	Data Error
817	16418018	Reuben SS	January-February-06	March-April-09	34	Data Manipulation
818	16413606	Yao D	January-06	February-07	13	Data Error

Results: Preliminary

- Author Issues=51
- Data Error=280
- Data Manipulation=133
- Duplicate Publication=112
- IRB Approval=54
- No Reason Given=79
- Other=108
- Plagiarism=262
- Self-Plagiarism=93
- Unable to Replicate Results=76

Methods: Challenges



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Monitoring Mechanisms

- **COPE** (Committee on Publication Ethics)
- **ICMJE** (International Committee of Medical Journal Editors)
- **Retraction Watch**

COPE (Committee on Publication Ethics)*



RETRACTION GUIDELINES

“COPE aims to define best practice in the ethics of scholarly publishing and to assist editors, editorial board members, owners of journals and publishers to achieve this. One of the ways in which it fulfills this mission is by the publication of its Code of Conduct and Best Practice Guidelines for Journal Editors.”

*<http://publicationethics.org/>

ICMJE (International Committee of Medical Journal Editors)



http://www.icmje.org/publishing_2corrections.html

**Uniform Requirements for Manuscripts Submitted to Biomedical Journals:
Publishing and Editorial Issues Related to Publication in Biomedical Journals:
Corrections, Retractions and "Expressions of Concern"**

“The retraction or expression of concern, so labeled, should appear on a numbered page in a prominent section of the print journal as well as in the online version, be listed in the Table of Contents page, and include in its heading the title of the original article. It should not simply be a letter to the editor. Ideally, the first author of the retraction should be the same as that of the article, although under certain circumstances the editor may accept retractions by other responsible persons. The text of the retraction should explain why the article is being retracted and include a complete citation reference to that article.”

Retraction Watch*

Retraction Watch

Tracking retractions as a window into the scientific process

- A blog that reports on retractions of scientific papers.
- An informal repository for retractions.
- Investigate how journals themselves deal with retractions.

*<http://retractionwatch.wordpress.com/>

Anti-Plagiarism Software

- **eTBlast**



eTBlast: a text-similarity based search engine

<http://etest.vbi.vt.edu/etblast3/>

- **Déjà vu**

Deja Vu: a Database of Highly Similar Citations*

Powered by eTBlast
Innovation Labs
Virginia Bioinformatics Institute

<http://dejavu.vbi.vt.edu/dejavu/>



- Developed by Virginia Bioinformatics Institute at Virginia Tech
- Can detect text similarities across several databases

Search eTBLAST

Enter your query text:

Select database

- MEDLINE
- CRISP
- NASA
- Medical Cases
- PMC Full Text
- PMC METHODS
- PMC

INTRODUCTION

- PMC RESULTS
- PMC (paragraphs)
- PMC Medical Cases
- Clinical Trials
- Arxiv
- Wikipedia
- VT Courses

--OR upload file-- (a ["text only"](#) file)

[A quick guide](#)

- Can detect highly similar citations in Medline
- *Users can:
 - (1) browse Déjà vu entries with no specific search method. Each entry links to the scientific citation along with full text whenever freely available;
 - (2) search Déjà vu content by authors, title word, abstract word, year and comment word;
 - (3) view Déjà vu results in a particular category or identified by a particular 'discovery method' (eTBLAST or manual);
 - (4) provide comments in order to contest a record or submit a potential duplication that will be reviewed by authors of this manuscript.

*Errami M, Hicks JM, Fisher W, Trusty D, Wren JD, Long TC, Garner HR. Déjà vu--a study of duplicate citations in Medline. *Bioinformatics*. 2008 Jan 15;24(2):243-9.

Questions & Contacts



Merle Rosenzweig
oriley@umich.edu

Anna Ercoli Schnitzer
schnitzr@umich.edu

Irina Zeylikovich
irinaz@umich.edu

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