Editorial

How *Pediatrics* validated erroneous British mercury data

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Abstract

John Stone presents more compelling evidence of high-level collusion between the CDC, the WHO, and British health officials over an epidemiological study presented, without independent peer review to the 2004 IOM committee and subsequently published in *Pediatrics.* Information acquired from public sources and through Freedom-of-Information-Act (FOIA) requests in both the U.K. and the U.S.A. suggest: a) the study was compromised by undisclosed conflicts of interest from its inception, b) the study made a knowingly false claim about the equivalence of the mercury burden in the WHO and the UK routine-vaccination schedules, c) the database used in the study was, at best, weak, and d) the authors deliberately excluded confounding evidence that clearly established the autism rate rose when the schedule was changed in the UK in 1990. When all this substantiation was presented to *Pediatrics* the journal declined to publish the evidence.

Keywords: Thimerosal, mercury, CDC, WHO, United Kingdom, Elizabeth Miller

1. Introduction

On February 8, 2004, the Immunization Safety Review Committee of the IOM met to re-examine the issue of vaccines and autism. There were five thimerosal-related epidemiological studies that convinced the committee that thimerosal was not a trigger for regressive autism. One of those studies was conducted in the United Kingdom. It had not yet been published when the committee met, but its data was presented by co-author Dr. Elizabeth Miller of the United Kingdom Health Protection Agency (formerly Public Health Laboratory Service).

The study was subsequently published in the September 2004 issue of *Pediatrics.* Nick Andrews, Elizabeth Miller, Andrew Grant, Julia Stowe, Velda Osborne, and Brent Taylor were listed as authors, in that order, and the publication was titled *Thimerosal Exposure in Infants and Developmental Disorders: A Retrospective Cohort Study in the United Kingdom Does Not Support a Causal Association* [1].

However, this publication was not widely discussed in the U.K., where the subject of thimerosal has never:

- Received the public attention as it has in the United States, and has never
- Competed in the media and the public interest with the MMR controversy.

It was only months after this publication that I began to look carefully at the historical record and realized that the study contained numerous anomalies in addition to those already cited in electronic responses by John Heptonstall and Mark and David Geier.

It is well known that electronic letters to a medical journal are usually published unless they are not relevant, contain offensive language or constitute a personal attack on someone. In fact, *Pediatrics* did accept three post publication peer reviews (P3Rs) that I sent concerning the Andrews *et al.* study. However, as months went by and I awaited a response from the authors, ever more problems presented themselves and I made three further attempts to address these to the journal with letters written in August 2005, February 2006 (after the publication of my three part investigation *Mercury and Autism in the United Kingdom,* originally published in *Red Flags* [2]) and November 2006. As of April 2007, none of these have been published. And, as it has now emerged in publications on the Vaccine Autoimmunity Project website (www.vaproject.org), this was not an isolated matter [3,4].

Appendices I through III present each of the submission letters that were refused. They contain information about the mercury in vaccines issue in the United Kingdom that may not be widely known in the United States.

2. Conclusion

The Andrews *et al.* study was fraught with severe flaws from its inception.

The authors had undisclosed, and, to this day, unacknowledged, conflicts of interest which should at least have, at least, been made known, and which should have effectively disqualified them from undertaking the research. They stated in reply to Mark and David Geier that:

> "The requirements by *Pediatrics* for the conflict of interest declaration were complied with…" [6],

so it would seem that the commercial conflicts were made known to the journal, but these were not initially passed on for the information of the readers. The question of the hidden commercial conflicts, though serious, was not as bad as the more fundamental problem of the historical involvement of the authors with the policy they were reviewing.

Pediatrics initially allowed serious criticism of the paper in electronic peer-to-peer review, which the authors responded to in part, though far from satisfactorily. However, when further and even more serious flaws were exposed, the editor simply refused to publish the documentary evidence. This has left the journal profoundly compromised.

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The study lies at the heart of the defence of a longstanding policy which was established before the study was even undertaken. It was commissioned in a triangular arrangement between British, United States, and World Health Organization (WHO) health officials, the very people who had heaviest responsibility for the policy in the first place. We now live with the official fiction that the science was correct.

In 2004, when the spotlight fell on the famous Wakefield *Lancet* study of 1998 [7], there was so little wrong with it that the ten authors who signed a letter of retraction could only dissociate themselves from "an interpretation" and not something which was stated in the paper [8].

On the other hand, the Andrews study is so flawed it is hard to know where to begin or where to end, but it remains a cornerstone of international health policy.

Scarcely a day passes without someone repeating "that based on reliable epidemiological evidence the Immunization Review Safety Committee has decreed that thimerosal in pediatric vaccines is not and never was related to autistic regressions." When the British data was presented at the committee meeting in February 2004, it had not been subjected to peer-review, which, in itself, is problematic. After the study was published, the authors only responded in a selective and incomplete way to published criticisms, while the journal blanked out the most serious criticisms of all. The editor and any U.S. reviewer could hardly have known all the details that I revealed, and, given all the methodological issues, the study certainly should not have been published in the first place.

Indeed, it is even possible that British reviewers were not aware of some of the details. The suppression of material criticism is inexcusable, and places infants across the world in jeopardy.

Author's letter to *Archive of Diseases in Childhood*

Contemporaneously with the last submission I sent one to *Archive of Diseases in Childhood* (27 November 2006), which was, in fact, published on-line, although not yet answered [5]:

Dear Editor,

Figure 1 in this study shows a rise in autism incidence (recorded) from 22 cases in the birth cohort of 1989 to 46 in 1991. R. Lingam, A. Simmons, N. Andrews, E. Miller, J. Stowe, and B. Taylor fail to take into consideration the introduction of the accelerated Diptheria, Pertussis, Tetanus (DPT) as a potential confounder, advancing the doses from 3, 5, and 10 months to 2, 3, and 4 months [1]: each dose also containing 50 μg Thiomersal (Thimerosal) including 25 μg mercury [1]. This is a surprising omission as N. Andrews, E. Miller, J. Stowe, and B. Taylor were also co-authors of [1], which, though not published at the time of this study, had already been delivered privately to the World Health Organization in June 2002 [1]. Equally in [1] they failed to note the aforementioned rise in this present study as possible evidence of a population effect of the accelerated schedule.

John Stone

Reference:

[1] Andrews N, Miller E, Grant A, Stowe J, Osborne V, Taylor B. Thimerosal Exposure in Infants and Developmental Disorders: A Retrospective Cohort Study in the United Kingdom Does Not Support a Causal Association. Pediatrics 2004 Sept.; 114(3):584–91 (doi:10.1542/peds.2003-1177-L), http://pediatrics.aappublications.org/cgi/content/full/114/3/584

John Heptonstall's "P3R" dispatch to *Pediatrics*

However, in November 2006 a further potential confounder to the Andrews study also came to light. A story appeared in the *Sun* newspaper that due to poor recording many British infants may have received the vaccine schedule more than once thus significantly increasing their mercury exposure. On 9 November 2006, John Heptonstall dispatched the following P3R submission to *Pediatrics.* Once again, it was not published.

ID: 114/3/584

Sir/Madam,

The UK media today (8th November 2006) contains information suggesting that the UK government and medical establishment is presiding over a major national scandal with respect to its vaccine programmes (http://www.thesun.co.uk/article/0..2-2006510771.00html).

"Child immunisation records are in such chaos that health chiefs across Britain have no idea what jabs have been given to hundreds of thousands of kiddies," says The Sun... "The scandal is exposed in top secret documents leaked to The Sun, which reveal records held by the NHS are a farce....up to 60% more shots have been given to children than should have been...some youngsters appear to have received 30 jabs—when they should have had just 13.... amazingly some children are shown as having nine jabs in a single day.....the shambolic records—dating back an astonishingly 20 years—are mainly blamed on incompetent paperwork in surgeries.... 6 records taken at random were all found to contain errors.... That means records for one million children in London alone are involved.... an insider said there is no reason to think that the rest of the country is any different, it's just that London is the first place any of this work has been done."

Dr. Elizabeth Miller, one of the authors and a noted employee and spokesperson for the U.K. Department of Health during the past two decades, could comment on this extremely serious developing situation and how it might affect the integrity and validity of this study and all others reliant on the accuracy of UK vaccination records and respective databases developed this past twenty years, not least the U.K. GPRD, a counterpart of which has long been maintained by the Boston Collaboration using constant updates from UK computerised medical records?

Assuming *The Sun* story holds merit, would it not now be wise for every parent to seriously consider withholding vaccination from their children until validated evidence-based studies are available to prove safety and efficacy of this medical intervention? Perhaps Dr. Miller can convey to the readers her expert opinion as to whether vaccines, which may now be devoid of proper evidence-based support from U.K.-based research, ought to be suspended until they can be scientifically declared safe?

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Regards,

John H.

Conflict of Interest: None declared

U.K. health regulator's letter to the author

I also wrote querying this matter with health minister, Caroline Flint. I received the following reply on her behalf from Dr Philip Bryan of the Medicines and Healthcare products Regulatory Agency on 18 January 2007:

Subject: THIOMERSAL IN VACCINES

Dear Mr. Stone,

Thank you for your e-mail of 10 November 2006 to Caroline Flint, Minister of State for Public Health, in relation to thiomersal in vaccines. As vaccine safety falls within the remit of Medicines and Healthcare products Regulatory Agency (MHRA), I have been asked to reply on her behalf.

As I have stated in our previous correspondence, the Commission on Human Medicines (CHM) and its Vaccine Expert Group has reviewed the available evidence in relation to the safety of thiomersal-containing vaccines and considers all relevant new evidence as it be comes available. The advice of the CHM, and the MHRA, remains that there is no evidence of adverse effects caused by levels of thiomersal in vaccines.

We have noted the information provided in your latest correspondence, in particular that in relation to the validity of the study by Andrews *et al* 2004 and the amount of thiomersal contained in some U.K. vaccines. As you are aware, through direct correspondence between yourself and MHRA during 2005 and 2006, we have tried our best with the information available to us to answer in full your many requests for information and clarification around issues relating to the safety of thiomersal in vaccines. Several of the points in our past correspondence also concerned the study by Andrews *et al.* 2004.

We wish to re-iterate that the study by Andrews *et al.* was published in a peer-reviewed journal and was given full consideration by the CHM (then the Committee on Safety of Medicines) Vaccine Safety Working Group. The Group considered that the study was robust, that the methodology and results were valid, and the conclusions justified. This also applied to the GPRD database in the study which has been used in many peer-reviewed vaccine studies previously. The MHRA has nothing further to add on the methodology of the study.

We are aware that the authors of this study have previously tried to address your, and others', concerns via correspondence on the *Pediatrics* journal on-line message board. If you have any further concerns over the methodology, you may wish to raise these with the authors directly.

Finally, we have clarified the issues around thiomersal content of DTP vaccines used in the UK in previous correspondence (I refer you to my letters of 3 August and 5 September 2005). I also understand that Professor Miller has answered similar questions via the *Pediatrics* journal on-line message board. We have nothing further to add on this matter.

Yours sincerely,
<s>

Dr. Philip Bryan
Senior Scientific Assessor
Vigilance and Risk Management of Medicines (VRMM)

Author's concluding note:

The implications of this letter are manifold:

1) A supposedly independent agency answers on behalf of a government minister.
2) Further evidence of potential flaws in study data are airily waved aside without reasons being offered.
3) The robustness of the methodology and data source of the study is once again asserted without contrary evidence ever having been addressed, or at best only peripherally. Scientific dialogue has once again been avoided.
4) Peer review status is held to validate the study irrespective of further evidence coming to light.

References

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[2] http://www.vaproject.org/stone/mercury-autism-in-uk-part-1-200602.htm
http://www.vaproject.org/stone/mercury-autism-in-uk-part-2-200602.htm
http://www.vaproject.org/stone/mercury-autism-in-uk-part-3-200602.htm
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[4] Trelka JA. How mercury was absolved: creativity, collusion and censorship. Medical Veritas 2007 Apr.;4(1):1390–2.
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[6] http://pediatrics.aappublications.org/cgi/eletters/114/3/584#1073
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[8] Murch SH, Anthony A, Casson DH, Malik M, Berelowitz M, Dhillon AP, Thomson MA, Valentine A, Davies SE, Walker-Smith JA. Retraction of an Interpretation. Lancet 2004 Mar. 6;363(9411):750.

Appendix I. First letter

19 August 2005:

ID: 114/3/584

Why a "retrospective cohort study" rather than a time-trend analysis?

Having noted the continuing silence of Nick Andrews, Elizabeth Miller, Andrew Grant, Julia Stowe, Velda Osborne and Brent Taylor [1] (not to mention Jon Heron and Jean Golding [2]) regarding the mysterious issue of the double dose of thimerosal [3], there is another event in the history of the UK dosage of thimerosal which is recorded by Andrews *et al.* but has yet to be discussed: the change in the U.K. DPT schedule in 1990 from 3, 5 and 10 months to 2, 3 and 4 months [1]. In addition to the greater immaturity of the infant metabolism in the new schedule—and presuming the thimerosal content to have remained the same—this represents an approximately 20% rise in dosage when measured against body-weight [4].

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Without going once again into the hugely problematic usage of the U.K. General Practitioner's Research Database [5, 6], I would like to suggest that there is another important source of data available in relation to this event which ought to have been considered and which is published in a contemporaneous study of MMR and autism in *Archives of Disease in Childhood (ADC)* which shared 4 of the same authors with the present study [7]. The study covers 5 districts of North-East London between 1979 and 1998 (perhaps my own son is one of the cases), and very speculatively the authors seem to attribute the entire rising trend to better diagnosis [8]. However, the cohorts, of 1990 and 1991 show a particularly alarming growth in the autism rate. According to my reading of their graph, cases rose from 21 for the birth cohort of 1989, to 37 in 1990 and 47 in 1991. (In 1992 incidentally, the trend continued to rise and that was the year HiB was introduced in the UK.)

This is highly unsatisfactory. It is apparent that the authors of the present paper chose the ground on which to explore the possible relationship between thimerosal and autism, and it was not autism prevalence in 5 north east London districts 1979-98. If they had done they would have had a little more explaining to do. As it is they did not mention the hike in thimerosal exposure in the *ADC* paper, or allude to the *ADC* paper here. Once again we are owed an explanation.

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Conflict of Interest: Autistic son

Appendix II. Second letter

7 February 2006:

ID: 114/3/584

I have just completed a 6-month-long three-part investigation into the present study[1] published in the on-line medical journal Red Flags [2-5]. In addition to the many unresolved points in the above correspondences (and I include not only my previous e-letters but also those from Mark and David Geier and John Heptonstall) I note the following issues:

i) The mercury load of the WHO program in 2001 exposed infants to 187.5 µg of mercury between birth and 14 weeks, and was not "the same" as the official U.K. load, as stated here [1,3,4].

ii) The study was under the control of the CDC, which was not transparent [4].

iii) The project was reviewed by the CDC after it had been announced in the British press, and was given the green light despite the fact that it was recognised that exposure in the official U.K. programme was a fraction of the WHO exposure, and despite recognised deficiencies in the U.K. database [4].

iv) Evidence exists from other Department of Health documents and a parliamentary answer that mercury exposure in the period examined varied greatly in the U.K. and may frequently have exceeded 75µg 2-4 month dose, which is given as standard in the study [3,5].

v) Four of the authors of the present study (Andrews, Miller, Taylor and Stowe) worked contemporaneously on a separate MMR focussed study published in Archives of Diseases in Childhood which disclosed a diagnosed 109% increase in lower continuum ASD between 1989 and 1991 in northeast London synchronous with the introduction of the accelerated DPT schedule in 1990.[6]. This dramatic trend is neither mentioned in the present study, nor is the introduction of the accelerated DPT schedule mentioned as a possible confounder in the MMR study. [5].

vi) Recording of developmental disorders and particularly autism is haphazard in the General Practitioners' Research Database. Results vary alarmingly between studies and seem to be below actual population levels by several orders of magnitude. [5].

vii) It was British Government policy to deny there was any concern regarding vaccine mercury from the time the issue arose in the US in 1999, and before any studies at all were carried out. This position was maintained while studies were carried out, and even after mercury had been removed from the programme in October 2004.[5].

Supporting documents supplied.

[1] Andrews N, Miller E, Grant A, Stowe J, Osborne V, Taylor B. Thimerosal Exposure in Infants and Developmental Disorders: a retrospective cohort study in the United Kingdom does not support a causal association. Pediatrics 2004;114:584-591.
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[5] Stone J. Mercury and Autism in the U.K. Part III: The PHLS Study Reviewed, http://www.redflagsdaily.com/articles/2006_ feb06.php
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Conflict of Interest: Autistic son

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Appendix III. Third letter

26 November 2006:

ID: 114/3/584

Sir,

Nick Andrews, Elizabeth Miller, Andrew Grant, Julia Stowe, Velda Osborne and Brent Taylor state concerning the mercury exposure in the UK:

> "Because the United Kingdom changed to an accelerated 2/3/4 month DTP immunization schedule in 1990 (replacing the former 3/5/10 month schedule) and because vaccinations are generally given on time in the United Kingdom, a substantial proportion of children in the GPRD cohort will have had a cumulative Hg exposure of 150 μg of thimerosal (75 μg of Hg) by 4 months of age. This level of Hg exposure, although lower than the maximum of 187.5 μg received in the United States by 6 months of age, is similar to the level received by 3 to 4 months of age in the United States. It is also the same as the amount of thimerosal used by developing countries that follow the expanded immunization schedule." [1]

It is odd that they do not give WHO schedule as a straight point of comparison with U.S. and U.K. practice. The WHO schedule is not widely publicised, however a UK Committee on the Safety of Medicines (CSM) document from 2001 gives the WHO mercury exposure as 187.5 μg between birth and 14 weeks, being similar in content but not time span to the US schedule. It is hard to see how, by intent, the UK and WHO schedules are in any way "the same". This is exceptionally disturbing given that this study is presented as evidence in support of WHO practice, and was indeed commissioned by the WHO for this purpose.

I note additionally a contemporaneous study also co-authored [by] Nick Andrews, Elizabeth Miller, Julia Stowe and Brent Taylor [2]. This study, while focussing on the MMR and autism, documents a rise in incidence in lower continuum autistic disorder in a north east London population from 22 cases in the cohort of 1989 to 46 cases in the cohort of 1991 coincident—though this is not mentioned—with the introduction of the accelerated DPT schedule in 1990. It must be a matter for grave concern that the authors failed to consider anywhere this evidence of a possible population effect for DPT and thimerosal, either here or as a potential confounder in the MMR study. Indeed, it [is] not obvious why a time-trend analysis in relation to the thimerosal problem was not undertaken. If there were strong arguments to discount the trend it would surely have looked better if they had been rehearsed at the time, as the authors were patently aware of it. Unfortunately, it is far more telling than the impenetrably crunched data of the probably inadequate GPRD (I commend John Heptonstall's analysis, above).

(CSM document submitted).

John Stone

[1] Andrews N, Miller E, Grant A, Stowe J, Osborne V, Taylor B. Thimerosal Exposure in Infants and Developmental Disorders: A Retrospective Cohort Study in the United Kingdom Does Not Support a Causal Association. Pediatrics 2004 Sep.;114(3):584–91. (doi:10.1542/peds.2003-1177-L), http://pediatrics.aappublications.org/cgi/content/full /114/3/584

[2] Lingam R, Simmons A, Andrews N, Miller E, Stowe J, Taylor B. Prevalence of autism and parentally reported triggers in a north-east London population. Archives of Disease in Childhood 2003;88:666–70. http://adc.bmj.com/cgi/content/full /88/8/666

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