Editorial

Mercury and autism in the United Kingdom

John Stone
Email: johndanstone@googlemail.com

Abstract

John Stone presents compelling evidence of high-level collusion between the CDC, the WHO, and British health officials in an epidemiological study presented at the 2004 IOM and subsequently published in *Pediatrics*. Information acquired from public sources and through Freedom-of-Information-Act (FOIA) requests in both the U.K. and U.S.A. suggest, among other things: (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. Hopefully, after reading this and the preceding narratives, the reader will understand something of the length U.S.A. and U.K. authorities and the journal *Pediatrics* appear to have gone to keep the truth from the public.

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

1. The British government and the WHO

In the United Kingdom, the issue of mercury in pediatric vaccines and autism has been consistently overshadowed by the longer-standing measles, mumps, rubella (MMR) controversy, which has rumbled in the British media since the publication of Andrew Wakefield's famous *Lancet* paper in February 1998 [1].

The mercury issue came to light publicly here on May 27, 2001—two years after the United States—in a report by Rosie Waterhouse in the *Sunday Times* [2], though it was not a front-page matter and was largely overshadowed by the last weeks of the 2001 general election campaign. At first, however, it seemed to be having some impact on policy. A week after the first article, the newspaper reported:

> "The government's medicines safety watchdog has taken action to warn patients and General Practitioners (GPs) of potential serious reactions to vaccines containing a preservative which is almost 50% mercury. Manufacturers have been told to add a warning to the summary of product characteristics for all vaccines with Thiomersal [the U.K. licensed brand name for Thimerosal]. A warning will also be added to the patient information leaflet." [3]

In retrospect, the one-sided implication of this is clear. While moral pressure continued to be applied on general practitioners and parents to accept the vaccine, the licensing authority, the Medicines Control Agency (MCA)—currently, the Medicines and Healthcare Products Regulatory Agency, or MHRA —had moved to protect themselves and the manufacturers legally, and to give the impression that something was actually being done to protect the public. But the MCA acted only *after* the matter became public knowledge, although officials had known about the problem for several years.

On June 17, 2001, the *Sunday Times* went on to report that the World Health Organization (WHO) was launching an inquiry into the safety of thimerosal led by epidemiologist Elizabeth Miller, head of the immunization division of the U.K. Public Health Laboratory (PHLS) [4]:

> "She will analyze records of 500 GP practices to check for a link between the use of vaccines that contain the preservative thiomersal—which is almost 50% mercury—and a range of neuro-developmental disorders which include autism.
>
> There has been a big rise in the number of children exhibiting mild to severe neurological problems such as dyslexia and autism. This follows the introduction of the measles, mumps and rubella (MMR) vaccine in 1988 and a sharp rise in the number of mercury-based vaccines given.
>
> The number of vaccinations that can be given before the age of two has risen from about eight in 1980 to 22 now.
>
> A key factor may be that mercury-based vaccines are being given to babies as young as two months old, when their bodies are less able to cope with it….
>
> Vaccines containing mercury include the triple DTP injection against diptheria, tetanus and whooping cough and some licensed brands of Hib, a meningitis vaccine. Mercury is not used in the MMR vaccine."

Another four weeks elapsed, however, before a letter from Miller, outlining the official position, appeared in the paper [5]:

> "Your articles, *Autism linked to mercury vaccine* (May 27) and *Inquiry launched into vaccine 'link' with autism* (June 17) implied that there has been increasing use of thiomersal-containing vaccines in the U.K. since 1988. In fact, the thiomersal content of vaccines given in the routine vaccination program has not increased

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over the past decade. The only vaccines for children used in the routine program that contain thiomersal are DPT (diptheria, tetanus, pertussis) and DT. Because of theoretical concerns that the small amount of mercury in thiomersal could be harmful, both European and United Kingdom regulators have recommended that manufacturers phase out its use wherever possible as a precaution.

As a further precautionary measure, the Public Health Laboratory Service, on behalf of the World Health Organization, will be undertaking research into any negative effects of thiomersal-containing vaccines in the near future.

Several studies and research papers have found no evidence that the MMR vaccine, which contains no thiomersal, is a factor in the cause of autism."

There are numerous anomalies and holes in Miller's response:

1. She shifts the ground in adjoining sentences from "increasing use of thiomersal-containing vaccines in the U.K. since 1988" to "the thiomersal content of vaccines given in the routine program" in "the past decade" (i.e., since 1991). On careful scrutiny, she does not deny that there has been "increasing use of thiomersal-containing vaccines in the U.K. since 1988," or an increase in the mercury content of "the routine program" between 1988 and 1991.
2. The assurance that thiomersal is only used in DPT and DT vaccines is in the present tense and does not necessarily cover any of the preceding period.
3. Reference to "the routine vaccination program … in the past decade," does not preclude greater exposure in non-routine practice, and does not place a limit on the extent of non-routine practice.
4. Reference to "the small amount of mercury in thiomersal" is scientifically erroneous (being 49.6 percent by weight) and prejudicial to the investigation. Moreover, the dosage was known to be toxicologically significant. According to the admitted level of .025 mg of mercury, the dose was by weight approximately 40 to 66 times the U.S. Environmental Protection Agency's reference dose for daily exposure to environmental mercury, tailing off to 30 to 48 times at four months [6].
5. It was perverse and prejudicial to refer to "theoretical concerns" of toxicity, when the substance was known to be highly toxic. The only theoretical proposition (not stated) was that the toxic material might be excreted from the infant body without doing damage. The concerns were *real*; the conjecture that no organic damage was being inflicted, *theoretical*.
6. The statement that the European and United Kingdom regulators had recommended phasing out thimerosal as a precaution did not mean that this was the policy of U.K. Department of Health, or that it was about to happen.
7. The assurance about MMR is virtually meaningless: absence of proof not being the same as proof of absence.
8. It was anomalous and compromising that Miller had been left to front an investigation into her own policy, and that her laboratory was funded by five vaccine manufacturers with a history of using thimerosal (GlaxoSmithKline, Aventis Pasteur [now, sanofi-aventis], Wyeth, Baxter Health Care and Chiron Biocine [now, part of Novartis]) [7].

So flawed is this submission that it would tend to confirm the substance of Rosie Waterhouse's report, rather than refute it.

One question that emerges from this is how routine was the "routine program" or, to put it another way, were variations from it common?

Part of the answer comes in a table once published by the Department of Health and now presented in Table 1 [8], which gives the uptake numbers for infant vaccines (figures are for those completing the schedule) in the period 1988-89 to 1997-98. This shows that administration of the component vaccines of the DPT was very far from standard, particularly at the beginning of the period. For instance, in 1988-89, the uptake of the historically controversial pertussis vaccine was 517,000, against 604,000 for diptheria and 644,000 for tetanus: a 25% variation. This narrowed year by year, until it had virtually leveled off between the three in 1996-97 (Table 1)

Table 1. Ratio of tetanus uptake to pertusis and diphtheria by year

Year	Ratio of tetanus uptake to pertussis	Ratio of tetanus uptake to diptheria
88-89	125.0%	106.6%
89-90	118.7%	107.5%
90-91	113.0%	106.2%
91-92	112.5%	107.4%
92-93	110.0%	106.7%
93-94	108.0%	105.5%
95-96	104.5%	102.3%
96-97	—	—

However, even in 1996-97, as a Department of Health web document shows, the pattern may not have been that clear-cut:

"Data collected from form KC50 and COVER (cover of vaccination evaluated rapidly) is presented in this document. Ninety six percent of children had been inoculated against polio, tetanus and diptheria before the age of two. The target of a 90% uptake for each vaccine was reached by all but three health authorities. During the year, 878,000 reinforcing doses were given against diptheria, 901,000 against tetanus and 910,000 against polio. Ninety two percent of infants had been immunized against whooping cough (pertussis) by the age of one, and 94% by the age of two." [9]

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There were, in fact, many licensed mercury-containing single vaccine products on the market, particularly toward the end of the period, none of which suggests a uniformly low-dose program based on the DPT and DT. At least 80 mercury-containing vaccines were licensed between 1993 and 2001, although none had been in the previous seven years [10]. Pertussis actually had a bad reputation at the beginning of the period, but it does not seem that there was an identity of uptake of diptheria and tetanus through the use of the DT either. On the other hand, in 1997-98, pertussis uptake was exceeding the uptake of the other two by about two percent (589,000 as against 576,000 for diptheria and 578,000 for tetanus) and this could only be achieved by the use of single-vaccine shots. This suggests statistically significant variations from the "routine program" leading to frequent additional mercury exposure in infants. (There are further anomalies in the historic record, which will emerge in section 2.)

The position became even more anomalous as it gradually emerged over the following months that, unlike the United States, there was no immediate attempt or intention to remove thimerosal from the recommended pediatric vaccinations pending the outcome of the investigation and further research. In fact, thimerosal continued to be used in the DPT vaccine in the United Kingdom until its phasing out of the schedule in October 2004 [11].

With remarkable strategic placement, however, it was not until the imminent removal of mercury from U.K. infant vaccine, more than three years later, in September 2004, that two British government studies—including the one announced in the *Sunday Times* in June 2001, which had been presented *in camera* to the WHO as early as June 2002—were published in *Pediatrics* [12,13]. The PHLS study had also been presented at the US Institute of Medicine Special Committee on Immunization in February 2004. But it was only with the publication of the study that it became possible to assess its methodology and conclusions, by which time it had been standing as guarantor for the WHO mercury policy for more than two years, (as is stated at the end of the published version):

> "The results of the two United Kingdom studies were presented to the WHO Global Advisory Committee on Vaccine Safety in June 2002. These studies contributed to the conclusion that there is currently no evidence of mercury toxicity in infants, children or adults who are exposed to thimerosal in vaccines, and that there is no reason to change current immunization practices with thimerosal-containing vaccines on grounds of safety. This conclusion is particularly important for developing countries that administer thimerosal-containing DTP vaccines according to the expanded immunization schedule." [12]

However, the study apparently makes a false claim about the relationship between the U.K. and the WHO schedule:

> "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."* (Italics added for emphasis) [12]

This claim is contradicted by a contemporaneous U.K. Committee on Safety in Medicines document that states:

> "The early childhood vaccination regimen recommended by the WHO involves exposure of 187.5μg EtHg in the first 14 weeks of life (table 2). Until recently, the same level of exposure had been recommended (sic) within the first six months of life in the U.S. schedule."

Incredibly, the PHLS study was initiated, funded and accepted by the World Health Organization, although the official level of U.K. exposure at 14 weeks was secretly known to be only just over one quarter of the exposure of the WHO schedule, while the study itself states that the level was "the same." Some of the hidden history of how this came about will be explored in the following section.

2. The long arm of the CDC

As noted previously, Elizabeth Miller, head of immunization at the U.K. Public Health Laboratory Service (PHLS), took four weeks to reply to a June 17, 2001 article in the *Sunday Times* that reported she was to lead a World Health Organization (WHO) investigation into autism and mercury-containing vaccines. When Miller's letter finally appeared in the newspaper on July 15, it apparently denied reporter Rosie Waterhouse's claims about an increasing mercury load in vaccine since 1988, although on careful scrutiny, there seemed little substance to the rebuttal.

Such a delay in responding is curious enough in the context of a weekly newspaper, and enhanced in this case by the level of indignation expressed in Miller's letter when it appeared. The reasons for this unusual occurrence, according to emails obtained under the U.S. Freedom of Information Act, would seem to lie with the U.S. Centers for Disease Control and Prevention (CDC). These few surrendered emails must surely represent a tiny proportion of the exchanges that would have gone on for weeks and months among the PHLS, the CDC, and the WHO.

Eleven days had elapsed from the publication of the *Sunday Times* article, when Elizabeth Miller emailed Robert Chen of the CDC:

> "Dear Bob,
>
> "The information given to me by the licensing authority is that the whole cell DTP/Hib vaccine we currently use contains 50 micrograms thiomersal per dose so that our children if on schedule would have 75 micrograms of ethyl Hg by 4 months of age. They originally told me that the whole cell DTP we used on its own from 1990 (when we adopted our accelerated schedule) up to

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1992/3 contained 100 micrograms thiomersal, so exposure to ethyl Hg would have been 150 micrograms by 4 months. We then started using combined DTP/Hib vaccines for which the thiomersal content apparently was 50 μg/dose. The authority is now saying that they have made a mistake and the vaccine we used up to 1992/3 only contained 50 micrograms thiomersal/dose. If this is true, then do we have sufficient exposure to ethyl Hg by 4-6 months of age to pick up an effect? Do I have to give my GPRD grant money from WHO back?

Liz"

There are several puzzles here. One is: How could it be that the head of the immunization division of the Public Health Laboratory Service needed to apply to the licensing authority to ascertain the content of the vaccines? Then, there is Miller's conviction that the dose had been higher, her annoyance that the U.K. mercury load was half what she had believed (which might have been considered good news), and her strongly expressed concern that she might lose the grant for the WHO research for this reason.

The WHO project was certainly in jeopardy. The following day, Thomas Verstraeten, Chen's colleague at the CDC, wrote to Chen:

"Bob,

"I think two issues are important in assessing the potential strength of the GPRD study:

1. Maximum exposure and 2. Unbiased controls.

The maximum exposure is indeed relatively low if that was the only T(himerosal) containing vaccine used. My estimate is that you need at least >50 by 3 months or >100 by 6 months to see an effect if there is one which you can barely make (50 at 2 mo and 75 at 4 mo in the UK).

The quality of the comparison group is maybe even more important if you consider all the criticism we have received of comparing high T exposure to no or low T exposure. I am not sure if the GPRD is that reliable that you can be sure that low exposure is really low exposure and not underascertainment in the database.

I hate to say this, but given these concerns, it may not be worth doing this after all. On the other hand, maybe the grant can be given to Harald in Sweden to do his follow-up of the DTaP trial kids…."

Verstraeten's note raises a catalogue of issues, which in light of events must continue to raise concern:

1. The given U.K. dosage at 3 months is only just over one quarter of the WHO schedule for birth to 14 weeks, and Verstraeten even doubts that the routine U.K. exposure would produce any effect.
2. Verstraeten casts serious doubt on the quality of the U.K. database, a matter to which it will be necessary to return at length in section 3.
3. The funding of the operation by the WHO is under the influence of the CDC, a factor that has not been transparent.

Verstraeten's qualms, nevertheless, seem to have been pushed aside in the following fortnight in time for Miller's letter to appear in the *Sunday Times* confirming, among other things, that her laboratory was to conduct a study on behalf of the WHO, as reported a month earlier. But all the participants in the discussions had known that the official U.K. mercury load was not the same as the WHO load, as the paper was eventually erroneously to state. Could it be that they were driven to this because removing the WHO funding would have drawn attention to the issue of the size of the WHO mercury load, and exposed the whole story to the glare of publicity once again, perhaps on an international basis? It seems impossible to resolve the mystery of the 100μg thimerosal/50μg mercury dose that Miller apparently had believed was contained in the DPT. For instance, the minutes of a Joint Committee on Vaccination and Immunization (JCVI) of Oct. 9, 2000 reported:

"A paper comparing the potential levels of thiomersal exposure at 6 months of age through the U.K. and U.S. immunization program was presented. The estimated potential thiomersal exposure through the U.K. program was calculated to range between 0.15 and 0.30 mg (equivalent to 75-150 ug of mercury)."

Another JCVI document from the second half of 1999 with the date blanked out seems to refer to the 0.3-mg exposure to thimerosal as current: "The estimated potential thiomersal exposure through the U.K. program is between 0.15 – 0.3mg."

Also, confirming the measurement in volume terms: "A solution of 0.01 or 0.02 percent thiomersal is commonly used in vaccines."

Following publication of the PHLS study, Miller and co-author Nick Andrews were unable to resolve this matter in public correspondence in on-line *Pediatrics* [14]. They cited letters written to the author by Philip Bryan of the MHRA:

"A subsequent review of the content of thiomersal-containing vaccines revealed that the '150 microgram' calculation was actually based on an incorrect assumption that the ethylmercury content of this vaccine brand was 50 micrograms per dose when it, in fact, was 50 micrograms per 1ml (i.e., 25 micrograms per 0.5ml dose). Ethylmercury exposure through doses of DTP vaccination by 4 months of age, therefore, did not exceed 75 micrograms. I hope this clarifies the confusion." (Letter: Aug. 3, 2005)

The vaccine product for which the incorrect information on quantity of thiomersal per dose was provided was Trivax AD. This information relating to Trivax AD was supplied some time ago in response to an urgent query at a time when many products containing thiomersal had to be identified. As stated, following subsequent requests for information, it was noted that the initial quantity per dose calculation was actually based on an incorrect assumption that the ethylmercury content of the vaccine brand was 50 micrograms per dose when, in fact, it was 50 micrograms per 1ml (i.e. 25 micrograms per 0.5ml dose). I hope this clarifies the matter." (Letter: Sept. 5, 2005)

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Bryan proposed this as an explanation of the Medicines Control Agency briefing note of June 7, 2001, provided by the Department of Health, which stated:

> "Thiomersal-containing vaccines have been in use for over 60 years and evidence does not support a causal link with autism. Indeed, reported rates of autism have been continuing to rise over the past decade as thiomersal content in routine U.K. childhood program has fallen."

It is worth noting, if it was true (and Bryan claims it was an error), that the rising trend in autism in 2001 would have been a product of the early '90s vaccination, when the routine program dose was said to be higher. Any lowering of dose in the later '90s would have been too recent to trace. This was a flawed argument, although as it turns out, it was never produced in public.

Interestingly, when I challenged Miller and Andrews publicly on the fact that the JCVI documents also gave the figure as a percentage of volume [15], they did not offer any further defense or explanation. Nor is it clear that the peculiar circumstances of this error as described by Philip Bryan would have been compatible with successive presentations over a 12-month period at the JCVI, including a paper discussing the higher level. (But Bryan also makes the common error of quoting the mercury level in thimerosal as for "ethylmercury" as opposed to mercury *per se* [16].)

It should also be noted that, according to an internal Merck memo *Re: Vaccine Task Force Assignment Thimerosal (Merthiolate) Preservative—Problems, Analysis, Suggestions For Resolution* written under the sub-heading "Problem" by Maurice Hilleman in March 1991 [17]:

> "The regulatory control agencies in some countries, particularly Scandinavia (especially Sweden). but also U.K., Japan, and Switzerland, have expressed concern for thimerosal, a mercurial preservative, in vaccines."

The evidence, therefore, is that there had been awareness of the mercury level problem by British health officials — and possibly "concern"—since at least 1991, even though the matter did not become publicly known until the *Sunday Times* highlighted it in 2001. Against this background, it is surprising that a mix-up of the kind described by Philip Bryan could have continued over an extended period.

By Aug. 14, 2001, Elizabeth Miller was requesting from Robert Chen access to background variable confounders in the unpublished CDC Vaccine Safety Datalink (VSD) study co-authored by Chen, and led by Thomas Verstraeten:

> "I am just about to receive the GPRD data which we propose to use to do the same kind of study you did on the VSD data set. It would be very helpful if you had a protocol describing what you did in your study, in particular what the background variables were that you included as possible confounders. I am on leave from 21 August to 10 September, but Nick, the statistician, who will be working on the data set, is around and you could liaise with him directly."

On Oct. 18, 2001, Miller was seeking further aid from CDC concerning the potential for irregularity in the outcome coding of GPRD. She wrote to Chen:

> "Dear Bob,
>
> We will shortly be starting our analyses on the GPRD data set and would be grateful if you or someone at your end could look at the list of conditions we have identified as relevant development outcomes (this I am faxing as I do not have it electronically). The codes in the GPRD are Read or Oxmis (Rdoxflaf O or R) and there is not a precise mapping to ICD 9. We have identified all the codes we think are relevant to the outcomes of interest, as you will see we have flagged them as follows:
>
> 1 = child psychoses
> 2 = specific psychopathological symptoms
> 3 = emotional disturbance
> 4 = hyperkinetic syndrome
> 5 = specific developmental delay
> 6 = mental retardation
>
> I would be interested in any comments. Have we got the right conditions (as judged by text field) and are there any other conditions that we might have missed?
>
> I don't know what the coding system is for medical conditions on your HMOs but if there is anything similar to the one on the GPRD and if you have a list of the conditions you flagged this would be very helpful to us, not only for the outcomes of interest but also the exclusions and other background conditions that you took account of in the analysis as potential confounders."

The one thing missing was autism.

3. The PHLS study reviewed

By the time the U.K. Public Health Laboratory Service (PHLS) study was published in September 2004, Elizabeth Miller's department had become the Communicable Disease Surveillance Centre, Immunization Department. The authors disclosed no competing interests. However, independent researchers Mark and David Geier wrote to *Pediatrics:*

> "The authors of the Andrews *et al.* study failed to disclose their significant conflicts of interests to the readership of *Pediatrics*: Elizabeth Miller disclosed in her 2001 publication [18] and in 2002 to the Committee on the Safety of Medicines previously disclosed that she has received funding to study vaccines from Aventis Pasteur, Wyeth Vaccines, SmithKline Beecham, Baxter Health Care, North American Vaccine, Wyeth-Lederle Vaccine, and Chiron Biocine; and Nick Andrews, Julia Stowe, and Brent Taylor all disclosed in 2001 that they had received funding to study vaccines from Wyeth Vaccines and SmithKline Beecham [18]. These companies all are or were makers of thimerosal-containing vaccines." [18]

To which Elizabeth Miller, Nick Andrews and Brent Taylor replied:

> "The requirements by *Pediatrics* for the conflict of interest declaration were complied with by the authors

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> and the Health Protection Agency's policy on the condition under which commercial funding is obtained for studies in [sic] available on our web site [19].

In other words, the authors did not deny these competing interests, although they had not declared them. They do not claim either to have adhered to the Health Protection Agency code, but merely allude to its existence. It is perhaps even more concerning that officials who bear responsibility for implementing the policy they are reviewing do not declare this as an interest, as if by implication they are above having an interest. This is a tactic that deceives a good many journalists and politicians, but it is by no means the reality. In fact, it makes little sense that they should be in the position of reviewing the policy at all. The conclusion of the PHLS study as stated in the abstract was succinct:

> "With the possible exception of tics, there was no evidence that thimerosal exposure via DPT/DT vaccine causes neurodevelopmental disorders." [12]

This, in itself, restricts the scope and value of the study, and poses certain questions. As noted in part I, Miller failed to deal with the claim of the *Sunday Times* that there was "increasing use of thiomersal-containing vaccines in the U.K." after 1988.

Evidence was available that the vaccine schedule was quite commonly not administered in the routine way, and there would have been increased exposure from the combined use of single vaccines. It was also documented that 80 thiomersal-containing vaccines, presumably manufactured on a commercial basis, were licensed for pediatric use between 1993 and 2001. These are important confounders that the study does not even consider.

The study apparently treats all infants as if they had the same load, and had received either DT or DPT. It excludes infants who had hepatitis B or influenza shots "in the first six months because such children are likely to be an atypical sub-group," not apparently because they would have had greater exposure. But it is also not clear what has happened to infants who received the schedule through combined single vaccines, who would have had higher dosages. These are simply not referred to. Were they included as if they had had the DT or DPT, or were they excluded? A sub-group that had had higher exposure would be of exceptional interest, but this was not studied. Salutary to consider the warning concerning the U.K. data source—the General Practitioners' Research Database (GPRD)—given by Thomas Verstraeten of the Centers for Disease Control and Prevention, and quoted in Section 2:

> "The quality of the comparison group is maybe even more important if you consider all the criticism we have received of comparing high T exposure to no or low T exposure. I am not sure if the GPRD is that reliable that you can be sure that low exposure is really low exposure and not underascertainment in the database."

These are quite likely to be the remarks of someone who had been able to access the database and been able to sample its data himself.

The other issue that Miller failed to deal with satisfactorily in her letter to the *Sunday Times* was that of thiomersal content in the routine program, which, as she said, had not increased "over the past decade" (1991-2001) but had actually increased between 1988, the date she first mentioned in the letter, and 1991. The reply had skirted the major event of the introduction of the accelerated DPT schedule in 1990, bringing forward vaccination at 3, 5 and 10 months to 2, 3 and 4 months, representing an approximately 20% increase in mercury content in relation to infant body weight, delivered to significantly more immature infants. This was originally recognized as a critical issue by Miller. She had written to Robert Chen on June 27, 2001:

> "The licensing authority has now definitely confirmed that the whole cell vaccine we used prior to 1996 did only contain the 50μg thiomersal dose. This is really annoying as we checked with them several times. I need to discuss the implications of this with WHO. What is the thiomersal exposure in the Harald Heibel study because I believe they used the U.K. whole cell vaccine for their 2, 4, 6 vs 3, 5, 12 month, so even with most accelerated schedule, the Swedish children would get less exposure than our kids routinely get."

The significance of this event became masked in the PHLS study. However, contemporaneous with the PHLS study was another study sharing four of the same authors (Miller, Taylor, Andrews and Stowe), which studied incidence of autism in a northeast London population in relation to MMR. Published in *Archives of Diseases in Childhood (ADC)*, and submitted in December 2002, six months after the mercury study was presented to the WHO, it was published a year ahead of it in August 2003. However, neither study references the other.

The *ADC* paper [20] chronicles the rise in autism—based on patient records—in five northeast London districts between 1979 and 1992, arguing that an exponential trend exists over the period independently of the introduction of the MMR in 1988. Without citing evidence, it concludes that this was due to institutional changes and better diagnosis. The authors further argue that this process tailed off from 1992 and that the trend should remain stable beyond the point at which their data begins to peter out in 1996:

> "The prevalence of autism, which was apparently rising from 1979 to 1992, reached a plateau at a rate of 2.6 per 1,000 live births. This leveling off, together with reducing age at diagnosis, suggests that the earlier recorded rise in prevalence was not a real increase, but was likely due to factors such as increased recognition, a greater willingness on the part of educationalists and families to accept the diagnostic label, and better recording systems. The proportion of parents attributing their child's autism to MMR appears to have increased since August 1997."

There was, in fact, no evidence presented whatsoever for the conclusion that the trend was a cultural phenomenon (as I pointed out on ADC Online at the time, without response [21]). One confounding factor, which the authors might have taken into account given that they were simultaneously engaged on a thimerosal study, was that diagnosed incidence of childhood and atypical autism (excluding Asperger Syndrome) rose from 22 in the birth cohort of 1989 to 36 in 1990 and 46 in 1991, *a rise of 109% synchronous with the introduction of the accelerated DPT schedule*. And yet right at the outset, reporter Rosie

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Waterhouse had aggravated Miller by her suggestion in the *Sunday Times* that:

> "A key factor may be that mercury-based vaccines are being given to babies as young two months old, when their bodies are less able to cope with it…."

But the data was available to health officials—the very same health officials—and they failed to even acknowledge it.

3.1 The PHLS study is based on an inadequate database

The U.K. General Practitioners' Research Database used in the PHLS study [24] is an inadequate tool, both quantitatively and qualitatively, to research neurodevelopmental disorders. The authors of the PHLS study, amid their opaque and unverifiable data, include only 104 cases of autism among term infants, and two among pre-term infants, representing an incidence of barely more than 0.1 percent. By comparison, a survey from the Office of National Statistics offers a much more plausible one percent incidence of autistic spectrum disorders (ASD) among children born between 1988 and 1999 [22].

The question further arises with the PHLS figure as to how much of it is interpretation. The study of Hershel Jick and James Kaye came up with much lower figures still, albeit rising dramatically from 1.6 boys in 10,000 in 1993 to 9.5 boys in 10,000 in 1999. Supposing four ASD boys to one ASD girl, this would amount to 1 in 10,000 in 1993 to 6 in 10,000 in 1999, so that in 1993, the median year of the PHLS study, they perhaps were only picking up one-tenth as many cases as the PHLS total using the same database [23]. This is a wide and unacceptable margin of error.

Another British government-sponsored study into autism and MMR testifies to the ramshackle nature of the data included in the GPRD:

> "Medical notes for 318 subjects were obtained. They varied in quality and exhaustiveness. For some children, GP records included several consultant reports, speech and language assessments, and educational psychology reports. For other children, the information available was scanty, with sometimes the only available data consisting of one, or a few, letters between the GPs and consultants. A high proportion of records had missing data on parental age, socio-economic status, and detailed psychometric assessment of the child and, therefore, the frequencies of these variables are not described here. Of the 318 children whose medical forms were obtained, the raters confirmed a diagnosis of PDD (pervasive developmental disorders) in 294 children (92.5%). Compared to children with a confirmed PDD diagnosis, children for whom the diagnosis was not confirmed (n = 24) had significantly fewer PDD symptoms (2.1 vs 6.2; $p < 0.001$), higher language level (phrase speech: 80% vs 45%; p=0.051), and more frequent parental concern arising for the first time after the age of 3 years (20% vs 2.9%; p=0.024)." [24]

It might be considered after initial assessment that drawing any significant conclusions from a database of this quality in this particular field would be rash. This, however, failed to stop a succession of studies related to the vaccine/autism issue from proceeding. Apart from the PHLS study, these included three by the Boston Collaborative Drug Surveillance Program, [9,10,7] and four studies by Smeeth *et al.* backed by the U.K. Medical Research Council [24,27,28,30].

Serious questions must arise as to the wisdom and motivation behind these enterprises, which were extensively reviewed by John Heptonstall in *BMJ Rapid Responses* and online *Pediatrics* [30,31]. There are, in fact, too many problems with the database even before starting to consider issues of method and transparency: for instance, there is the likelihood that the vast bulk of the cases are lost in the control group and adversely weighting the sample. Moreover, the PHLS study takes the precaution of removing all the most vulnerable clinical cases as stated under the heading "exclusion criteria":

> "Children with Read and OXMIS codes relating to a variety of prenatal, perinatal and postnatal conditions that occurred before 6 months of age were excluded as were children who were recorded as having an outcome event in the first 6 months of life. These children were excluded from the main analysis because the presence of such a condition is likely to affect both vaccination and future neurodevelopmental outcomes. Examples of exclusions were birth asphyxia, cerebral palsy, meningitis, encephalitis and head injury. Children were also excluded when they received either hepatitis B or influenza vaccination in the first 6 months of life because such children are likely to be an atypical subgroup. Children who were born preterm (<37 weeks' gestation) are likely to be of low birth weight and many stay small. Such infants might be more susceptible to standard doses of thimerosal. Preterm infants were therefore analyzed separately." [12]

Since the listed exclusions are, based on their own testimony, only "examples," this is the epidemiological equivalent of a blank check. Significantly, perhaps, when authors Andrews and Miller attempted to answer criticism by Heptonstall, they did not respond to point 12 in his online letter to *Pediatrics* of Oct. 30, 2004 [31]:

> "12. The excluded group of children, postnatal and 'outcomes,' who might have suffered mercury damage from vaccines—a tiny fraction of the 103,043 cohort but a fair proportion of approximately 5,000 cited as having outcome conditions. Andrews *et al.* state the exclusions were made 'because the presence of such a condition is likely to affect both vaccination and future developmental outcomes.' Aren't these the very children the study should have focused on?"

4. Conclusions

The most illuminating response I received from a Freedom of Information inquiry came in reply to questions fired off in irritation to the U.K. Department of Health after having an earlier query passed on to the licensing authority, the MHRA. Aside from the collection of interesting material supplied were these two astounding answers (June 1, 2005):

> "Q: At what point was it that the Department of Health became aware that there might be a problem with thiomersal/ thimerosal?"

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"A: The Department of Health is not aware of problems with Thiomersal, only that concerns had been raised in the U.S. based on the U.S. immunization schedule and the EPA recommendations. The Department's interest followed the U.S. information that was in the public domain."

"Q: Who knew, and when?"

"A: This was public knowledge amongst numerous Department of Health officials from the time of publications from the U.S."

In other words, officially speaking, the hypothesis that mercury vaccine could cause autism was never, ever considered by U.K. officials. It was not considered in 1999, 2001, 2002, 2004 or 2005. Apparently, it never will be in the U.K.

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