Neurodevelopmental Disorders Following Thimerosal-Containing Childhood Immunizations: A Follow-Up Analysis

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The authors previously published the first epidemiological study from the United States associating thimerosal from childhood vaccines with neurodevelopmental disorders (NDs) based upon assessment of the Vaccine Adverse Event Reporting System (VAERS). A number of years have gone by since their previous analysis of the VAERS. The present study was undertaken to determine whether the previously observed effect between thimerosal-containing childhood vaccines and NDs are still apparent in the VAERS as children have had a chance to further mature and potentially be diagnosed with additional NDs. In the present study, a cohort of children receiving thimerosal-containing diphtheria-tetanus-acellular pertussis (DTaP) vaccines in comparison to a cohort of children receiving thimerosal-free DTaP vaccines administered from 1997 through 2000 based upon an assessment of adverse events reported to the VAERS were evaluated. It was determined that there were significantly increased odds ratios (ORs) for autism (OR = 1.8, $p < .05$), mental retardation (OR = 2.6, $p < .002$), speech disorder (OR = 2.1, $p < .02$), personality disorders (OR = 2.6, $p < .01$), and thinking abnormality (OR = 8.2, $p < .01$) adverse events reported to the VAERS following thimerosal-containing DTaP vaccines in comparison to thimerosal-free DTaP vaccines. Potential confounders and reporting biases were found to be minimal in this assessment of the VAERS. It was observed, even though the media has reported a potential association between autism and thimerosal exposure, that the other NDs analyzed in this assessment of the VAERS had significantly higher ORs than autism following thimerosal-containing DTaP vaccines in comparison to thimerosal-free DTaP vaccines. The present study provides additional epidemiological evidence supporting previous epidemiological, clinical and experimental evidence that administration of thimerosal-containing vaccines in the United States resulted in a significant number of children developing NDs.

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Potential conflict of interest: David Geier has been a consultant in cases involving vaccines before the no-fault National Vaccine Injury Compensation Program (NVICP) and in civil litigation. Dr. Mark Geier has been a consultant and an expert witness in cases involving vaccines before the no-fault NVICP and in civil litigation.

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We previously published the first epidemiological evidence from the United States showing an association between thimerosal-containing childhood vaccines and neurodevelopmental disorders (Geier and Geier 2003a). Specifically, it was determined that there was from a two- to sixfold statistically significantly increased reporting rate of neurodevelopmental disorders, depending on the specific symptom or disorder, to the Vaccine Adverse Event Reporting System (VAERS) database following thimerosal-containing diphtheria-tetanus-acellular pertussis (DTaP) (administered from 1992 to 2000) in comparison to thimerosal-free DTaP vaccine (administered from 1997 to 2000), whereas control adverse events were reported similarly following both vaccines under study.

In light of the fact that a number of years have gone by, the present study was undertaken to determine whether the previously observed effect between thimerosal-containing childhood vaccines and neurodevelopmental disorders are still apparent in the VAERS database as children have had a chance to further mature and potentially be diagnosed with a neurodevelopmental disorder. The results of the present analysis should allow one to be able to determine whether the previous observations represented a transient artifact, or whether the previous results are indeed robust, representing a true effect of thimerosal-containing childhood vaccines on neurodevelopmental disorders.

MATERIALS AND METHODS

The VAERS database is an epidemiological database that has been maintained by the Centers for Disease Control and Prevention (CDC) since 1990. Specific vaccine-adverse events following vaccination are required to be reported to this database as mandated by law. The VAERS Working Group of the CDC has previously reported that less than 5% of the total adverse events submitted to VAERS are reported by parents. The VAERS Working Group of the CDC and the Food and Drug Administration (FDA) analyze and publish epidemiologic studies based

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TABLE 1
The composition of the DTaP vaccines under study

Vaccine component	Thimerosal-containing DTaP vaccine A	Thimerosal-containing DTaP vaccine B	Thimerosal-free DTaP vaccine C
Pertussis toxin (μg/dose)	23.4	3.5	25
Filamentous hemagglutinin (μg/dose)	23.4	35	25
Pertactin (μg/dose)	—	2	8
Fembrial agglutinogens (μg/dose)	—	0.8	—
Diphtheria toxoid (Lf/dose)	3.7	9	25
Tetanus toxoid (Lf/dose)	5	5	10
How toxoided	Formaldehyde	Formaldehyde	Formaldehyde
Aluminum (mg/dose)	0.17	0.23	0.50
Diluent	Phosphate-buffered saline	Phosphate-buffered saline	Saline
Preservative	Thimerosal	Thimerosal	Phenoxyethanol
Trace constituents	Formaldehyde, gelatin, polysorbate-80	Formaldehyde, gelatin, polysorbate-80	Formaldehyde, polysorbate-80

upon analyses of VAERS. The VAERS Working Group of the CDC published that VAERS is simple to use, flexible by design, and the data are available in a timely fashion. The authors also warn that the potential limitations in VAERS may include underreporting, erroneous reporting, frequent multiple exposures, multiple outcomes, and lack of precise denominators (Singleton et al. 1999).

In order to examine VAERS correctly, in this study, a technique developed by Rosenthal, Chen, and Hadler from the National Immunization Program (NIP) of the CDC (Rosenthal, Chen, and Hadler 1996) was employed. This technique involves comparing two vaccine groups in VAERS that were administered to similarly aged populations, and using the net number of doses distributed (this number takes into account doses not distributed or returned during the period) from the Biological Surveillance Summaries (BSS) of the CDC to calculate incidence rates of reported adverse events to VAERS following the vaccines under study. The incidence rates of adverse events reported to VAERS for the vaccines under study were compared to determine the relative safety (ratio of reported adverse events and statistical significance) of the vaccines analyzed.

Analysis Methods

A retrospective examination of the VAERS database (online public access version; reports entered through 28 February 2004) was undertaken using Microsoft Access™. VAERS was analyzed for neurodevelopmental adverse events reported in a cohort receiving thimerosal-containing DTaP vaccines in comparison to a cohort receiving thimerosal-free DTaP vaccines (1997 through 2000), including autism, mental retardation, ataxia, speech disorders, thinking abnormalities, and personality disorders. Descriptions of these adverse events were based upon those reporting them and defined fields contained within VAERS.

The BSS of the CDC broken down by vaccine manufacturer determined the number of thimerosal-containing and thimerosal-free DTaP vaccine (1997 through 2000) doses distributed/administered. The BSS indicated that 53,579,940 thimerosal-containing DTaP vaccines and 16,915,700 thimerosal-free DTaP vaccines were distributed/administered from 1997 through 2000. In Table 1, the composition of the DTaP vaccines analyzed are summarized. We are precluded from identifying the vaccine manufacturers analyzed in this study because of an agreement with the CDC not to release such information as a condition of the CDC providing us with a breakdown of the number of doses of vaccines distributed/administered by manufacturer. The CDC maintains that this information is proprietary between themselves and the manufacturer.

Controls

It has been hypothesized that because of compelling presentations in the popular media implicating an association between autism and thimerosal-containing vaccines, biases might result in population prejudice favoring the reporting of autism adverse events to the VAERS associated with vaccines containing thimerosal. If this were the case, it would be expected that increases in the incidence rates of reported autism adverse events following thimerosal-containing vaccines would have occurred, and this might result in an over estimate of the risk association between thimerosal and autism. In examining the risk for the other types of neurodevelopmental disorders examined in this study in comparison to the risk for autism, one can evaluate what potential effects the media had on the association we observed between thimerosal and autism.

To evaluate potential general biases present in the reporting of adverse events, a series of control adverse events were employed including fevers and total reports, as well as neurological adverse events including seizures and encephalitis/encephalopathy.

The distribution and geographical dispersion of the populations analyzed in VAERS were also evaluated as controls. In determining the distribution of the populations reviewed the

TABLE 2
A summary of the distribution of the populations analyzed in VAERS

Vaccine type	Reported female reports per million vaccines [no. of reports]	Reported male reports per million vaccines [no. of reports]	Reported male/female ratio	Reported mean age (years)
Thimerosal-containing DTaP	54 [2,874]	63 [3,368]	1.2	2.03 ± 3.3
Thimerosal-free DTaP	52 [887]	59 [997]	1.1	2.16 ± 4.04
Odds ratio for reported adverse events	1.02	1.07	1.04	—
95% odds ratio confidence interval for reported adverse events	0.95–1.1	0.99–1.1	0.94–1.1	—
p value	.55	.07	.43	.20*

Note. All p values determined using the likelihood ratio chi-square test statistic, except where marked with an *, which was determined using the t test statistic.

overall mean age, total numbers of male and female reports, and male/female ratios of those reporting adverse events to VAERS were examined. Similarly, in reviewing the geographical dispersion of the populations analyzed, the total number of adverse event reports submitted to VAERS from large representative states from the western (California), central (Illinois), and eastern (Florida) regions of the United States were examined.

Statistical Methods

In performing the statistical analyses employed in the present study, the premise of equality between the cohorts examined forms the basis of the null hypothesis. The statistical method involved constructing 2×2 contingency tables. We determined odds ratios (ORs), 95% OR confidence intervals (CIs) for reported adverse events, and p values from our 2×2 contingency tables. The statistical package in Microsoft Excel™ and SISA™ were utilized, and the t test statistic, likelihood ratio chi-square statistic, or Fisher's exact test statistic ($n < 5$) were employed to determine statistical significance. In order for statistical significance testing to be preformed for an outcome, there had to be at least a total of 20 outcomes identified in VAERS. A double-sided p value $< .05$ was considered statistically significant.

RESULTS

Tables 2 and 3 compare the distribution and geographical dispersion of those reporting adverse events following the vaccines under study to VAERS. It was found that the vaccines under study were overall administered to cohorts with a similar distribution and geographical dispersion. Table 4 and Figure 1 evaluate neurodevelopmental disorders reported to VAERS following thimerosal-containing DTaP vaccines in comparison to thimerosal-free DTaP vaccines. It was found that there were significantly increased ORs for autism (OR = 1.8, 95% OR CI = 1.0–3.3, $p < 0.05$), speech disorders (OR = 2.1, 95% OR CI = 1.1–4.0, $p < 0.02$), mental retardation (OR = 2.6, 95% OR CI = 1.3–5.2, $p < 0.002$), personality disorders (OR = 2.6, 95% OR CI = 1.2–5.7, $p < 0.01$), and thinking abnormalities (OR = 8.2, 95% OR CI = 1.1–60, $p < 0.05$) reported following thimerosal-containing DTaP vaccines in comparison to thimerosal-free DTaP vaccines. Table 5 examines control adverse events reported to VAERS in the cohorts under study. It was determined that fever (OR = 0.99, 95% OR CI = 0.89–1.1, $p = 0.91$), seizure (OR = 1.09, 95% OR CI = 0.88–1.4, $p = 0.41$), and encephalitis/encephalopathy (OR = 1.4, 95% OR CI = 0.61–3.5, $p = 0.37$) control adverse events were reported similarly in the cohorts under study, whereas there was

TABLE 3
A summary of geographical dispersion in the populations analyzed in VAERS

Vaccine type	Reported California reports per million vaccinations [no. of reports]	Reported Florida reports per million vaccinations [no. of reports]	Reported Illinois reports per million vaccinations [no. of reports]
Thimerosal-containing DTaP	10 [540]	4.7 [253]	4.7 [253]
Thimerosal-free DTaP	11 [186]	3.7 [63]	5.4 [92]
Odds ratio for reported adverse events	0.92	1.3	0.87
95% odds ratio confidence interval for reported adverse events	0.78–1.1	0.96–1.7	0.68–1.1
p value	.31	.08	.25

Note. All p values determined using the likelihood ratio chi-square test statistic

TABLE 4
A summary of neurodevelopmental disorders reported following the vaccines under study in VAERS

Type of vaccine	Autism	Speech disorders	Mental retardation	Personality disorders	Thinking abnormalities	Ataxia
Reported incidence per million thimerosal-containing DTaP [no. of reports]	1.3 [72]	1.2 [66]	1.3 [74]	1.1 [58]	0.40 [26]	0.48 [26]
Reported incidence per million thimerosal-free DTaP [no. of reports]	0.77 [13]	0.59 [10]	0.53 [9]	0.40 [7]	0.059 [1]	0.24 [4]
Odds ratio for reported adverse events	1.8	2.1	2.6	2.6	8.2	2.1
95% odds ratio confidence interval for reported adverse events	1.0–3.2	1.1–4.0	1.3–5.2	1.2–5.7	1.1–6.0	0.72–5.9
p value	$<.05$	$<.02$	$<.002$	$<.01$	$<.001$*	.20*

Note. All p values determined using the likelihood ratio chi-square test statistic, except where marked with an *, which were determined using the Fisher's exact test statistic.

a clinically non-significant statistical increase in total adverse events (OR = 1.06, 95% OR CI = 1.0–1.1, $p < 0.05$) reported to the VAERS following thimerosal-containing DTaP vaccines in comparison to thimerosal-free DTaP vaccines.

DISCUSSION

The VAERS database showed that a significant risk factor for the development of a neurodevelopmental disorders was the amount of mercury children received from thimerosal-containing childhood immunizations. It was observed that those children receiving thimerosal-containing DTaP vaccines in comparison to thimerosal-free DTaP vaccines were at increased risk for reported neurodevelopmental disorder adverse events based upon our assessment of the VAERS database. A number of controls to determine if biases or confounders were present in the reporting of adverse events examined in the VAERS database for

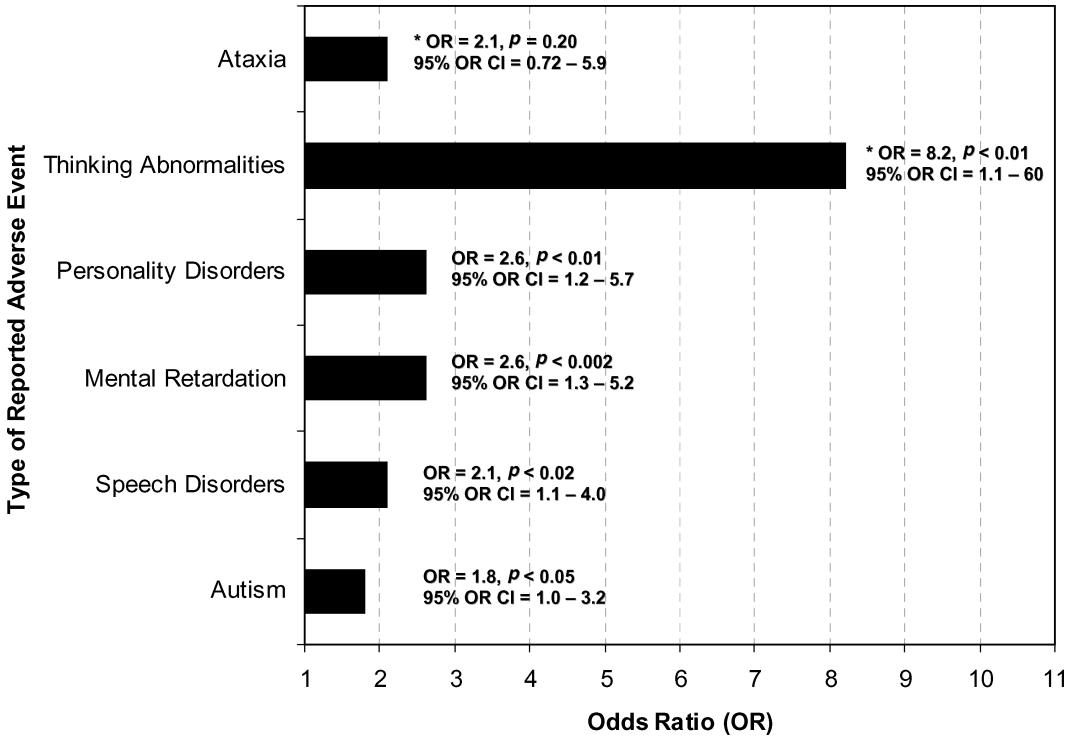

FIGURE 1
All p-values determined using the likelihood ratio chi-square test statistic, except * determined using the Fisher's exact test statistic, OR = Odds Ratio; CI = Confidence Interval.

TABLE 5
A summary of control adverse events reported following the vaccines under study to VAERS

Type of vaccine	Seizures	Fever	Total reports	Encephalitis/encephalopathy
Reported incidence per million thimerosal-containing DTaP [no. of reports]	6.7 [361]	29 [1,563]	120 [6,397]	0.52 [28]
Reported incidence per million thimerosal-free DTaP [no. of reports]	6.1 [104]	29 [497]	113 [1,907]	0.36 [6]
Odds ratio for reported adverse events	1.09	0.99	1.06	1.4
95% odds ratio confidence interval for reported adverse events	0.88–1.4	0.89–1.1	1.0–1.1	0.61–3.5
p value	.41	.91	$<.05$	.37

Note. All p values determined using the likelihood ratio chi-square test statistic.

the cohorts under study were evaluated, and the results indicate that they had a minimal effect upon the results of the study. It was even observed, although the media has reported a potential association between autism and thimerosal exposure, that the other neurodevelopmental disorders analyzed in our assessment of the VAERS had significantly higher ORs than autism following thimerosal-containing DTaP vaccines in comparison to thimerosal-free DTaP vaccines.

The results of the present study demonstrate that the thimerosal effect previously observed is not a mere particularity of the years examined in the VAERS, but a broad-based effect that may be seen with different years of examination. The results of the present study also took into account the number of years of follow-up among the cohorts examined in the VAERS database, so as to allow a sufficient chance for the populations under study to receive a diagnosis of a neurodevelopmental disorder. The thimerosal-containing and thimerosal-free DTaP vaccines examined in the present study were administered from 1997 through 2000, so that the minimum age in the cohorts examined was 3 years and 4 months-old. This minimum age assumes that the youngest individual in either cohort received their first DTaP vaccine on the last day of each study period, calculated based on VAERS reports received through February 28, 2004. The CDC has previously published that the approximate median age of diagnosis for autism (3.9 years), speech or language delay (2.9 years), and coordination disorder (3.8 years), which were all consistent with the minimum age of children in the cohorts examined in the VAERS database (Verstraeten et al. 2003).

In further considering the results of the present study, it must be noted that none of the children we examined in this study from the VAERS database truly represent a background population that received no thimerosal. It was observed among the reports examined in the VAERS database that other vaccines containing thimerosal, such as hepatitis B vaccine, *Haemophilus influenza* type b (Hib) vaccine, or influenza vaccine, were concurrently administered in the birth cohorts examined. The central difference in the total amounts of mercury received from thimerosal-containing vaccines in the children examined in the VAERS database stems from the fact that some children received additional doses of mercury from thimerosal-containing DTaP vaccine in comparison to those children receiving thimerosal-free DTaP vaccine. As a result, the increased risks observed for neurodevelopmental disorders, probably represent a considerable underestimation of the true risk of additional doses of mercury from thimerosal-containing vaccines. As far as exposure from other sources that may have had significant concentrations of mercury such as Rh_o immune globulin, seafood, manufacturing plant emissions, dental amalgams, and/or other pharmaceuticals, although potentially significant, probably had a limited effect on the results of this study because the populations analyzed were large, and there should have been equal exposure to other sources of mercury among the populations examined. The probability that exposure to other sources of mercury were similar in the thimerosal-containing and thimerosal-free DTaP vaccine cohorts examined in the VAERS database is further supported by the fact that there were similar geographical dispersions in the populations examined.

In considering the technique employed in the present study, it is important to recognize that it continues to be employed by the NIP of the CDC to evaluate the safety of vaccines in the VAERS database (Lloyd et al. 2003). Chen and Rosenthal from the NIP have published potential limitations in VAERS, such as underreporting, erroneous reporting, frequent multiple exposures, multiple outcomes, and lack of precise denominators, should apply equally to both vaccines administered to similarly aged populations, and allow for determination of accurate relative quantitative relationships between vaccines and adverse outcomes (Chen and Rosenthal 1996). Additionally, a recent review has examined the utility of this method to analyze the VAERS database, and has concluded that studies examining the VAERS database using the methods of analysis developed by Rosenthal, Chen, and Hadler (1996) had good positive predictive value for determining vaccine-associated adverse events that were consistent with observations made in vaccine clinical trials and other databases, including the CDC Vaccine Safety Datalink (VSD) database (Geier and Geier 2004a).

In considering the results from the present study, published epidemiological studies conducted in the United States have

shown significant overall and dose-response relationships between increasing doses of mercury from thimerosal-containing childhood vaccines that are in accord with the observations made in this study (Geier and Geier 2003a, 2003b, 2003c, 2004b). A study by Verstraeten et al. (2003), the only other epidemiological study outside of previously mentioned studies that was conducted in the United States, reported to have initially found a significant relationship between thimerosal-containing childhood vaccines and some types of neurodevelopmental disorders, but upon further examination of a different data set did not find a consistent effect. The lead author concluded that their study was neutral (i.e., could neither accept nor reject a causal relationship) regarding the relationship between thimerosal and neurodevelopmental disorders (Verstraeten 2004).

The only potential studies showing a negative relationship between thimerosal and autism have been conducted in Denmark and Sweden (Hviid et al. 2003; Madsen et al. 2003; Stehr-Green et al. 2003). These studies have very little applicability to the US experience with thimerosal, because in both Denmark and Sweden, much lower levels of thimerosal were administered to children as part of the childhood immunization schedule. Overall, these countries administered approximately one-third the thimerosal dose administered in the United States, and these countries administered the thimerosal dose in a much less rigorous schedule than in the United States (i.e. in the US thimerosal dosing began on the day of birth). Additionally, the studies in Denmark have been shown to suffer from the fact that (1) only inpatient diagnosed autistics were initially identified, and then later in these studies both inpatient and outpatient diagnosed autistics were identified, (2) different diagnosis codes of neurodevelopmental maladies, i.e., psychosis infantilis posterior (ICD-8 299.01) versus atypical (i.e., regressive) autism (ICD-10 F84.1), before and during the presumed increase in autism incidence, respectively; and (3) data from additional clinics with a significant portion of the autistics in the entire country were added as the studies progressed.

The results of the present epidemiological study appeared to be supported by recently emerging clinical, molecular, and animal model observations concerning thimerosal and its relationship with neurodevelopmental disorders in the United States.

A recent clinical study by Bradstreet et al. (2003) has evaluated the concentration of heavy metals in the urine among children with autistic spectrum disorders in comparison to a neurotypical control population based upon excretion following a 3-day treatment with meso 2,3-dimercaptosuccinic acid (DMSA). The authors observed that there was approximately six-times significantly greater urinary mercury concentrations among vaccinated cases matched to vaccinated neurotypical controls, whereas children with autistic spectrum disorders had similar urinary cadmium and lead concentrations in comparison to controls. Similar urinary mercury concentrations were observed among matched vaccinated and unvaccinated neurotypical children following DMSA treatment. Similarly, Holmes et al. (2003) have evaluated body-burdens of mercury by examining postnatal mercury elimination in first baby hair cut samples from 94 children diagnosed with autism in comparison to 45 age- and gender-matched controls. Information on diet, dental amalgam fillings, vaccine history, Rho D immunoglobulin administration, and autism symptom severity was collected through a maternal survey questionnaire and clinical observation. Hair mercury levels in the autistic group were 0.47 parts-per-million (ppm) versus 3.63 ppm in controls, a significant difference. The mothers in the autistic group had significantly higher levels of mercury exposure through Rho D immunoglobulin injections and amalgam fillings than control mothers. Within the autistic group, hair mercury levels varied significantly across mildly, moderately, and severely autistic children, with mean group levels of 0.79, 0.46, and 0.21 ppm, respectively. Hair mercury levels among controls significantly correlated with exposure to mercury through childhood vaccines, a correlation that was absent in the autistic group. Together, these clinical observations suggest that autistic children have significantly higher body-burdens of mercury than neurotypical children following exposure to mercury.

The biochemical and genomic basis for the increased body-burden of mercury in autistic children have been identified. James et al. (in press a) have evaluated the methionine cycle and transsulfuration metabolites in autistic children in comparison age- and sex-matched control children. It was determined that there were significant decreases in the plasma concentration of cysteine (19% reduction) and glutathione (46% reduction), both are crucial for mercury excretion, in autistic children in comparison to control children. Additionally, consistent with the DMSA treatment and first baby haircut study results, it was determined that autistic children had significantly increased oxidative stress (3-fold decrease in glutathione/oxidized glutathione redox ratio) in comparison to control children. Boris et al. (in press) have identified specific genomic polymorphisms for enzymes in the methionine cycle and transsulfuration pathways in autistic children that would account for the distinct transsulfuration metabolite profiles observed by James et al. in autistic children.

A decreased ability to excrete mercury is troubling because thimerosal has been reported by a researcher from the Food and Drug and Administration (FDA) to cross the blood-brain and placental barriers, and result in appreciable mercury content in tissues, including the brain (Slikker 2000). In addition, it has recently been shown there was an approximate 28 day half-life of mercury in the brains of young primates injected with thimerosal solutions that had similar concentrations to thimerosal-containing childhood vaccines (Institute of Medicine 2004).

Baskin et al. (2003) have demonstrated that micromolar concentrations of thimerosal induced membrane and DNA damage, and initiated caspase-3–dependent apoptosis in human neurons and fibroblasts. In addition, James et al. (in press b) have reported that the neurotoxicity of thimerosal is associated with depletion of glutathione. The ethylmercury in thimerosal binds to cysteine thiol (-SH) groups on intracellular proteins and inactivates their function. The cysteine-SH group of glutathione, binds mercury and protects essential proteins from functional

inactivation. Glutathione is the major mechanism of mercury excretion, and individuals with genetic deficiencies in glutathione synthesis will be less able to excrete mercury and will be more sensitive to its adverse effects.

Leong, Syed, and Lorscheider (2001) recently examined neurite outgrowth following exposure to the same concentrations of mercury, aluminum, lead, cadmium, and manganese, demonstrating that nanomolar concentrations of mercury markedly disrupted membrane structure and linear growth rates of imaged neurites in 77% of all nerve growth cones. It was observed that the tubulin/microtubule structure disintegrated following mercury exposure. In contrast, exposure to other metal ions did not affect growth cone morphology, or their motility rate. The authors reported in the presence of mercury, neuronal somata failed to sprout, whereas the other metals examined did not affect growth patterns of the neurons examined, providing visual and biochemical evidence that strongly, implicated mercury as an etiological factor in neurodegeneration. Similar results have been observed in tissue culture systems with thimerosal (Brunner, Albertini, and Wurgler 1991; Parry 1993; Wallin and Hartely-Asp 1993).

Waly et al. (2004) have reported that methylation events play a critical role in the ability of growth factors to promote normal development. The authors found that insulin-like growth factor-1 (IGF-1)– and dopamine-stimulated methionine synthase (MS) activity and folate-dependent methylation of phospholipids in SH-SY5Y human neuroblastoma cells, occurred via a phosphoinositol (PI) 3-kinase– and mitogen-activated protein (MAP) kinase–dependent mechanism. The stimulation of this pathway increased DNA methylation, whereas its inhibition increased methylation-sensitive gene expression. Thimerosal inhibited both IGF-1– and dopamine-stimulated methylation, with an IC_{50} of 1 nM, and eliminated MS activity. The authors concluded that the discovery of the PI 3-kinase/MAP kinase/MS pathway, and its potent inhibition by thimerosal, a vaccine component, provides a molecular explanation for how increased use of vaccines could promote an increase in the incidence of autism and attention deficit–hyperactivity disorder (ADHD). In addition, Deth and Waly (2004) have reported that folate-dependent, phospholipid methylation in the lymphoblasts of autistic children were in a dose-response manner significantly more sensitive to thimerosal exposure than in unaffected siblings.

Hornig, Chian, and Lipkin (2004) have reported on administering thimerosal to mice. The authors demonstrated that a genetically susceptible mouse strain developed an autism-like disorder following administration of thimerosal mirroring the childhood immunization schedule in the United States, and the mice shared features in common with autism including growth delay, reduced locomotion, exaggerated response to novelty, increased brain size, decreased numbers of Purkinje cells, significant abnormalities in brain architecture, affecting areas subserving emotion and cognition, and densely packed hyperchromic hippocampal neurons with altered glutamate receptors and transporters. The authors concluded that their findings implicate genetic influences and maturational factors as critical determinants of postnatal thimerosal-related sequelae and highlight the importance of interactions of gene, environment, and timing in the pathogenesis of neurodevelopmental disorders.

CONCLUSION

The present study provides additional epidemiological evidence linking thimerosal with neurodevelopmental disorders. From the 1980s to the late 1990s, the level of thimerosal in childhood vaccinations based upon the recommended vaccine schedule within the first 6 months of life increased from 75 μgrams of ethylmercury starting at 2 months (3 DTP vaccines at 25 μgrams of ethylmercury each) to approximately 200 μgrams of ethylmercury starting on the day of birth (three DTP vaccines [25 μgrams of ethylmercury each], three Hib vaccines [25 μgrams of ethylmercury each], three hepatitis B vaccines [12.5 μgrams of ethylmercury each], and in many children influenza vaccine [12.5 μgrams of ethylmercury each]). Based on the information elucidated in this publication, children exposed to these greater levels of mercury through thimerosal in vaccinations are at much greater risk of neurodevelopmental disorders evidenced by analysis of the VAERS database. Despite, the recent conclusion of the National Academy of Sciences' Institute of Medicine that there is no evidence of a relationship between thimerosal and autism, and that no further scientific research should be undertaken to evaluate the relationship between thimerosal and autism (Institute of Medicine 2004), the results of the present study, taken with data recently published by a number of researchers, demonstrate a connection between mercury exposure via infant vaccinations and the dramatic increase in autism and other neurodevelopmental disorders in the United States. It is clear that the results of the present study mandate that additional research should be undertaken, not only for autism, but other childhood neurodevelopmental disorders, by evaluating childhood mercury-associated exposures, especially from thimerosal-containing childhood vaccines.

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