Autism as a Minamata disease variant: analysis of a pernicious legacy

Kenneth P. Stoller, MD, FAAP
International Hyperbaric Medical Association
404 Brunn School Rd. #D
Santa Fe, NM 87505
Phone: +1 505 955 8560
Email: info@hbotnm.com

Abstract

Minamata Disease is a myriad of neurological and neurodevelopmental symptoms stemming from the pollution of Minamata Bay, Japan with 27 tons of organic mercury by the Chisso Corporation. The corporation denied responsibility and continued to pollute waterways for three decades. While research findings showing mercury was the cause of Minamata disease were concealed by the corporation, a number of committees, of which Chisso Corporation employees were members, were formed to research the problem. The committees denied this information and refuted the direct link of mercury. Today, the causes of autism and several neurodevelopmental disorders may be linked to mercury. Genetic and environmental risk factors are involved, but the epidemic increase in autism parallels cumulative mercury exposure through Thimerosal containing vaccines. Children with autism have a decreased detoxification capacity with a higher mercury exposure during pregnancy due to maternal dental amalgam and Thimerosal containing immunoglobulin shots. In vitro, mercury and Thimerosal in levels found after vaccination inhibit methionine synthase (MS) by 50%. Normal function of MS is crucial in biochemical steps necessary for brain development, attention and production of glutathione, an important mercury-detoxifying agent. Autistic children have significantly decreased levels of reduced glutathione. Numerous committees from numerous agencies have met in response to the growing evidence in support of mercury as the etiology of a growing epidemic. Research papers were created and reports generated all apparently predetermined to exonerate Thimerosal and control vaccine policy, from both within and outside the United States. Today, Thimerosal has been reintroduced back into the routine vaccine schedule with pressure from the WHO and the CDC based on the strength of what appears to be flawed and/or fabricated data whose influence remains unchecked; meanwhile, mercury exposure continues to increase the number of learning disabled and dependent children.

Keywords: mercury poisoning, Minamata Disease, Thimerosal, neurodevelopmental disorders, autism

"The right to search for truth implies also a duty. One must not conceal any part of what one has recognized to be true." Albert Einstein (engraved in stone on the National Academy of Sciences building in Washington, D.C., home to the NIH and the IOM).

1. Minamata

Over 3,000 victims have been recognized as having Minamata disease, the result of the Chisso Corporation dumping 27 tons of mercury compounds into Minamata Bay, Japan from 1932 to 1968. Thousands of people whose normal diet included fish from the bay unexpectedly developed symptoms of methyl mercury poisoning. It is known that all forms of mercury are neurotoxic, especially during brain development [1,2].

By the mid-1950's, Minamata residents were diagnosed as having degeneration of their nervous systems. Numbness and other neuropathies occurred in their limbs and lips. Their speech became impeded and they experienced visual disturbances as well. Some lost consciousness while others developed extra pyramidal symptoms. Meanwhile, cats were committing suicide and birds dropped dead on the wing.

The Chisso Corporation denied all accusations that the mercury they were dumping was causing any illness and continued their pollution. By 1958, Chisso Corporation transferred their dumping from the Minamata Bay to the Minamata River in an inane attempt to mitigate the disaster they had created. The Minamata River flows past the town Hachimon, and into the Shiranui Sea, and the people of this area also began developing symptoms after a few months.

In July 1959, researchers from Kumamoto University concluded that organic mercury was the cause of the Minamata disease. A number of committees, of which Chisso Corporation employees were members, formed to research the problem. The committees denied this information and refuted the direct link of mercury to the brain damage, gross deformities, and death caused to the citizens of Minamata and Niigata. Chisso deliberately concealed their own research implicating mercury as the cause of the disease, and it was only a deathbed confession by one of Chisso's own researchers that led to a 1973 verdict against the corporation [3-5].

2. Autism

Autism was first described in 1943 in children born in the 1930s and has increased worldwide [6-9]. The increase of autism has been linked to the increase in mercury exposure through fish and industrial sources, amalgam[10] and additionally, through increased parenteral exposure to ethylmercurithiosalicate (Thimerosal), first introduced by Eli Lilly in the 1930s as a preservative in vaccinations [6,7,11]. In 1982, an expert panel at the FDA reviewed Thimerosal and called for its removal in over the counter products. The panel reported that Thimerosal was "toxic, caused cell damage, was not effective in killing bacteria or halting their replication" and that Thimerosal is "not generally recognized as being safe or effective" (1982 vol. 47, No. 2 Federal Register). In 1991, senior executives of Merck were concerned that infants were getting too much mercury. The March 1991 memo, obtained by the *Los Angeles Times* (February 8, 2005), said that six month old children who

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received shots on schedule would get a mercury dose 87 times higher than the maximum daily consumption guideline of mercury from fish—"the mercury load appears rather large," said the memo from Maurice R. Hilleman written to the president of Merck's vaccine division. "The key issue is whether Thimerosal, in the amount given with the vaccine, does or does not constitute a safety hazard." (He retired as a senior VP at Merck in 1984.)

In 1988, the FDA ruled that Thimerosal be removed from OTC products, but gave the industry another 16 years to phase out Thimerosal's presence. In 1999, the FDA stated that mercury exposure from vaccines exceeded Federal Safety Guidelines. On November 15, 1999 the FDA nominated Thimerosal to the Center for the Evaluation of Risks to Human Reproduction and on at least two occasions the core Scientific Advisory Board recommended further evaluation.

Also in 1999, the Public Health Service (PHS) and the American Academy of Pediatrics (AAP) first announced that Thimerosal should be removed from vaccines:*"…because any potential risk is of concern, the Public Health Service (PHS), the American Academy of Pediatrics (AAP), and vaccine manufacturers agree that Thimerosal-containing vaccines should be removed as soon as possible. Similar conclusions were reached this year in a meeting attended by European regulatory agencies, European vaccine manufacturers, and FDA, which examined the use of Thimerosal-containing vaccines produced or sold in European countries* [12]*."*

The prevalence of autism in the United States became epidemic (increase of 5 in 10,000 to 60 in 10,000) when additional Thimerosal-containing vaccines were introduced for newborns in the early 1990s (then, newborns up to the age of six months were regularly exposed to a cumulative Thimerosal dose of 187.5 μg) [13]. At the same time, most other countries, such as Germany and Denmark, where Thimerosal doses were reduced, reported a much lower autism prevalence. In California, for example, the autism rate increased by 634% between 1987 and 2002, which was not to be attributed to shifts in the interpretation of diagnostic criteria, migration of the population, improved diagnostic accuracies, or better reporting [8,9,14].

The study that concerned the CDC—Stajich GV, Lopez GP, Harry SW, Sexson WR. Iatrogenic exposure to mercury after hepatitis B vaccination in preterm infants. *J Pediatr* 2000 May;136(5):79–81—showed post-vaccination mercury levels were significantly higher in preterm infants as compared with term infants in regard to the Hepatitis B injections at birth. The concern did not appear to be about the impact mercury could have on newborns but on the impact it could have on the vaccination compliance rates. To mitigate any problems the Stajiich study might have, or if word leaked out about the then embargoed Verstraeten data [15] (showing a direct link between Thimerosal and the epidemic of neurodevelopmental disorders and discussed in detail below), the CDC contracted with Dr. Pichichero, a strong proponent of Thimerosal, to undertake a study similar to Dr. Stajich but produce different results.

The results of this alliance between the CDC/NIP officials and Pichichero, at the University of Rochester, resulted in what was hoped would be the definitive Thimerosal study [20] to prove that Thimerosal is not toxic in amounts found in childhood vaccines. A number of governmental (CDC, FDA, etc) committees, of which vaccine manufacturer employees were members, formed to review the problem as well [16]. Verstraeten (CDC/GlaxoSmithKline) diluted his original epidemiological study to show that there was no causation between Thimerosal and autism or any other neurodevelopmental problem [17]. Verstraeten published this article identifying himself as a CDC employee without divulging he was working for a major vaccine manufacturer. He diluted this data several times until all significance had vanished and then "lost" all the data so it could not be reviewed. Then, J. Codero, Assistant Surgeon General and Director of the National Center on Birth Defects and Developmental Disabilities, attached a cover to a manuscript that was eventually published as *Thimerosal and the occurrence of autism: negative ecological evidence from Danish population-based data* [18]. This Danish study, critiqued below, is also now known to have significant methodological flaws.

Between 1999 and 2000, several meetings were held to discuss the safety of the vaccines, especially in relationship to Thimerosal use, such as The National Vaccine Advisory Committee Sponsored Workshop on Thimerosal Vaccines held August 11, 1999 at Lister Hill Auditorium, Bethesda, MD, and the Simpsonwood Retreat [16]. The salient commonality at these meetings is the discussion about heavy metal toxicity sans any recognized experts in heavy metal toxicity. Dr. Martin Myers, Director of the National Vaccine Program Office, Department of Health and Human Services, stated, "Perhaps the most important thing that I took away from the last meeting (Lister Hill) was that those of us who deal with vaccines have really very little applicable background with metals and toxicological research (HHS, National Vaccine Program Office Workshop on Aluminum in Vaccines, May 11, 2000, San Juan, Puerto Rico)."

In 2001, the CDC and its Office of the NIP also contracted with the Institute of Medicine (IOM) to create the Immunization Safety Review Committee (ISRC) presumably for damage control against the mounting Thimerosal vaccine injury evidence (The transcripts of the IOM meetings are available online at *www.nomercury.org/iom.htm).* The IOM's first report on Thimerosal was issued in October of 2001 [19]. "(*The CDC) wants us to declare, well, these things are pretty safe on a population basis,"* stated Dr. Marie McCormick, Chairman of the ISRC. This committee met to address the question if exposure to Thimerosal-containing vaccines could be associated with adverse neurodevelopmental disorders, and the committee stated they found the hypothesis "biologically plausible." They had different marching orders despite being told, "*We said this before you got here, and I think we said this yesterday, the point of no return, the line we will not cross in public policy is to pull the vaccine, change the schedule. We could say it is time to revisit this, but we would never recommend that level. Even recommending research is recommendations for policy. We wouldn't say compensate, we wouldn't say pull the vaccine, we wouldn't say stop the program,*" by Kathleen Stratton, Ph.D., IOM staff and Study Director ISRC. "*We are not ever going to come down that it is a true side effect*," said McCormick even before the IOM had considered any evidence. Nevertheless, the IOM committee concluded, "*The committee recommends that full consideration be given by appropriate professional societies and governmental agencies to removing Thimerosal from*

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vaccines administered to infants, children, or pregnant women in the United States."

The CDC called the IOM committee to meet most recently in 2004 after it was made clear they would reach the unequivocal conclusion that there is no causality between vaccines and autism or any other neurological injury. The IOM would base its final conclusions on epidemiological research already proven to be flawed or fabricated [17,18,20]. The IOM ignored anything that was not aligned with its orders from the CDC; no evidence was embraced that was in conflict with that policy, and on May 18, 2004, the IOM's ISRC issued their final report which found the body of epidemiological evidence favors a rejection of a causal relationship between vaccine Thimerosal exposure and autism.

In the two years since it was issued, the IOM report has been successfully used to silence media inquires into vaccine safety, as a defense for ignoring 4,500 petitions for vaccine injuries in federal court, as justification for eliminating federal funding on research of the vaccine/autism link, and as justification for the federal preemption of vaccine control.

The FDA has never ordered recall of mercury-laden vaccines which continued to be used almost exclusively through 2002-2003. In 2005, when it appeared that autism rates were starting to decrease coincident with the removal of Thimerosal from the vaccines in the routine schedule [21], the CDC significantly broadened its flu-shot recommendations, so that by age 5 years, children exposed to an all-Thimerosal schedule of flu shots would get 53% of the mercury children received from all shots in 1999. If this was done on purpose, to obfuscate the falling autism rates, there was a reason.

The WHO Strategic Group of Experts (SAGE) met in June of 2001, and stated their objective clearly: "*WHO was extremely anxious to preserve the production of vaccines. Industry is expecting clear signals from WHO on the Thiomersal issue, and has been confirmed by informal consultations with some manufacturers during the first half of 2001."* At the WHO HQ in Geneva, a meeting was held on May 21 2002, "WHO informal meeting on removal of Thiomersal from vaccines and its implications for global vaccine supply." From the meeting summary more objectives were enumerated, such as: (1) Obtaining regulatory approval for the new formulated Thiomersal-reduced or removed vaccines involves complex activities that are costly and time consuming; (2) WHO is concerned about the current situation whereby manufacturers in developed countries have been forced to lower the Thiomersal content of their vaccines; (3) The option of using single dose vaccines is not feasible for WHO … upgrading the infrastructure would result in huge increase in vaccine cost. The meeting memo went on to state, "*In view of the situation, WHO is faced with…support maintenance of Thimerosal as an effective preservative in multidose and possibly also in single dose vaccines*." Lastly, the memo stated, "*The actions required from WHO in order to ensure continued availability of these vaccines include the following: …Develop a strong advocacy campaign to support ongoing use of Thimerosal."*

In other words, agencies outside of the USA, such as the WHO [22], the Global Alliance for Vaccines and Immunization (GAVI), and the International Brighton Collaboration seem to be having untoward influence on vaccine policy inside the U.S. This influence apparently brought the Thimerosal-laden flu vaccine into the routine vaccine schedule years after the AAP recommended the elimination of Thimerosal. Since WHO will not use any multidose vaccine that is not licensed in the USA, and it insists on using multi-dose vaccine, it therefore must keep the uses of Thimerosal vaccine viable in the USA. This problem would be solved if a vaccine maker substituted a non-Thimerosal preservative, but that would require them to submit a new drug application even though only the preservative has changed. The fee that must be paid to the FDA for each new application is in the millions. The solution would be to have Congress request that the FDA waive the fee if for the purpose of removing Thimerosal from a biologic/vaccine – this would be the logical approach – but obfuscation seems to rule the day. In the meantime, development (behavioral) disorders like attention deficit disorders (ADD) or attention deficit hyperactivity disorders (ADHD) have also increased up to 1 out of every 6 children in the United States [23].

3. Amalgam

In 1830, amalgam fillings were first used in the U.S. By 1840, organized dentistry denounced the use of amalgam as a poor filling material due to concerns about mercury poisoning. The American Society of Dental Surgeons was formed and required members to sign a pledge promising not to use mercury fillings. The American Dental Association was formed in 1859 by those dentists that supported the use of mercury amalgam as the filling material of choice, which it still does today. In 1926, a chemist, Dr. Alfred Stock, noted that mercury amalgam fillings in the mouth were a source of mercury vapor. Fifty years later, the FDA pronounced acceptance of amalgam fillings and "grandfathered" their approval under the G.R.A.S. (generally recognized as safe) category, due to its long-term usage and has never budged from that position.

That amalgam fillings are a source of mercury nephrotoxicity was demonstrated by Boyd *et al.* [24] in an animal model and by Mortada *et al.* [25] in 101 humans. Animal and in vitro studies have shown that exposure to inorganic and metallic mercury cause neuronal damage [26,27] and biochemical alterations (inclusive induction of β-amyloid) found in Alzheimer's disease [28-33], even at very low levels (where other metals like Al, Cd, Pb, Mn, Zn, Fe, Cr, Cu, were not able to cause this type of neuronal alterations). Mercury levels in human placentas correlate with the number of maternal amalgam fillings and a substantial amount of mercury from amalgam reaches the fetus [34.35].

Mercury from dental amalgam in pregnant women was reported by Holmes to contribute to the development of autism in their children [36]. In this study mothers of 94 autistic children had statistically more amalgam fillings during pregnancy than 49 mothers of normal controls. In contrast to their higher mercury exposure during pregnancy, these autistic children had reduced mercury levels in their first haircut reflecting a reduced capacity to excrete mercury from their body which in turn may lead to elevated brain mercury levels. It is interesting to compare this study to that of Grandjean *et al.* who found that infants who reached milestone criteria early had significantly higher mercury concentrations in the hair at 12 months of age [37].

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This is completely consistent with Holmes making it clear that the ability to excrete mercury (high hair levels of mercury) is neuroprotective, and an inability to excrete mercury (low hair levels) is not neuroprotective. The neurobehavioral effects resulting from exposure to low levels of mercury from dental amalgam have been described [38-42]. Low dose exposure to inorganic mercury may be a cofactor in the development of autoimmune diseases as well [43-49].

First and foremost, the Holmes findings have been duplicated by other research units, for example by Hu *et al.* [50]. Nevertheless, a certain faction has been keen to dismiss the Holmes study without offering data to contradict it. Conveniently, the CDC has, in effect, said it will not fund Thimerosal related research, based on the 2004 IOM recommendations, and threats have been received by those who hold and seek NIH grants to drop and have no further involvement in Thimerosal research.

While mercury levels in blood, urine and hair are definitely not a reliable measure of total mercury body burden or clinical symptoms, effective excretion of mercury will lead to higher hair, blood and urine mercury levels in a population that is being exposed to mercury at a constant, chronic, low level. Mercury must enter cells before it can be partly detoxified by formation of the glutathione–mercury–glutathione complex. It is this same glutathione–mercury–glutathione complex that is transported out of the cells into the blood, where it is excreted by the kidney or by the bilary transport system of the liver into the feces. It is also this complex of glutathione and mercury that is apparently taken up by hair follicles from the blood over a longer period of time, since hair levels represent an integral of blood mercury levels during hair growth time. Increased excretion from cells into the blood results in higher blood mercury levels and increased blood delivery to the hair follicle (and liver for detoxification). Similar observations are consistent with the fact that higher levels of hair and blood mercury seem to indicate better cellular excretion ability and therefore better health [37]. When considering a population with identical exposures to mercury, the relative increase of mercury in the hair, blood and urine of the subjects is an indicator of a better ability to excrete the mercury from intracellular compartments and body tissues rather than of an increased exposure. The point of contention is about those who lack the ability to effectively excrete mercury and are then exposed to a large dose.

Berlin suggested that the frequency of pathological side effects from amalgam due to a genetically determined susceptibility is about 1% [51]. The German Commission on Human Biological Monitoring states that genetically susceptible individuals may develop immune mediated responses to amalgam. The portion of persons in the general public is about 1 to 4% [52]. Richardson concludes that approximately 20% of the general public may experience subclinical central nervous system and/or kidney function impairment due to amalgam fillings [53].

4. Efficacy and Safety?

In the early 20th century, the epidemic of Acrodynia (Pink's Disease) affected up to 1 in 500 infants in some industrial countries until teething powders which contained mercury as Calomel (Hg_2Cl_2) was removed from the market. Calomel, when given orally, is about 100-fold less toxic than ethyl mercury to neurons in vitro [54] and works by poisoning the nerves in the baby's gums. In 1953, immunizations with Thimerosal containing vaccines preceded the onset of Acrodynia in several cases [55]. After that, Acrodynia fell below the clinicians' radar although it continued to affect children, but the often mild, self-limiting, exfoliating rash on the hands of children was not recognized as a reaction to mercury.

No controlled, randomized study regarding the safety of amalgam or Thimerosal exists, yet these exposures seem to be crucial in the pathogenesis of autism [36,56]. Furthermore, with the exception of Mortada [25] that evaluated nephrotoxicity, there are no studies comparing the health of individuals' pre/post exposure or exposure versus non-exposure. As with the adverse side effects of hormone replacement therapy, the lack of a prospective controlled, randomized study may lead to completely false conclusions. In Minamata, a single corporation was able to obfuscate the damage they were causing with mercury for decades, but the situation with the mercury in biologics is much more pernicious as the FDA, NIH, and CDC seem to have been unduly influenced by vaccine manufacturers or dental boards and even seem to share co-employees thereof [22,57-61].

Why have Thimerosal and dental amalgam, both of which consist of about 50% of the most toxic non-radioactive element known [10], been allowed to bypass toxicological testing? As with Thimerosal, the literature on amalgam toxicity [10,30,62,63] is used inappropriately to attest to its harmlessness [64-72]. Why is there so much effort being expended to keep mercury biologics in use?

5. The Biochemistry of Mercury Exposure

"There are just a host of neurodevelopmental data that would suggest that we've got a serious problem … To think there isn't some possible problem here is unreal." Bill Weil, M.D., pediatrician/nephrologist, representing American Academy of Pediatrics at the Simpsonwood meeting June 2000 [16].

Because of the apparent disinformation surrounding Thimerosal, it is worth noting what toxicologists have understood for the last two decades regarding *The comparative toxicology of ethyl and methyl mercury* [73], "*There was little difference in the neurotoxicities of methyl mercury and ethyl mercury when effects on the dorsal root ganglia or coordination disorders were compared," further "the neurological signs and symptoms of methyl and ethyl mercury intoxication are identical…"* A recent study, using infant Macaca fascicularis primates exposed to injected ethylmercury or those exposed to equal amounts of ingested methylmercury, showed that ethylmercuy was retained twice as much inorganic mercury in their brains in comparison to the methylmercury exposed primates [74]. These primates were exposed to mercury levels at a rate equal to what children in the United States received via standard childhood vaccines from 1991-2003.

The Environmental Protection Agency considers any material that has greater than 200 ppb of mercury to be hazardous waste. A Thimerosal vaccine (1:10000 Thimerosal) exceeds this value by 250 times or 50,000 ppb mercury. The developing

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fetus would receive a dose of mercury that exceeds the federal limits by several hundred-fold when the mother is injected with a Thimerosal-containing vaccine. Furthermore, fetal blood mercury concentrations have been shown to be as much as 4.4 times greater than in maternal blood (Methylmercury [MeHg] [CASRN 22967-92-6] www.epa.gov/iris/subst/0073.htm) which would result in an even greater relative distribution to the fetus. In other words, the developing fetus acts as a mercury sink for its mother.

Cysteine and glutathione synthesis are crucial for mercury detoxification, and are reduced in autistic children, possibly due to genetic polymorphisms [53,75]. Therefore, autistic children have 20% lower levels of cysteine and 54% lower levels of glutathione, which adversely affect their ability to detoxify and excrete metals like mercury [53,76]. This leads to a higher concentration of free mercury in blood, which then transfers into tissues and increases the half-life of mercury in the body, as compared to children with normal levels of cysteine and glutathione [54]. As was shown by Bradstreet *et al.* in a study involving 221 autistic children, vaccinated autistic children showed about 6 fold elevation of urinary mercury than normal controls after appropriate mobilization with the chelating agent DMSA [22,77].

Delayed detoxification of mercury severely impairs methylation reactions (required for the correct expression of DNA, RNA, and neurotransmitters), which further adversely affects growth factor derived development of the brain and attention abilities. Phospholipid methylation, which is crucial for attention, is impaired in autistic and attention deficit hyperactivity disorders [54]. Ethyl mercury levels, seen ten days after vaccination [20] with Thimerosal doses lower than what infants received during the 1990s, produced greater than 50% inhibition of methylation [22,75]. In vitro studies have shown that Thimerosal was more than 100-fold more potent than inorganic mercury in inhibiting such essential methylation reactions [74]. Inorganic mercury was found to be 10 fold more potent than lead in inhibition of neuronal microtubule [78,79].

Inorganic mercury also leads to growth inhibition and denudation of neuronal growth cones [27]. This was seen already 15 min. after exposure to very low levels of inorganic mercury, levels which were about 100 to 1000 fold lower than found in brains of individuals with dental amalgam or Alzheimer's disease [80]. It was also shown that concentrations of Thimerosal, which can occur after vaccination, induce membrane and DNA damage and initiate apoptosis in human neurons [81]. Genotoxic effects were also observed in another in vitro study [82].

Autistic children seem to be genetically more susceptible for toxin derived inhibition of methylation processes [54]. It has been estimated that up to 15% of the population may show enhanced susceptibility to mercury exposure [22].

Pichichero *et al.* argued that ethyl mercury administered through vaccines is eliminated rapidly from the blood and rapidly excreted in stool [20]. In this study, only 33 children at age of 2 and 6 month were used for blood mercury assessment only, thus overlooking individuals with impaired mercury excretion. Furthermore, blood levels were obtained days to weeks after vaccination, thus peak levels were not measured and the Thimerosal dose was much lower than that given via vaccination in the 1990s. Furthermore, the stool was not examined to determine if that was where the mercury ended up. Nevertheless, the authors concluded, "*This study gives comforting reassurance about the safety of ethyl mercury as a preservative in childhood vaccines*." This study has already been criticized including possible conflicts of interest [61,83].

Levels of ethyl mercury found eight days after vaccination leads to 50% inhibition of methionine synthase (MS) [54,75]. Compounding this toxic sequela of Thimerosal, neurons are unable to synthesize cysteine, the rate limiting amino acid for glutathione synthesis [84]. Thus, neurons are most sensitive to mercury toxicity since glutathione is the major intracellular agent in mercury and heavy metal detoxification. It is known that Thimerosal and inorganic mercury depletes intracellular glutathione levels, which subsequently leads to oxidative stress, neuronal cytotoxicity and death [31,32,84,85]. The toxic effects of ethyl mercury appear to be essentially identical to methyl mercury as indicated by James *et al.* [84].

6. Autoimmunity

Autoimmunity as a cause of autism, triggered by bacterial antigens, dietary peptides and mercury has been proposed [86] as has an increased risk of multiple sclerosis from Thimerosal-containing Hepatitis B vaccines [80]. Autopsied brains of autistic children demonstrated chronic activation of microglia and astrocytes indicative of an autoimmune process [88]. Mercury is a potent inducer of haptene mediated autoimmune reactions [10], especially when exposure is repetitive, which is the case in children exposed early to iatrogenic mercury during pregnancy (from amalgam) and than after birth in the form of vaccines. Most studies neglect the importance of repetitive mercury exposures for the induction of autoimmunity. In autoimmune sensitive mouse strains, vaccinations with Thimerosal in doses and timing equivalent to the pediatric immunization schedule of the U.S. in 2001 lead to profound behavioral and neuropathologic disturbances comparable to autism, and in another study the autoimmune reaction persists long after mercury can no longer be detected [89,90]. These reactions were noted despite Thimerosal doses lower than the ones given to newborns in the 1990s in the U.S. It was also shown that the risk of Thimerosal sensitization is increased in individuals with gene deletions of the glutathione S-transferases M1 and T1 [91]. Mercury also increases cytotoxicity of glutamate [80] which has been described in many neurodegenerative diseases.

In vitro studies suggest that the neurotoxicity of Thimerosal is enhanced through neomycin and aluminium hydroxide (ingredients in vaccines) and testosterone, while estrogen decreases the toxic effects [92]. Estrogen has been shown to decrease the toxicity of inorganic mercury [32] which may explain the 4 to 1 ratio of boys to girls in autism. Lead may play a synergistic pathogenetic role in neurodevelopment disorders and autism. Combination of lead and mercury resulted in an increase of toxicity in vitro [93].

7. Epidemiological Obfuscation

Epidemiological studies have been scientifically compromised; nevertheless, using data from the Vaccine Adverse

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Events Reporting System (VAERS), Vaccine Safety Data (VSD), Biological Surveillance Summaries of the CDC and the U.S. Department of Education datasets, a significant correlation was found between the risk of autism, mental retardation, speech disorders and heart disease and the cumulative Thimerosal dose given parenterally, which far exceeds (11 to 150 fold) the EPA and FDA established maximum permissible levels for the daily oral ingestion of methyl mercury [94-98]. After the publication of this data, access to the VSD was restricted for independent scientists [58].

In a first analysis of the VSD datasets, Verstraeten *et al.* [15] had described a 7.6 to 11.4 fold increase of autism risk in children at one month, with the highest mercury exposure levels compared to children with no exposure [58]. In four subsequent separate generations of the analysis, which involve the exclusion of children with no Thimerosal exposure and less than two polio vaccines, the statistical significance disappeared [17,58,98]. Verstraeten added in information from another HMO (Harvard Pilgrim) to dilute the significance of his original findings – referred to as Generation Zero. This HMO was in receivership by the state of Massachusetts because its records were in shambles and therefore virtually worthless except for the fact that by adding in the numbers from this HMO it statistically made the true data, from his Generation Zero analysis, disappear by rendering it all statistically insignificant.

While other studies that did not find an association between Thimerosal and autism in United Kingdom [99] or in Denmark [100-102], these studies did not use controls, or used children who were never exposed to mercury [103]. An example of an apparently insidious methodological flaw is where Madsen *et al.* compared the number of newly recorded autism cases prior to 1992, when Thimerosal-containing vaccines were used, with those after 1992, when such vaccines were no longer produced in Denmark [100]. The authors observed a rise in autism rates after removal of Thimerosal, and thus conclude that Thimerosal plays no role in the aetiology of autism. However, the autism rates used after 1994 included children from the entire population while prior to 1994 only included hospitalized autistic children, hence the reported increase in the number of autistic children.

Again, Madsen *et al.* reported Danish autism rates for children born in the 1990's of 5 per 10,000 [18]. These Danish rates are very low in the 1990's compared to the U.S. or the United Kingdom [13]. Madsen *et al.* report also inpatient rates for the pre-1993 "psychosis protoinfantilis" (the term used at that time for autism) at well below 1 per 10,000 [100]. This low rate would contradict the single published survey of autism rates from Denmark, which indicated an autism rate of over 4 per 10,000 as far back as the 1950's [104]. The rate of increase was elevated every time the Danes changed either the *in* versus *out* patients, the inclusion of a large Copenhagen clinic's data, and the change in the diagnostic criteria for autism.

Also, additional confounders were present in countries with high prevalence of autism that were not present in Denmark: During 1970-92, the only childhood vaccine given in Denmark until five months of age was the monovalent pertussis vaccine. In the United States, children were exposed to multiple doses of diphtheria, pertussis, tetanus, polio, hepatitis B and *haemophilus* influenza B (Hib) vaccines before five months of age in the 1990s. In the United Kingdom, injections before age five months included multiple doses of meningitis C, polio, diphtheria, tetanus, Hib, and pertussis vaccines. Denmark did not administer Thimerosal containing RhoD immunoglobulin during pregnancy [36]. Comparing the Danish autism rate with that of the USA rate is statistically invalid since the amount of Thimerosal exposure and the age of exposures of Danish infants and USA infants were vastly different. The Danish study is like studying the effect of mosquitoes on the spread of malaria but doing the study in Minnesota versus Panama.

The four published articles that are collectively known as the Danish Study [18,100-103] compromise a deliberate and coordinated effort to overshadow the emerging evidence connecting Thimerosal to autism by a single network of authors almost all beholden to a single employer. This coordination involved individuals as high as the Assistant Surgeon General as mentioned above. The four articles were based on a slightly different, but analytically non-comparable, view of the same overtly flawed data. The authors all had ties to a for-profit Danish vaccine manufacturer, the Statens Serum Institut (SSI), and this significant conflict of interest was not disclosed or reported in any of the journals that published the Danish study. CDC employees and consultants were 3 of the 17 authors. SSI directly employed 6 of the remaining 15 authors, and SSI, through the Danish Epidemiology Science Centre, indirectly employed the remaining authors. SSI has a direct financial interest in the assessment of past Thimerosal vaccine issues as well as in maintaining the continued viability of Thimerosal-laden vaccines. Their overshadowing of these studies and direct participation via SSI employees has compromised the integrity of all these articles.

8. Conclusion

In a real sense, this is a form of Minamata disease including analogous denials, deceptions, governmental-corporate collusion, lack of accountability, and the arrogant continued use of mercury-laden biologics. The FDA panel in 1982 said Thimerosal was "toxic, caused cell damage, was not effective in killing bacteria or halting their replication" and that Thimerosal is "not generally recognized as being safe or effective" (1982 Vol. 47, No. 2 Federal Register). Learning disabled and autistic children are living the burden of proof. So, what happened? Where is the precautionary principle? When something atrocious is done there always seems to be the justification that it is preventing something even more atrocious.

As the evidence continues to mount on what may be the largest iatrogenic public health disaster to affect this nation, so too does it appear that the apparent justification for deliberately letting this continue was about protecting the vaccine program's viability (or profitability). However, such rationalizations have propelled matters down a slippery slope. What little altruism there is in this justification belies individuals protecting careers, status and reputations. This disaster did not come out of nowhere, and ultimately it will be found that it could have been mitigated if not for the irresponsible use of power and influence by an unholy alliance between corporation and state. It also calls into question whether this public health fiasco was an isolated scenario.

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Mercury in biologics is a clear and present danger to the public health, and the only sane thing to do is end the obfuscation of an issue that may literally be destroying our society. Thimerosal has been banned in virtually all first world countries, while the Autism pandemic continues in the United States unabated with the hope of mercury free childhood vaccines dashed with the introduction of the flu vaccine into the routine infant immunization schedule. Of course, this will have a cost just as the Roman Empire was destroyed by the untoward effects of lead plumbing, lead used in wine and a runaway malaria epidemic, so too will a country of jobless and dependent learning disabled and autistic children change the United States as we know it. Fifteen years from now the United States may no longer be a first world country because of this.

On May 20, 2004, the Office of Special Counsel (OSC) forwarded to Congress hundreds of disclosures relating to the link between Thimerosal and autism. But the OSC requires a federal employee, specifically one from within the FDA or CDC, to come forward and whistleblow. The OSC would then have jurisdiction in this matter. "I believe these allegations raise serious continuing concerns about the administration of the nation's vaccine program and the government's possibly inadequate response to the growing body of scientific research on the public health danger of mercury in vaccines…(but) because OSC lacks jurisdiction, we are closing our files on these cases…. sincerely (Special Counsel) SJ Bloch."

Who does have jurisdiction? The justice department has jurisdiction, but they have been recruited to defend HHS against any vaccine injury claim even though the vaccine injury compensation program was intended to be no-fault. Over the years, HHS has systematically eliminated any vaccine injury category for which a child could seek compensation. It is now virtually impossible for a child to receive compensation for a vaccine injury. Every time HHS paid out a claim, the condition that allowed that injured child to tap into the compensation program was eliminated as being a compensatable condition for subsequent claimants.

It is an ironic reality that we now live in where the dissemination of a known poison and the disinformation surrounding it is being used against us as if we were the enemies in some military campaign to benefit who? This goes beyond just individuals that do not want to lose their jobs or accept culpability that might injure their careers. Removing Thimerosal out of vaccines does not destroy the vaccination program, but it does require the infrastructure to change, and there are organizations that simply do not want that change to take place, so they are making sure it is being added back into the vaccine schedule in the form of the flu vaccine.

Disinformation surrounding this issue is as much a danger as the mercury, but where there is danger there is also opportunity; however, the public can only perceive what is shown to them. So, more galling than anything has been the effort to keep the public from knowing, and the intimidation of many to violate the public trust. Regrettably it seems, we have entrusted the public safety to others whose conscious awareness of the common well-being often fades in the face of compromising interests. This is illogical for these individuals have put these interests above children and grandchildren, except for those like Dr. Johnston who was clear about protecting his own family. Dick Johnston, M.D., University of Colorado School of Medicine and National Jewish Center was Chairman of the Simpsonwood meeting [16] that met in June of 2000 to review Verstraeten's Phase One/Generation Zero data and this is what he said at this meeting (page 198), "*Forgive this personal comment, but I got called out at eight o'clock for an emergency call and my daughter-in-law delivered a son by C-section. Our first male in the line of the next generation, and* ***I do not want that grandson to get a Thimerosal-containing vaccine until we know better what is going on.*** *It will probably take a long time. In the meantime, and I know there are probably implications for this internationally, but in the meantime I think I want that grandson to only be given Thimerosal-free vaccines."*

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