

Scientific Papers Showing Linking Thimerosal Exposure to Autism

September 10, 2015

Brian S. Hooker, Ph.D., P.E.

1. Rose et al. 2015 J Toxicol "Increased Susceptibility to Ethylmercury-Induced Mitochondrial Dysfunction in a Subset of Autism Lymphoblastoid Cell Lines" PMID 25688267.

In a comparison of lymphoblast cells from children with autism and matched non-autistic controls, a significantly higher number of "autistic" cell lines showed a reduction in ATP-linked respiration, maximal respiratory capacity and reserve capacity when exposed to mercury as compared to control cell lines. This supports the notion that a subset of individuals with autism may be vulnerable to mitochondrial dysfunction via thimerosal exposure.

2. Geier et al. 2015 Clin Chim Acta "Thimerosal: Clinical, Epidemiologic and Biochemical Studies," PMID 25708367.

This review article includes a section on numerous papers linking thimerosal exposure via infant vaccines to autism. This also includes a critique of studies from the U.S. Centers for Disease Control that deny any type of link.

3. Yassa 2014 Environ Toxicol Pharmacol "Autism: A Form of Mercury and Lead Toxicity" PMID 25461563.

Blood levels of mercury and lead were much higher in autistic children as compared to normal controls. Upon chelation, the blood levels of these heavy metals decreased and autistic symptoms improved.

4. Hooker et al. 2014 BioMed Research International, "Methodological Issues and Evidence of Malfeasance In Research Purporting to Show that Thimerosal-Containing Vaccines are Safe" PMID 24995277.

This review article shows methodological flaws in six separate CDC studies claiming that thimerosal does not cause autism. In three specific instances (Madsen et al. 2003, Verstraeten et al. 2003 and Price et al. 2010) evidence of malfeasance on the part of CDC scientists is shown. Background data (not reported in print) from these three publications suggest a strong link between thimerosal exposure and autism.

5. Geier et al. 2014 J Biochem Pharmacol Res "The risk of neurodevelopmental disorders following a Thimerosal-preserved DTaP formulation in comparison to its Thimerosal-reduced formulation in the vaccine adverse event reporting system (VAERS)" 2:64.

A comparison of autism reports from thimerosal-containing versus thimerosal free DTaP formulations showed a relative risk of 7.67 for autism when children were exposed to thimerosal via the DTaP vaccine.

6. Koh et al. 2014 Mol Brain, "Abnormalities in the zinc-metalloprotease-BDNF axis may contribute to megalencephaly and cortical hyperconnectivity in young autism spectrum disorder patients" PMID 25182223.

This protein (zinc-metalloprotease-BDNF) is upregulated by the presence of organic mercurials including thimerosal and it is responsible for large brains (megalencephaly) and cortical hyperconnectivity in children with autism.

7. Geier et al. 2013 Translational Neurodegeneration, "A two-phase study evaluating the relationship between Thimerosal-containing vaccine administration and the risk for an autism spectrum disorder diagnosis in the United States" PMID 24354891.

This study included a comparison of VAERS (Vaccine Adverse Event Reporting System) reports of autism following DTaP (Thimerosal containing and Thimerosal free). In addition the link between thimerosal containing HepB vaccine administration and autism was elucidated with a dose-dependent effect, using the CDC's Vaccine Safety Datalink.

8. Gorrindo et al. 2013 PLOS One "Enrichment of Elevated Plasma F_{2t}-Isoprostane Levels in Individuals with Autism Who Are Stratified by Presence of Gastrointestinal Dysfunction" DOI: 10.1371.

This paper showed significant levels of oxidative stress in children with autism with comorbid gastrointestinal problems. Thimerosal as well as vaccines in general contributes markedly to the amount of oxidative stress sustained physiologically.

9. Gronborg et al. 2013 JAMA Pediatrics, "Recurrence of Autism Spectrum Disorders in Full and Half-Siblings and Trends over Time A Population-Based Cohort Study" doi10.1001jamapediatrics.2013.2259.

This publication shows that ASD prevalence rates in Denmark decreased by 30% of the time period from 1994 to 2004 after Denmark removed thimerosal from their vaccines in 1992. This is directly counter to the fraudulent CDC Madsen et al. 2003 publication.

10. Sharpe et al. 2013 J Toxicol "B-lymphocytes from a population of children with autism spectrum disorder and their unaffected siblings exhibit hypersensitivity to thimerosal" PMID 23843785.

This paper shows that peripheral blood lymphocytes specific to antibody based immunity, from autistic subjects and their unaffected siblings, were much more sensitivity and exhibited higher rates of cell death than those of unaffected, unrelated control children. Thimerosal levels required to kill the cells from the subjects were less than 40% of those required to kill the cells of unrelated, non-autistic controls.

11. Duszczyk-Budhathoki et al. 2012 Neurochem Res “Administration of thimerosal to infant rats increases overflow of glutamate and aspartate in the prefrontal cortex: protective role of dehydroepiandrosterone sulfate” PMID 22015977.

The study authors determined that since excessive accumulation of extracellular glutamate is linked with excitotoxicity, data implies that neonatal exposure to thimerosal-containing vaccines might induce excitotoxic brain injuries, leading to neurodevelopmental disorders.

12. Li et al. 2012 PLoS One “Thimerosal-induced apoptosis in mouse C2C12 myoblast cells occurs through suppression of the PI3K/Akt/survivin pathway” PMID 23145070.

The study authors demonstrated cell death by low levels of thimerosal exposure, via a mitochondrial pathway. Study data revealed that cytochrome c leaked from the mitochondria and that caspase 9 and 3 were activated, causing apoptosis.

13. Kern et al. 2012 Acta Neurobiol Exp (Wars) “Evidence of parallels between mercury intoxication and the brain pathology in autism” PMID 22810216.

The study authors discuss 20 specific similarities between mercury intoxication and autism brain pathologies. The evidence suggests that mercury might be causal or contributory in the brain pathology of autism, with a possibility of working with other toxins or pathogens.

14. Sharpe et al. 2012 J Toxicol “Thimerosal-Derived Ethylmercury Is a Mitochondrial Toxin in Human Astrocytes: Possible Role of Fenton Chemistry in the Oxidation and Breakage of mtDNA” PMID 22811707.

Thimerosal significantly damaged the mitochondrial membranes and DNA in human astrocytes (which are also implicated in autism spectrum disorder). The enzyme caspase-3, which signals cell death was upregulated by 5 times in the presence of thimerosal and mitochondrial membranes showed significant depolarization.

15. Sulkowski et al. 2012 Cerebellum “Maternal thimerosal exposure results in aberrant cerebellar oxidative stress, thyroid hormone metabolism, and motor behavior in rat pups; sex- and strain-dependent effects” PMID 22015705.

Rat pups were exposed to thimerosal levels in utero (similar to the maternal flu shot) and exhibited aberrant brain oxidative stress (in the cerebellum) as well as autistic like behaviors. These effects were reserved primarily to males in the “Spontaneously Hypersensitive Rat” strain.

16. Garrecht et al. 2011 Toxicol Environ Chem “The plausibility of a role for mercury in the etiology of autism: a cellular perspective” PMID 22163375.

Key areas of focus include: (1) route and cellular mechanisms of Hg exposure in autism; (2) current research and examples of possible genetic variables that are linked to both Hg sensitivity and autism; (3) the role Hg may play as an environmental toxin fueling the oxidative stress found in autism; (4) role of mitochondrial dysfunction; and (5) possible role of Hg in abnormal neuroexcitatory and excitotoxicity that may play a role in the immune dysregulation found in autism.

17. Kern et al. 2011 *Toxicol Environ Chem* "Toxicity biomarkers among US children compared to a similar cohort in France: a blinded study measuring urinary porphyrins" PMID 24482554

This age and gender matched cohort study of 28 autism cases and 28 controls showed significantly higher urinary porphyrin levels in children with autism, specifically in those porphyrins (hexacarboxyporphyrin and precoproporphyrin) associated with mercury toxicity.

18. Gallagher et al. 2010 *J Toxicol Env Health A* "Hepatitis B vaccination of male neonates and autism diagnosis, NHIS 1997-2002" PMID 21058170.

The study authors investigated the National Health Inventory Survey (a very large national database) and found that boys receiving the full HepB series were 3 times as likely to receive an autism diagnosis as compared to those not receiving any HepB vaccine (statistically significant). Non-white boys had a significantly worse outcome.

19. Kern et al. 2010 *Acta Neurobiol Exp (Wars)* "Evidence of parallels between mercury intoxication and the brain pathology in autism" PMID 20628444.

The study authors explain parallels between autism spectrum disorder and mercury toxicity, including sexual dimorphism, neuronal cell migration and division, and cell death. Also, reports of regression into autism spectrum disorder are reported after significant mercury exposures.

20. Minami et al. 2010 *Cell Biol Toxicol* "Induction of metallothionein in mouse cerebellum and cerebrum with low-dose thimerosal injection" PMID 19357975.

The study authors determined that in combination with the brain pathology observed in patients diagnosed with autism, the present study helps to support the possible biological plausibility for how low-dose exposure to mercury from thimerosal-containing vaccines may be associated with autism.

21. Geier et al. 2009 *J Neurol Sci* "Biomarkers of environmental toxicity and susceptibility in autism" PMID 18817931.

Mercury toxicity was assessed in a cohort of 28 children with autism. The cohort showed significantly higher levels of urinary porphyrins associated with mercury toxicity as well as decreased plasma levels of reduced glutathione, cysteine and sulfate, also indicating active mercury toxicity and an inability to detoxify heavy metals.

22. Geier et al. 2009 *Toxicol Environ Chem* "Mitochondrial dysfunction, impaired oxidative-reduction activity, degeneration, and death in human neuronal and fetal cells induced by low-level exposure to Thimerosal and other metal compounds" PMID 24538666.

Three types of human cell lines were subjected to increasing concentrations of thimerosal, along with other toxic metal compounds. Thimerosal exhibited the greatest toxicity in each of the cell lines tested and the damage was similar to that observed in autism pathophysiologic studies.

23. Adams et al. 2009 *J Toxicol* "The severity of autism is associated with toxic metal body burden and red blood cell glutathione levels" PMID 20107587.

This study focused on correlations between overall body burden of toxic metals, including mercury, and the severity of autistic disorder. Higher body burden associated strongly with more severe autistic disorder as did low red blood cell levels of glutathione.

24. Geier et al. 2009 *Neurochem Res* "A prospective study of transsulfuration biomarkers in autistic disorders" PMID 16812812.

This study focuses on biomarkers associated with mercury detoxification, where autistic patients showed metabolic profiles consistent with increased oxidative stress and decreased detoxification capacity as compared to matched controls.

25. Young et al. 2008 *J Neurol Sci* "Thimerosal exposure in infants and neurodevelopmental disorders: an assessment of computerized medical records in the Vaccine Safety Datalink" PMID 18482737.

The study authors determined that significantly increased risk ratios were observed for autism and autism spectrum disorders as a result of exposure to mercury from Thimerosal-containing vaccines using the CDC's Vaccine Safety Datalink.

26. Geier et al. 2008 *Neuro Endocrinol Lett* "Neurodevelopmental disorders, maternal Rh-negativity, and Rho(D) immune globulins: a multi-center assessment" PMID 18404135.

Mothers receiving thimerosal via Rho(D) immune globulin injection saw a significantly higher rate of autism in the children exposed to mercury in utero. Overall, twice as much autism was seen in the exposed group of children versus the non-exposed control group.

27. Deth et al. 2008 *Neurotoxicol* "How environmental and genetic factors combine to cause autism: A redox/methylation hypothesis" PMID 18031821.

This paper explains how deficits in sulfur metabolism along with toxic heavy metals exposure could lead to autistic disorder. It also points out that genetic polymorphisms in sulfur metabolism are more frequent in autistic patients.

28. Wu et al. 2008 Chem Res Toxicol "Thiol-modulated mechanisms of the cytotoxicity of thimerosal and inhibition of DNA topoisomerase II alpha" PMID 18197631.

This paper showed how high levels of glutathione are protective against specific mechanisms related to thimerosal toxicity. It should be noted that autism is associated with lower levels of plasma glutathione.

29. Adams et al. 2007 J Tox Environ Health A "Mercury, lead, and zinc in baby teeth of children with autism versus controls" PMID 17497416

Children with autism showed significantly higher levels of mercury in their baby teeth than non-autistic controls, indicated marked exposure to mercury during gestation and early infancy.

30. Geier et al. 2007 J Matern Fetal Neonatal Med "A prospective study of thimerosal-containing Rho(D)-immune globulin administration as a risk factor for autistic disorders" PMID 17674242.

Children with autism were twice as likely as non-autistic controls to be born from mothers who had Rh incompatibilities with the developing fetus during pregnancy and thus were exposed to thimerosal via Rho(D) immune globulin injections during pregnancy.

31. Geier et al. 2007 J Toxicol Env Health A "A case series of children with apparent mercury toxic encephalopathies manifesting with clinical symptoms of regressive autistic disorders" PMID 17454560.

This case series of eight autistic patients showed a history of excretion of significant amounts of mercury post chelation challenge, biochemical evidence of decreased function in their glutathione pathways and had no known significant mercury exposure except from Thimerosal-containing vaccines/Rho(D)-immune globulin preparations; and had alternate causes for their regressive ASDs ruled out.

32. Desoto et al. 2007 J Child Neurol "Blood Levels of Mercury Are Related to Diagnosis of Autism: A Reanalysis of an Important Data Set" 22:1308.

This study is a correction to a previous study that claimed mercury levels in children's blood did not correlate with the presence of autism. In this reanalysis, Desoto shows clearly that a statistically significant link appears between blood mercury levels and autistic disorder in children.

33. Geier et al. 2006 J Toxicol Env Health A "An evaluation of the effects of thimerosal on neurodevelopmental disorders reported following DTP and Hib vaccines in comparison to DTPH vaccine in the United States" PMID 16766480.

This study shows significantly increased risk ratios for autism, speech disorders, mental retardation, infantile spasms, and thinking abnormalities reported to VAERS found following

thimerosal-containing DTP vaccines in comparison to thimerosal-free DTPH vaccines, with minimal bias or systematic error.

34. Nataf et al. 2006 *Toxicol Appl Pharmacol* "Porphyrinuria in childhood autistic disorder: implications for environmental toxicity" PMID 16782144

Children with autism showed statistically elevated levels of urinary porphyrins that specifically show mercury toxicity due to environmental exposure. This was a large study of 106 children with autism compared to children with Asperger's and control children. Neither the Asperger's or control group showed elevations in urinary porphyrin levels.

35. Herdman et al. 2006 *Toxicol Sci* "Thimerosal induces apoptosis in a neuroblastoma model via the cJun N-terminal kinase pathway" PMID 16624850.

Human neuroblastoma cells in culture were treated with thimerosal, leading to cell death within a 4 hour time period. This type of programmed cell death is mediated by the cJun protein.

36. Maya et al. 2006 *Ann Fac Med (Lima)* "Thimerosal and children's neurodevelopmental disorders" 67(3):243 [Spanish].

This review article cites epidemiological, ecological, biomolecular, toxicology, biosecurity, fetal toxicology and reproductive health studies that signal the possible causal association of thimerosal exposition and neurodevelopmental disorders in children.

37. Herbert 2005 *Neuroscientist* "Large brains in autism: the challenge of pervasive abnormality" PMID 16151044.

The author of this study links large brain size with neuroinflammation associated with toxic heavy metal exposure. The author posits that this type of inflammation could be treatable and increase the success of medical interventions for autism.

38. Burbacher et al. 2005 *Environ Health Perspect* "Comparison of blood and brain mercury levels in infant monkeys exposed to methylmercury or vaccines containing thimerosal" PMID 16079072.

Infant macaques retained significantly higher levels of elemental mercury in their brain tissue when exposed to thimerosal in infant vaccines versus methylmercury. The half-life of the mercury associated with thimerosal exposure was indefinite as it lasted much longer than the overall testing period.

39. Yel et al. 2005 *Int J Mol Med* "Thimerosal induces neuronal cell apoptosis by causing cytochrome c and apoptosis-inducing factor release from mitochondria" PMID 16273274

Thimerosal at levels comparable to infant exposure via vaccines caused neuronal cell death through changing the mitochondrial microenvironment. Thimerosal induced cell death was

associated with mitochondrial depolarization and a significant level of reactive oxidative stress intracellularly.

40. Humphrey et al. 2005 Neuro Toxicol "Mitochondrial mediated Thimerosal-induced apoptosis in a human neuroblastoma cell line (SK-N-SH)" PMID 15869795.

The study authors report a mechanism for human cell apoptosis via accumulation of organic and inorganic mercury in the mitochondria. This was followed by cytochrome c leakage from the mitochondria and caspase 9 activation, which induces mitochondrial depolarization.

41. James et al. 2005 Neurotoxicol "Thimerosal neurotoxicity is associated with glutathione depletion: protection with glutathione precursors" PMID 15527868.

This study investigated the cellular response to thimerosal toxicity including a very profound decrease in intracellular glutathione levels. Earlier research by this same author showed that autistic children had significantly lower glutathione levels as compared to neurotypical control children.

42. Parran et al. 2005 Toxicol Sci "Effects of Thimerosal on NGF signal transduction and cell death in neuroblastoma cells" PMID 15843506.

Thimerosal exposure caused programmed cell death (apoptosis) in neuroblastoma cells. At 48 hours incubation, concentrations of thimerosal typical of those present in the blood stream after vaccination caused neuronal death.

43. James et al. 2004 Am J Clinical Nutrition "Metabolic biomarkers of increased oxidative stress and impaired methylation capacity in children with autism" 80:1611.

Children with autism have a diminished methylation capacity leading to higher sustained levels of oxidation stress, due to deficiencies primarily in glutathione. Vaccines produce a very high level of oxidation stress to the body upon administration.

44. Waly et al. 2004 Mol Psychiatr "Activation of methionine synthase by insulin-like growth factor-1 and dopamine: a target for neurodevelopmental toxins and thimerosal" PMID 14745455.

This study shows that a novel growth factor signalling pathway regulates methionine synthase(MS) activity and thereby modulates methylation reactions. The potent inhibition of this pathway by ethanol, lead, mercury, aluminum and thimerosal suggests that it may be an important target of neurodevelopmental toxins.

45. Hornig et al. 2004 Mol Psychiatr "Neurotoxic effects of postnatal thimerosal are mouse strain dependent" PMID 15184908.

Specific mouse strains showing autoimmune disease sensitivity exhibited autistic behaviors and autistic-like brain pathologies after being exposed to thimerosal. Normal strains of mice

did not exhibit these behaviors or neurological features.

46. Juul-Dam et al. 2003 Pediatrics "Prenatal, perinatal and neonatal factors in autism, pervasive development disorder-not otherwise specified, and the general population" PMID 11335784.

This paper shows that mothers of children with autism had a statistically significant greater level of Rh-factor disease than mothers in the general population. Rh-factor disease is an indicator of thimerosal exposure as, at the time, all available anti-Rho IgG (therapeutic drug for Rh-factor disease) doses given to these mothers contained at least 12.5 micrograms of mercury via thimerosal.

47. Holmes et al. 2003 Int J Toxicol "Reduced levels of mercury in first baby haircuts of autistic children" PMID 12933322.

This study shows that autistic children are poor secreters of mercury via hair, which a normal physiological mode of mercury detoxification. Thus, autistic children subjected to mercury exposure would likely experience a longer, sustained toxicological effect.

48. Baskin et al. 2003 Toxicol Sci "Thimerosal induces DNA breaks, caspase-3 activation, membrane damage, and cell death in cultured human neurons and fibroblasts" PMID 12773768.

The study authors show that thimerosal exposure at micromolar levels initiates a cascade of events leading to cell death in human neurons and fibroblasts. Cell death is preceded by DNA breakage, caspase-3 activation and mitochondrial membrane depolarization.

49. Aschner et al. 2002 Mol Psychiatr "The neuropathogenesis of mercury toxicity" PMID 12142946.

The study elucidates "little" difference between methylmercury and ethylmercury (breakdown product of Thimerosal) toxicity to cells counter to CDC sponsored studies that declared that ethylmercury was "safe mercury."

50. Makani et al. 2002 Genes Immun "Biochemical and molecular basis of thimerosal-induced apoptosis in T cells: a major role of mitochondrial pathway" PMID 12140745

This study shows that thimerosal causes cell death in T lymphocytes (immune cells) via a mitochondrial depolarization mechanism.

51. Bernard et al. 2002 Mol Psychiatr "The Role of Mercury in the Pathogenesis of Autism" PMID 12142947.

This paper links thimerosal exposure via infant vaccines to autism based on the pathologies associated with autism as well as the timing of autistic regression. Emphasis is made on the total mercury exposure to infants in the vaccination schedule used in the 1990's and early 2000's.

52. Bernard et al. 2001 Med Hypotheses "Autism: A Novel Form of Mercury Poisoning" PMID 11339848.

Parallels are made between the signs and symptoms of mercury poisoning and infantile autism. A comprehensive analysis is included on the comorbidities of autism and their corresponding analogs due to mercury exposure.

53. Verstraeten et al. 1999 Internal CDC Abstract for the Epidemic Intelligence Service Meeting of 2000 "Increased risk of developmental neurologic impairment after high exposure to thimerosal-containing vaccine in first month of life."

This original version of the Verstraeten et al. paper (that was ultimately "watered down" before it was published in final form in 2003) shows risks of autism at 7.6-fold for children exposed to thimerosal in the first month of life compared to unexposed controls.