From Epidemiology, Clinical Medicine, Molecular Biology, and Atoms, to Politics:

A Review of the Relationship between Thimerosal and Autism

by

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Autism Epidemic Evidence

Publications I:

- California Department of Developmental Services. Autistic spectrum disorders: Changes in the California caseload an update: 1999 through 2002. Sacramento, CA: California Health & Human Services Agency, 2003.
- Blaxill MF, Baskin DS, Spitzer WO. Commentary: Blaxill, Baskin, and Spitzer on Croen et al. (2002), the changing prevalence of autism in California. J Autism & Dev Dis 2003;33:223-226.
- Yeargin-Allsopp M, Rice C, Karapurkar T, et al. Prevalence of autism in a US metropolitan area. JAMA 2003;49-55.
- Bertrand J, Mars A, Boyle C, et al. Prevalence of autism in a United States population: The Brick Township, New Jersey, investigation. Pediatrics 2001;108:1155-1161.
- Geier MR, Geier DA. Response to critics on the adverse effects of thimerosal in childhood vaccines. J Am Phys Surg 2003;8:68070.
- Yazbak FE. Autism in the United States: A perspective. J Am Phys Surg 2003;4:103-107.

Statements I:

California Department of Developmental Services reported that since the 1980s, California has experienced dramatic increased in the number of children diagnosed with autism. Autism, once a rare disorder, was found to be more prevalent than childhood cancer, diabetes, and Downs' Syndrome. Between 1987 and December 2002, the population of persons with autism increased by 634 percent. In examining potential biases or confounders resulting in the increased prevalence of autism in the state of California, it was observed that population migrations, shifts in the interpretation of diagnostic criteria, or differences in diagnostic accuracy had limited affects on the increasing prevalence of autism. The authors concluded that the increased prevalence of autism in California was a genuine phenomenon.


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SIGMA
Thimerosal
(Mercury-[(o-carb
SigmaUltra
Minimum 97% (H
Light sensitive
Store at room
temperature
Very toxic
Sehr giftig
Très
toxique
Muy tóxico
Molto
tossico
Zeer
vergiftig
SIGMA-ALDRICH CO

Thimerosal & Vaccines: Background Information I

- **Thimerosal is an organic mercury compound that is metabolized to ethylmercury and thiosalicylate and has been present since the 1930s as a preservative in some vaccines and pharmaceutical products to prevent bacterial and fungal contamination.**

- **The FDA in 1999, under the recommended childhood immunization schedule, determined infants might be exposed to cumulative doses of ethylmercury that exceed some federal safety guidelines established for exposure to methylmercury, another form of organic mercury.**

Thimerosal & Vaccines: Background Information II
(Institute of Medicine 2001)

- **The relationship between thimerosal from vaccines and neurodevelopmental disorders is biologically possible**

Biological Plausibility Evidence

Theoretical

Publications I:

- Bernard S, Enayati A, Redwood L, et al. Autism: A novel form of mercury poising. Med Hypothesis 2001;56:462-471.
- Ball LK, Ball R, Pratt RD. An assessment of thimerosal use in childhood vaccines. Pediatrics 2001;107:1147-1154.
- Bernard S, Enayati A, Roger H, et al. The role of mercury in the pathogenesis of autism. Mol Pschiatry 2002;7:S42-S43.
- National Toxicology Program. Chemical Repository – Statement on Thimerosal.
- Stecher PH (ed). The Merck Index: An Encyclopedia of Chemicals and Drugs, 8th Edition. Rahway NJ: Merck & Co, Inc., 1968, pg. 438.
- Redwood L, Bernard S, Brown D. Predicted mercury concentrations in hair from infant immunizations: Cause for concern. Neurotoxicology 2001;22:691-697.

Publications II:

- Geier MR, Geier DA. Thimerosal in childhood vaccines, neurodevelopment disorders, and heart disease in the United States. J Am Phys Surg 2003;8:6-11.

- Geier DA, Geier MR. An assessment of the impact of thimerosal in childhood neurodevelopmental disorders. Pediatr Rehabil 2003;6:97-102.

- Rohyans J, Walson PD, Wood GA, et al. Mercury toxicity following merthilate ear irregations. J Pediatrics 1984;104:311-313.

- Stetler HC, Garbe PL, Dwyer DM, et al. Outbreaks of Group A Streptococcal abscesses following Diphtheria-Tetanus-Toxoid-Pertussis vaccination. Pediatrics 1985;75:299-303.

Statements I:

Bernard et al. have compared the similar biological abnormalities commonly found in autism and the corresponding pathologies arising from mercury exposure. Distinct similarities were found between autism and mercury exposure in their effects upon biochemistry, the immune system, the central nervous system structure, neuro-chemistry and neurophysiology.

Geier and Geier have evaluated the instantaneous exposure of children to mercury from thimerosal-containing childhood vaccines administered as part of the routine childhood immunization schedule and determined that in some cases children were exposed to more than 100-fold in excess of the Federal Safety Guidelines for exposure to orally ingested methylmercury.

Statements II:

The National Toxicology Program (NTP), U.S. Department of Health and Human Services, National Institutes of Health's National Institute of Environmental Health Sciences (NIEHS) Statement on Thimerosal states that thimerosal is a Poison by ingestion, subcutaneous, intravenous and possibly other routes. An experimental neoplastigen and teratogen. Experimental reproductive effects. They report that among the symptoms of thimerosal exposure include mental retardation in children, loss of coordination in speech, writing, and gait, stupor, and irritability and bad temper progressing to mania.

Stetler et al. from the Centers for Disease Control and Prevention have evaluated higher concentrations of mercury than those present in a single dose of whole-cell Diphtheria-Tetanus-Pertussis (DTP) vaccine (i.e. 25 micrograms of mercury per dose). They concluded that they had serious reservations about administering higher doses of mercury from thimerosal-containing childhood vaccines because of, "the need to assure safety of the preservative."

Demonstrated

Publications I:

- Warkany J, Hubbard DM. Acrodynia and mercury. J Pediatr 1953;42:365-386.
- Derban LKA. Outbreak of food poisoning due to alkyl-mercury fungicide. Arch Environ Health 1974;28:49-52.
- Cinca I, Dumitrescu I, Onaca P, et al. Accidental ethyl mercury poisoning with nervous system, skeletal muscle, and myocardium injury. J Neurology, Neruosurgery, Psychiatry 1979;43:143-149.
- Pfab R, Muckter H, Roider G, et al. Clinical course of severe poisoning with thiomersal. Clin Toxicology 1996;34:453-460.
- Lowell J, Burgess S, Shenoy S, et al. Mercury poisoning associated with hepatitis B immunoglobulin. Lancet 1996;347:480.
- Axton JHM. Six cases of poisoning after a parenteral organic mercurial compound (Merthiolate). Postgraduate Medical Journal 1972;48:417-421.

Publications II:

- Zhang J. Clinical observations in ethyl mercury chloride poisoning. Am J Ind Med 1984;5:251-258.
- Kiffe M, Christen P, Arni P. Characterization of cytotoxic and genotoxic effects of different compounds in CHO K5 cells with the comet assay (single-cell gel electrophoresis assay). Mutation Research 2003;537:151-168.
- Takahashi N. Cytotoxicity of mercurial preservatives in cell culture. Ophthalmic Research 1982;14:63-69.
- Mukai N. An experimental study of alkylmercurial encephalopathy. Acta neuropathy (Berl.) 1972;22:102-109.
- Uchida T, Naito S, Kato-Hiroshi, et al. Thimerosal induces toxic reaction in non-sensitized animals. Int Arch Allergy Immunol 1994;104:296-301.
- Nelson EA, Gottshall RY. Enhanced toxicity for mice of pertussis vaccines when preserved with merthiolate. Applied Microbiology 1967;15:590-593.

Statements I:

Warkany and Hubbard have reported, "In several children of our series and in some recently reported, various immunization procedures preceded the onset of acrodynia in addition to mercurial exposure. This could be purely coincidental or the vaccination may play a role as an accessory factor. It is noteworthy that many vaccines and sera contain small amounts of mercury as preservatives which are injected with the biological material."

Mukai undertook an autoradiographic study in order to evaluate the distribution of ethylmercuri-S-cysteine (EMC) cells of the central nervous system. Mice were injected intraperitoneally with EMC labeled with tritium at a concentration of 0.3 mg/0.5 mL saline per day. The extent and distribution of cell damage were highly predictable, and selective necrosis of the small granular neurons in the koniocortex and neostriatum was a constant finding. Autoradiographic study suggested that the astroglial cell compartment played a role in conveying the mercury-protein complex into neurons.

Articles Reporting

Methyl- & Ethylmercury

Are

Similar

Publications I:

- Ball LK, Ball R, Pratt RD. An assessment of thimerosal use in childhood vaccines. Pediatrics 2001;107:1147-1154.

- Tan M, Parkin JE. Route of decomposition of thiomersal (thimerosal). International J Pharmaceutics 2000;208:23-34.

- Friberg L, Nordberg GJ, Vouk VB (eds). Handbook on the Toxicology of Metals, 2nd Edition, Volume II: Specific Metals. New York, NY: Elsevier, 1986, pg 418.

- Fagan DG, Pritchard JS, Clarkson TW, et al. Organ mercury levels in infants with omphaloceles treated with organic mercurial antiseptic. Arch Dis Child 1977;52:962-964.

- Zhang J. Clinical observations in ethyl mercury chloride poisoning. Am J Ind Med 1984;5:251-258.

Publications II:

- Yonaha M, Ishikura S, Uchiyama. Toxicity of organic mercury compounds. III. Uptake and retention of mercury in several organs of mice by long term exposure of alkoxyethylmercury compounds. Chem Pharm Bull 1975;23:1718-1725.

- Pichard A. Mercury and its Derivatives. INERIS, Compilation of Toxicological and Environmental Data on Chemicals, July 2000, pgs. 1-45.

- Magos L, Brown AW, Sparrow S, Bailey E, et al. The comparative toxicology of ethyl- and methylmercury. Arch Toxicol 1985;57:260-267.

- Ueha-Ishibashi T, Oyama Y, Nakao H, et al. Effect of thimerosal, a preservative in vaccines, on intracellular Ca2+ concentrations of rat cerebellar neurons. Toxicology 2004;195:77-84.

- Report of an International Committee (Berlin MH, Clarkson TW, Friberg LT, Gage JC, Goldwater LJ, Jernelov A, Kazantzis G, Magos L, et al.). Maximum allowable concentrations of mercury compounds. Arch Environ Health 1969;19:891-905.

Publications III:

- Miller VL, Klavano PA, Jerstad AC, et al. Absorption, distribution, and excretion of ethylmercury chloride. Toxicology & Applied Pharmacology 1961;3:459-468.

- Brooks AGF, Bailey E, Snowden RT. Determination of methyl- and ethylmercury in rat blood and tissue samples by capillary gas chromatography with electron-capture detection. J Chromatography 1986;374:289-296.

- Sylversen TLM. Distribution of mercury in enzymatically characterized subcellular fractions from the developing rat brain after injections of methylmercuric chloride and diethylmercury. Biochem Pharmacology 1974;23:2999-3007.

- Winship KA. Organic mercury compounds and their toxicity. Adv Drug React Ac Pois Rev 1986;3:141-180.

Publications IV:

- Platonow N. A study of the metabolic fate of ethylmercuric acetate. Occup Health Rev 1968;20:1-8.

- Platonow N. A study of the metabolic fate of methylmercuric acetate. Occup Health Rev 1968;20:9-19.

Statements I:

Ball et al. from the Food and Drug Administration reported, "Because higher-dose exposure to ethylmercury from thimerosal results in toxicity comparable to that observed after high-dose exposure to methylmercury, and because of the chemical similarity of the 2 compounds, it appears reasonable to consider toxicity of low doses of methylmercury and ethylmercury to be similar."

An International Committee (including Berlin, Clarkson, and Magos) concluded that the elimination of methyl- and ethylmercury is very slow, especially in man and primates, and consequently there is a considerable risk of mercury accumulation. It was determined that women of childbearing age should not be exposed to an occupational risk from methyl- and ethlmercury compounds. The authors concluded that for methyl- and ethylmercury salts, the ceiling value for mercury in whole blood should not exceed 10 micrograms of mercury/100 mL, as total mercury.

If Methyl- and Ethylmercury are Similar:

The National Research Council (NRC) of the Unites States' National Academy of Sciences has concluded in 2000 (Toxicological Effects of Methylmecury) that overall, data from animal studies, including nonhuman primates, indicate that the developing nervous system is a target for low-dose methylmercury exposure. Results from animal studies have reported effects on cognitive, motor, and sensory functions.

The NRC has also concluded that the Environmental Protection Agency safety guideline for the oral ingestion of methylmercury of 0.1 ug/Kg bodyweight/day is a scientifically justifiable level for the protection of public health.

Animal Model

for

Thimerosal-Induced

Autism

Hornig M, Chian D, Lipkin WI. Susceptibility of mice to disturbances of behavior and brain architecture following postnatal thimerosal exposure paralles strain sensitivity to thimerosal. IMFAR 2002, Orlando, FL, pgs 85-86.

The authors found that **early postnatal administration of thimerosal using doses and timing that mimic the childhood immunization schedule induces mouse strain-specific effects on weight gain, locomotor and exploratory activity, stereotypic behaviors, and size of CA regions of hippocampus**.

The authors concluded that their findings suggest that **brain architecture and function may be altered in genetically susceptible hosts following postnatal thimerosal exposure**, and support the utility and relevance of this model as a tool for identifying genetic and maturational factors underlying vulnerability to toxin-induced CNS injury and understanding the pathogenesis of human neurodevelopmental disorders. .

Epidemiological Evidence

Publications I:

- Geier MR, Geier DA. Neurodevelopmental Disorders Following Thimerosal-Containing Vaccines. Experimental Biology & Medicine 2003;228:660-664.
- Geier MR, Geier DA. Thimerosal in childhood vaccines, neurodevelopment disorders, and heart disease in the United States. Journal of American Physicians & Surgeons 2003;8(1):6-11.
- Geier DA, Geier MR. An Assessment of the Impact of Thimerosal on Childhood Neurodevelopmental Disorders. Pediatric Rehabilitation 2003;6:97-102.
- Geier DA, Geier MR. A Comparative Evaluation of the Effects of MMR Immunization and Mercury Doses From Thimerosal-Containing Childhood Vaccines on the Population Prevalence of Autism. Medical Science Monitor (in press).

Publications II:

- Stehr-Green P, et al. Autism and thimerosal-containing vaccines: Lack of consistent evidence for an association. Am J Prev Med 2003;25:101-106.

Statements I:

Geier & Geier

Thimerosal-Containing vs Thimerosal-Free DTaP Vaccines

Type of Reaction	Relative Risk	Attributable Risk	Percent Association	Statistical Significance
Mental Retardation	6.1	5.1	86	$p < 0.002$
Autism	6.0	5.0	86	$p < 0.05$
Speech Disorders	2.2	1.2	69	$p < 0.05$

Statements II:

Stehr-Green P, et al.

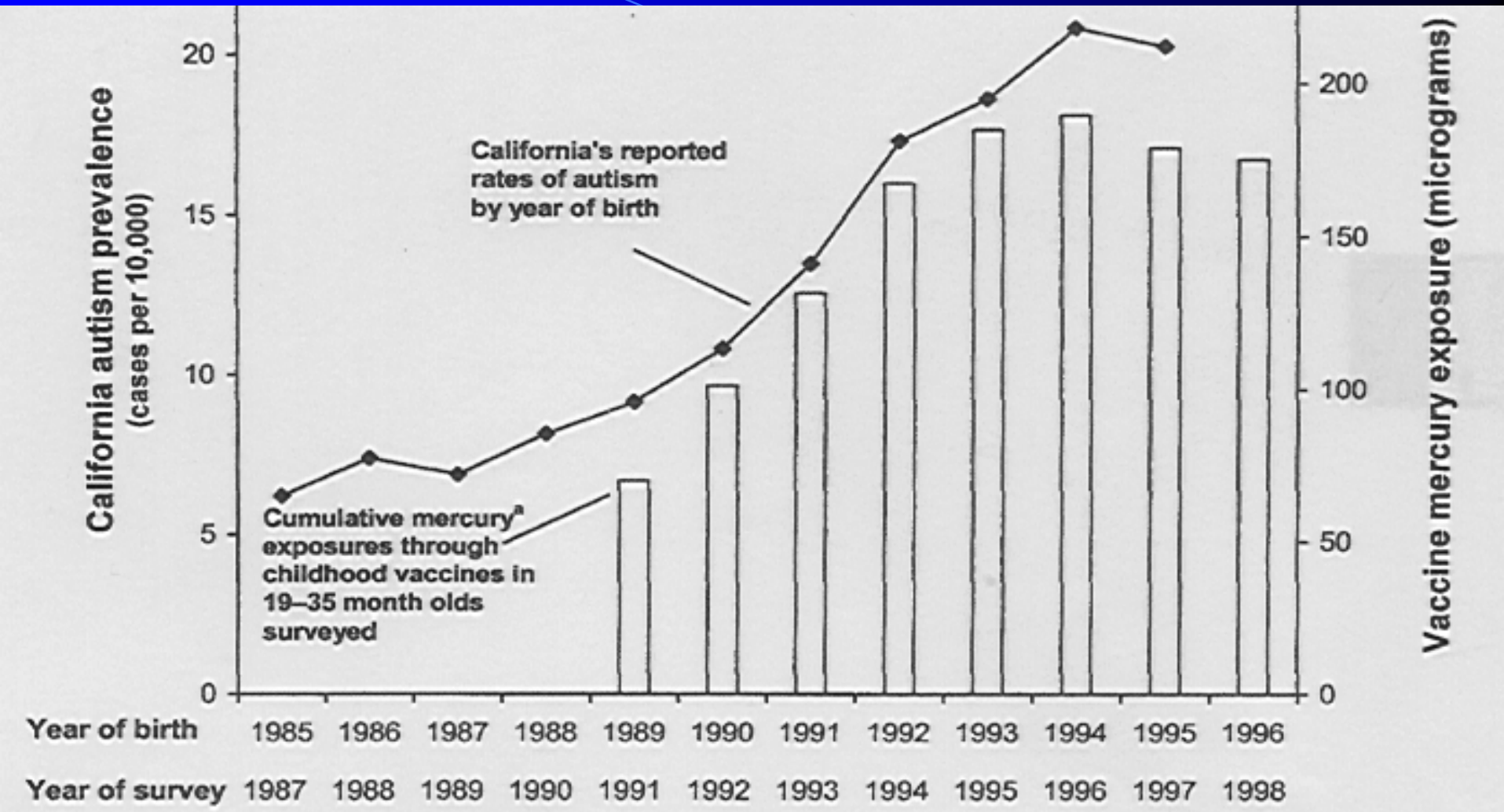


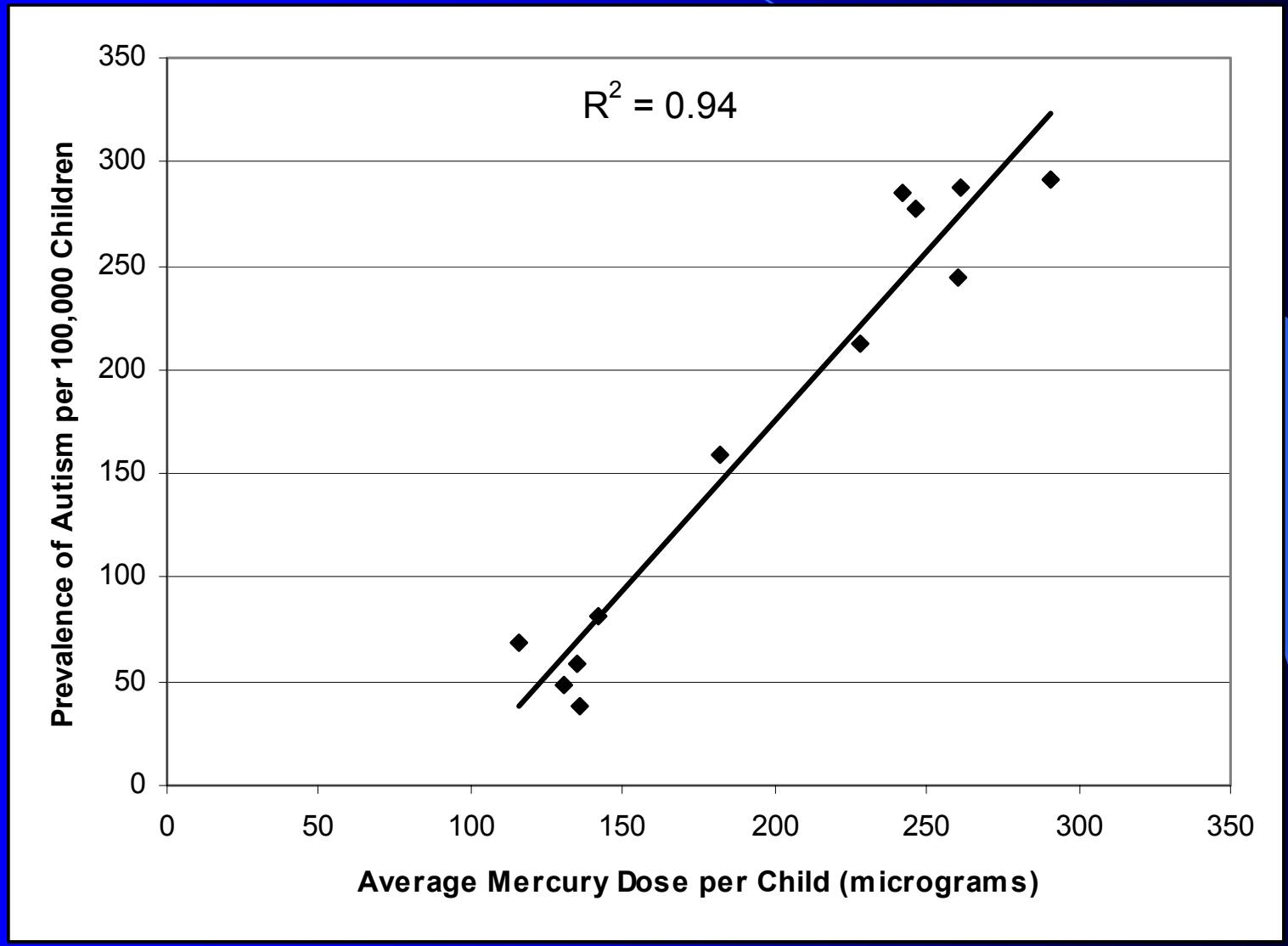
Figure 1. Graphical ecologic analysis presented by Blaxill[5] to the Institute of Medicine on July 16, 2001, comparing the estimated average cumulative dose of mercury exposure in the United States from vaccines, and the estimated prevalence (per 10,000 population) of children diagnosed with autism-like disorders seeking special education services for autism in California from 1987 to 1998, by birth-year cohort.

[a]Includes DPT, *Haemophilus influenza* B, and hepatitis B exposures weighted by survey year compliance.

Statements III:

Geier & Geier

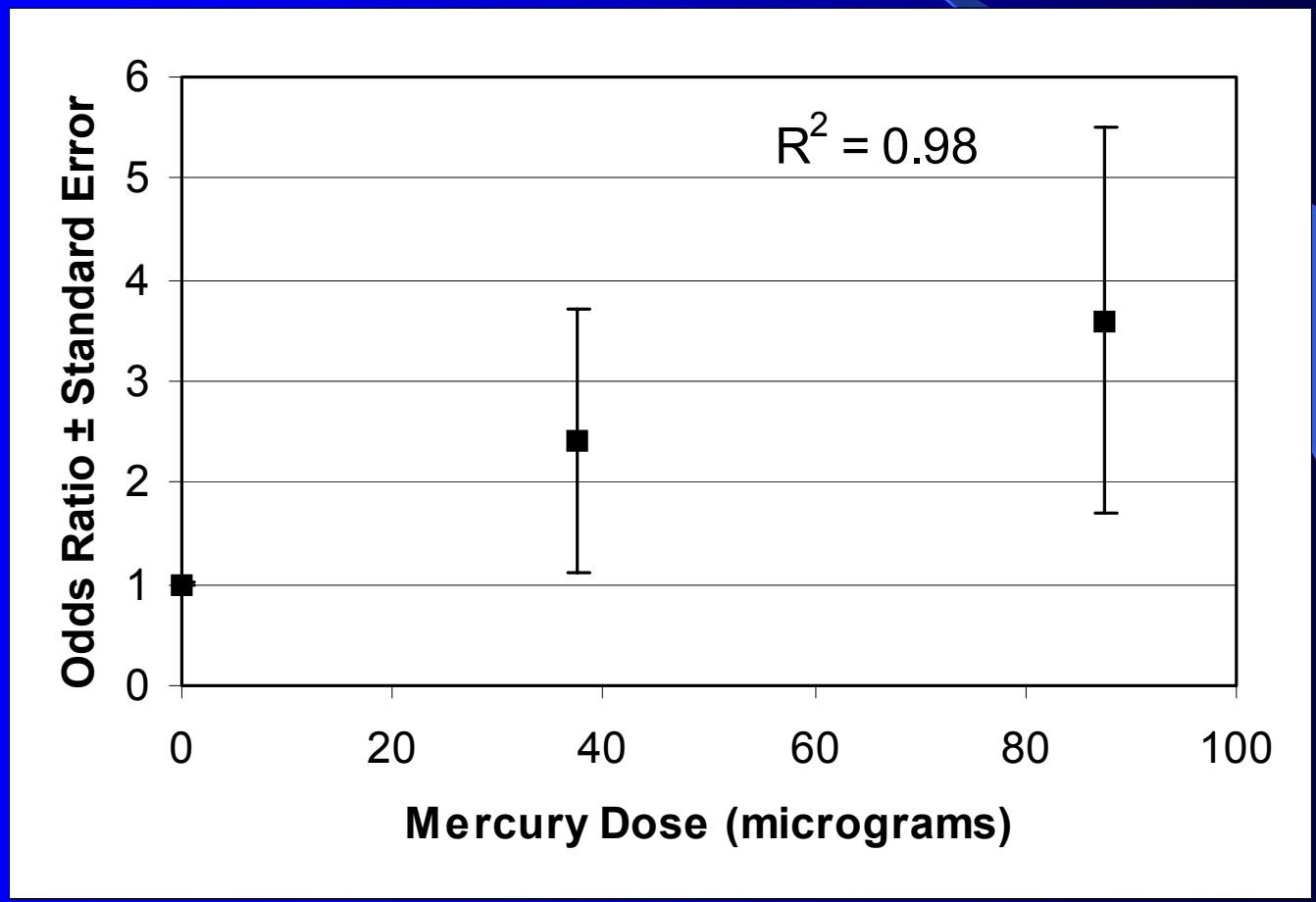
US Department of Education Report



Statements IV:

Geier & Geier

Outcome: Autism
Thimerosal-Containing vs Thimerosal-Free DTaP Vaccines

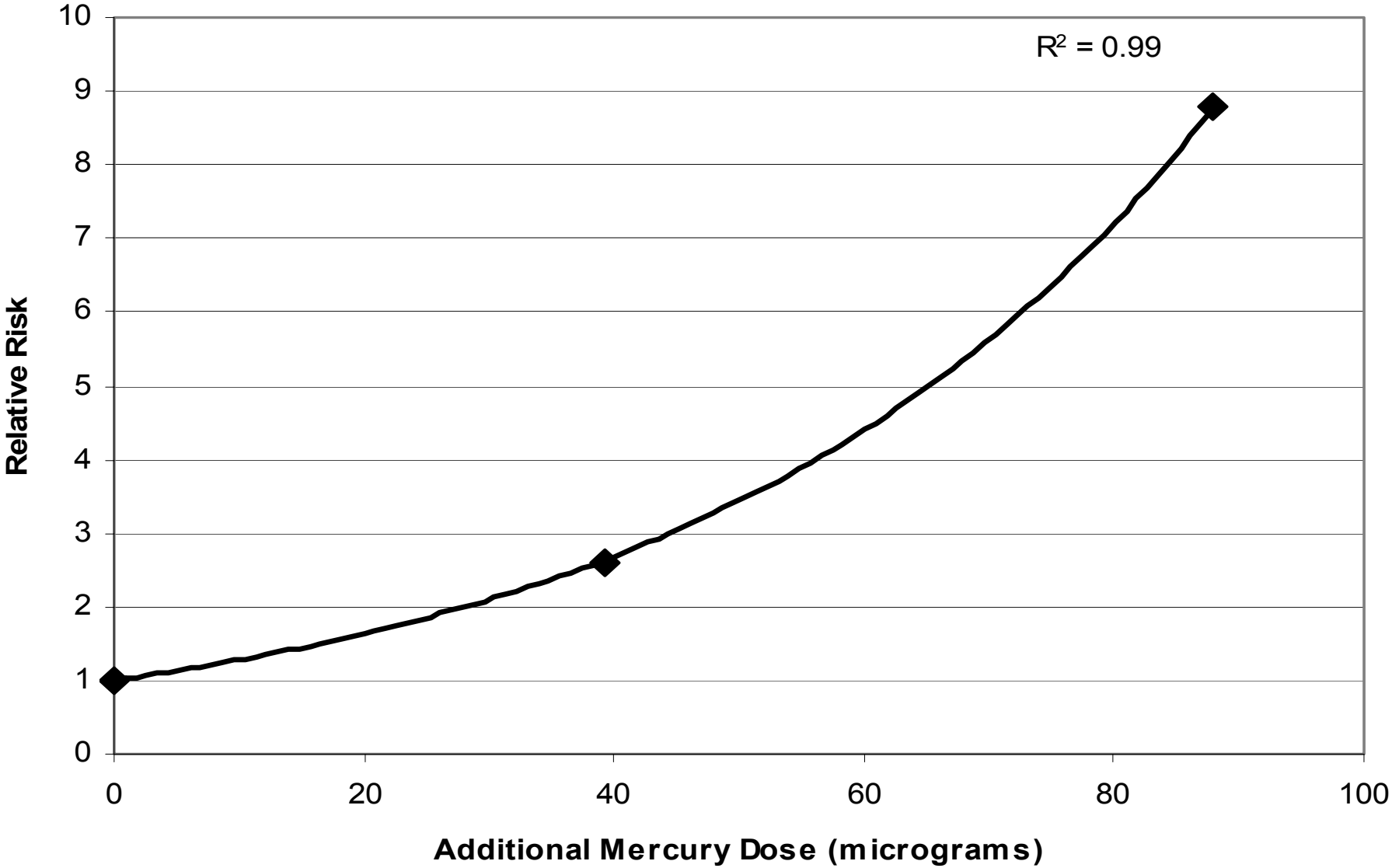


Geier & Geier

Vaccine Safety Datalink Results

Children Receiving 4 Doses of Thimerosal-Containing DTaP or Thimerosal-free DTaP Vaccines in Various Combinations

Autism (ICD-9: 299.0)



Mercury Retention Evidence

Publications I:

- Gale GR, Smith AB, Jones MM, et al. Meso-2,3-Dimercaptosuccinic acid monoalkyl esters: effects on mercury levels in mice. Toxicology 1993;81:49-56.
- Zhang J. Clinical observations in ethyl mercury chloride poisoning. Am J Ind Med 1984;5:251-258.
- Bradstreet J, Geier DA, Kartzinel JJ, et al. A case-control study of mercury burden in children with autistic spectrum disorders. J Am Phys Surg 2003;8:76-79.
- Holmes AS, Blaxill MF, Haley BE. Reduced levels of mercury in first baby haircuts in autistic children. International J Toxicology 2003;22:277-285.
- Godfrey ME, Wojcik DP, Krone CA. Apolipoprotein E genotyping as a potential biomarker for mercury neurotoxicity. J Alzheimer's Dis 2003;5:189-195.

Statements I:

Bradstreet et al.

A summary of heavy metal levels following a 3-day DMSA treatment in autistic spectrum disorder cases matched to control children for age, sex, and vaccination status

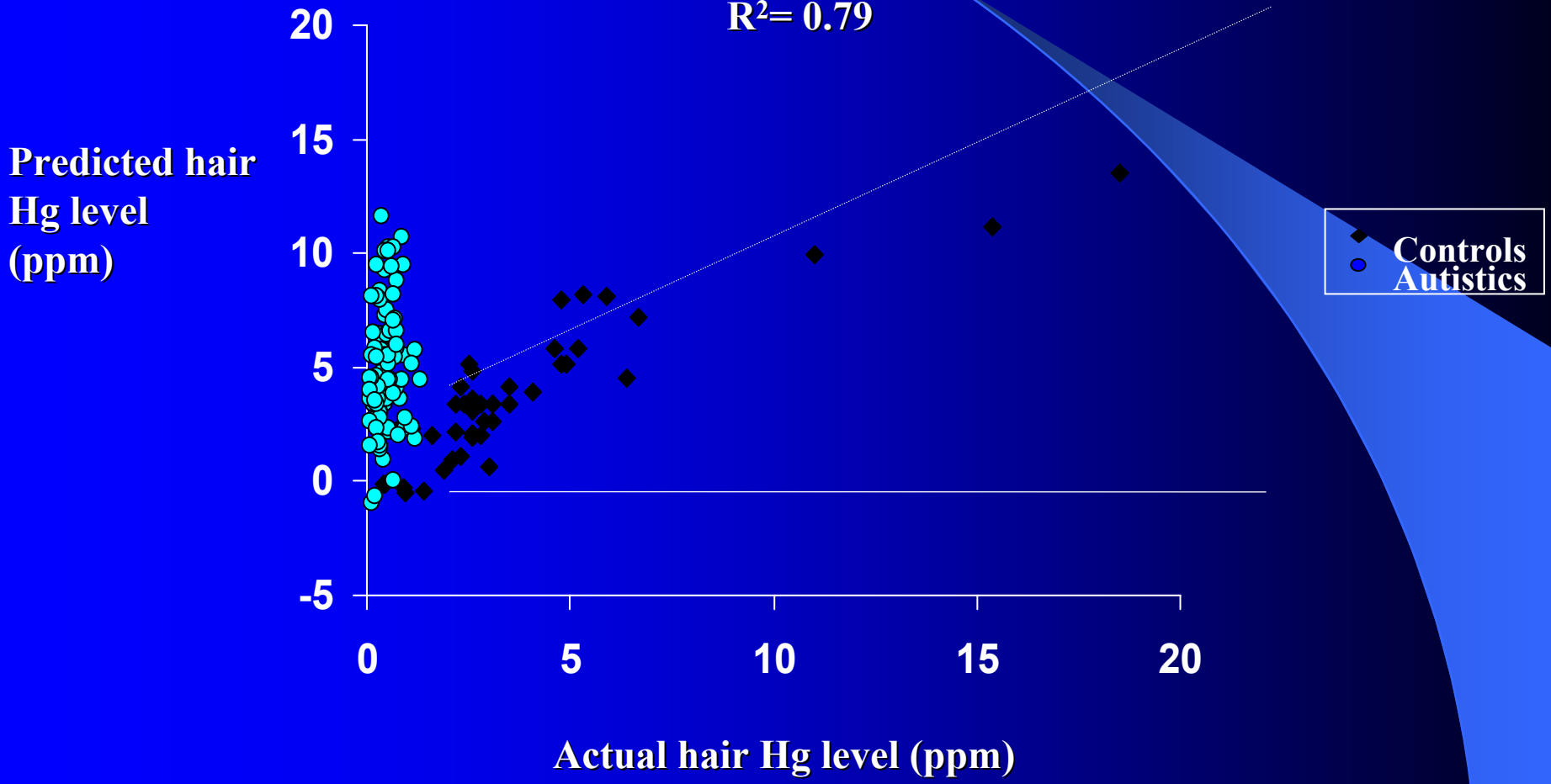
	Heavy Metal Examined	Population Examined	Heavy Metal Level (microgram/gram of creatinine)
	Mercury	55 Cases	6.42 ✂ 12.69
	Mercury	8 Controls	1.08 ✂ 1.12
Statistical Assessment			Relative Increase = 5.9 p < 0.005 95% CI: 1.90 to 8.79
	Cadmium	55 Cases	0.48 ✂ 0.42
	Cadmium	8 Controls	0.36 ✂ 0.22
Statistical Assessment			Relative Increase = 1.3 p = 0.35 Not Significant
	Lead	55 Cases	18.2 ✂ 43.3
	Lead	8 Controls	11.8 ✂ 8.6
Statistical Assessment			Relative Increase = 1.5 p = 0.34 Not Significant

Statements II:

Holmes et al.

ACTUAL VERSUS PREDICTED BIRTH HAIR MERCURY LEVELS

Hair Hg level= (5.60)+0.04(amalgam volume)+1.15(fish consumption)+0.03(vaccine):
R^2= 0.79



Impaired Sulfation

&

Oxidative Stress

in

Autistic Children

Evidence

Publications I:

- James SJ. Impaired transulfation and oxidative stress in autistic children: Improvement with targeted nutritional intervention. Fall DAN! 2003 Conference, Portland, Oregon, October 3-5, 2003.

- Bradstreet J, Geier DA, Kartzinel JJ, et al. Plasma cysteine and plasma sulfate levels in children with autistic spectrum disorders. [unpublished material]

- Alberti A, Pirrone P, Elia M, et al. Sulphation deficit in "low-functioning" autistic children: A pilot study. Biol Psychiatry 1999;46:420-424.

- Yorbik O, Sayal A, Akay C, et al. Investigation of antioxidant enzymes in children with autistic disorder. Protaglandins, Leukotrienes and Essential Fatty Acids 2002;67:341-345.

Statements I:

James

The plasma sulfur-group profile observed in the autistic children is severely abnormal.

Table 1	Control Children n=33	Autistic Children n=20	p value
Methionine (μmol/L)	30.6 ± 6.5	19.3 ± 9.7	0.001
SAM (nmol/L)	90.0 ± 16.2	75.8 ± 16.2	0.01
SAH (nmol/L)	20.1 ± 4.3	26.1 ± 5.4	0.001
Homocysteine (μmol/L)	6.3 ± 1.2	5.4 ± 0.9	0.01
Adenosine (μmol/L)	0.28 ± 0.16	0.39 ± 0.19	0.05
Cysteine (μmol/L)	210 ± 18.5	163 ± 14.6	0.001
Total glutathione (μmol/L)	7.9 ± 1.8	4.1 ± 0.5	0.001
Oxidized Glutathione (nmol/L)	0.3 ± 0.1	0.55 ± 0.2	0.001
GSH/GSSG Ratio	25.5 ± 8.9	8.6 ± 3.5	0.001

Genotypes

Associated

With

Thimerosal/Mercury Sensitivity

Publications I:

- Westphal GA, Schnuch A, Schulz TG, et al. Homozygous gene deltions of the glutathione S-transferases M1 and T1 are associated with thimerosal sensitization. Int Arc Occup Environ Health 2000;73:384-388.

- Godfrey ME, Wojcik DP, Krone CA. Apolipoprotein E genotyping as a potential biomarker for mercury neurotoxicity. J Alzheimer's Dis 2003;5:189-195.

Statements I:

Wesphal et al.

The authors determined that the glutathione system was involved in the metabolism of thimerosal or its decomposition products (organomercury alkyl compounds).

The authors found that certain genotypes were associated with polymorphisms in the glutathione system, resulting in certain individuals being more sensitive to thimerosal then others.

Distribution

of

Thimerosal & Ethylmercury

in the

Body

Publications I:

- Takeda Y, Kunugi T, Terao T, et al. Mercury compounds in the blood of rats treated with ethylmercuric chloride. Toxicology & Applied Pharmacology 1968;13:165-173.

- Gasset AR, Itoi M, Ishii Y, et al. Teratogenicities of ophthalmic drugs II. Teratogenicities and tissue accumulation of thimerosal. Arch Ophthalmol 1975;93:52-55.

- Slikker W. Developmental neurotoxicology of therapeutics: Survey of novel recent findings. Neurotoxicology 2000;21:250.

- Blair AMJN, Clark B, Clarke AJ, et al. Tissue concentrations of mercury after chronic dosing of squirrel monkeys with thiomersal. Toxicology 1975;3:171-176.

Publications II:

- Miller VL, Klavano PA, Jerstad AC, et al. Absorption, distribution, and excretion of ethylmercury chloride. Toxicology & Applied Pharmacology 1961;3:459-468.

- Yonaha M, Ishikura S, Uchiyama. Toxicity of organic mercury compounds. III. Uptake and retention of mercury in several organs of mice by long term exposure of alkoxyethylmercury compounds. Chem Pharm Bull 1975;23:1718-1725.

- Wright FC, Palmer JS, Riner JC. Retention of mercury in tissues of cattle and sheep given oral doses of a mercurial fungicide, Ceresan M. J Agr Food Chem 1973;21:614-615.

- Platonow N. A study of the metabolic fate of ethylmercuric acetate. Occup Health Rev 1968;20:1-8.

Statements I:

Slikker from the Food and Drug Administration reported, "Thimerosal (sodium ethylmercurithiosalicylate) crosses the blood-brain and placental barriers and results in appreciable mercury content in tissues including brain."

Molecular Evaluations

of the

Effects of Thimerosal/Mercury

On

Neuron Degeneration

Publications I:

- Baskin DS, Ngo H, Didenko VV. Thimerosal induces DNA breaks, caspase-3 activation, membrane damage, and cell death in cultured human neurons and fibroblasts. Toxicological Sciences 2003;74:361-368.
- Leong CCW, Syed NI, Lorscheider FL. Retrograde degeneration of neurite membrane structural integrity of nerve growth cones following in vitro exposure to mercury.
- Brunner M, Albertini S, Wurgler FE. Effects of 10 known or suspected spindle poisons in the in vitro porcine brain tubulin assembly assay. Mutagenesis 1991;6:65-70.
- Parry JM. An evaluation of the use of in vitro tubulin polymerisation, fungal and wheat assays to detect the activity of potnetial chemical aneugens. Mutation Res 1993;287:23-28.

Publications II:

- Wallin M, Hartley-Asp B. Effects of potential anueploidy inducing agents on microtubule assembly in vitro. Mutation Research 1993;287:17-22.

- Waly M, Olteanu H, Banerjee R, et al. Activation of methionine synthase by insulin-like growth factor-1 and dopamine: a target for neurodevelopmental toxins and thimerosal. Mol Pschiatry 2004;1-13.

Statements I:

Waly et al. (Johns Hopkins University, US Dept. Agriculture)

A recent analysis of the VAERS found a significant correlation between the use of thimerosal-containing DTaP vaccines in comparison to thimerosal-free DTaP vaccines for autism. The discovery of the PI3-kinase/MAP-kinase/MS pathway, and its potent inhibition by the vaccine component of thimerosal, provides a potential explanation for how increased use of vaccines could promote an increase in the incidence of autism. The increased incidence of ADHD could represent an alternate manifestation of vaccine-associated neurodevelopmental toxicity since the D4 dopamine receptor is linked to ADHD and its PLM function depends upon MS.

Molecular Evaluations

of the

Effects of Thimerosal

On

Neuron Degeneration

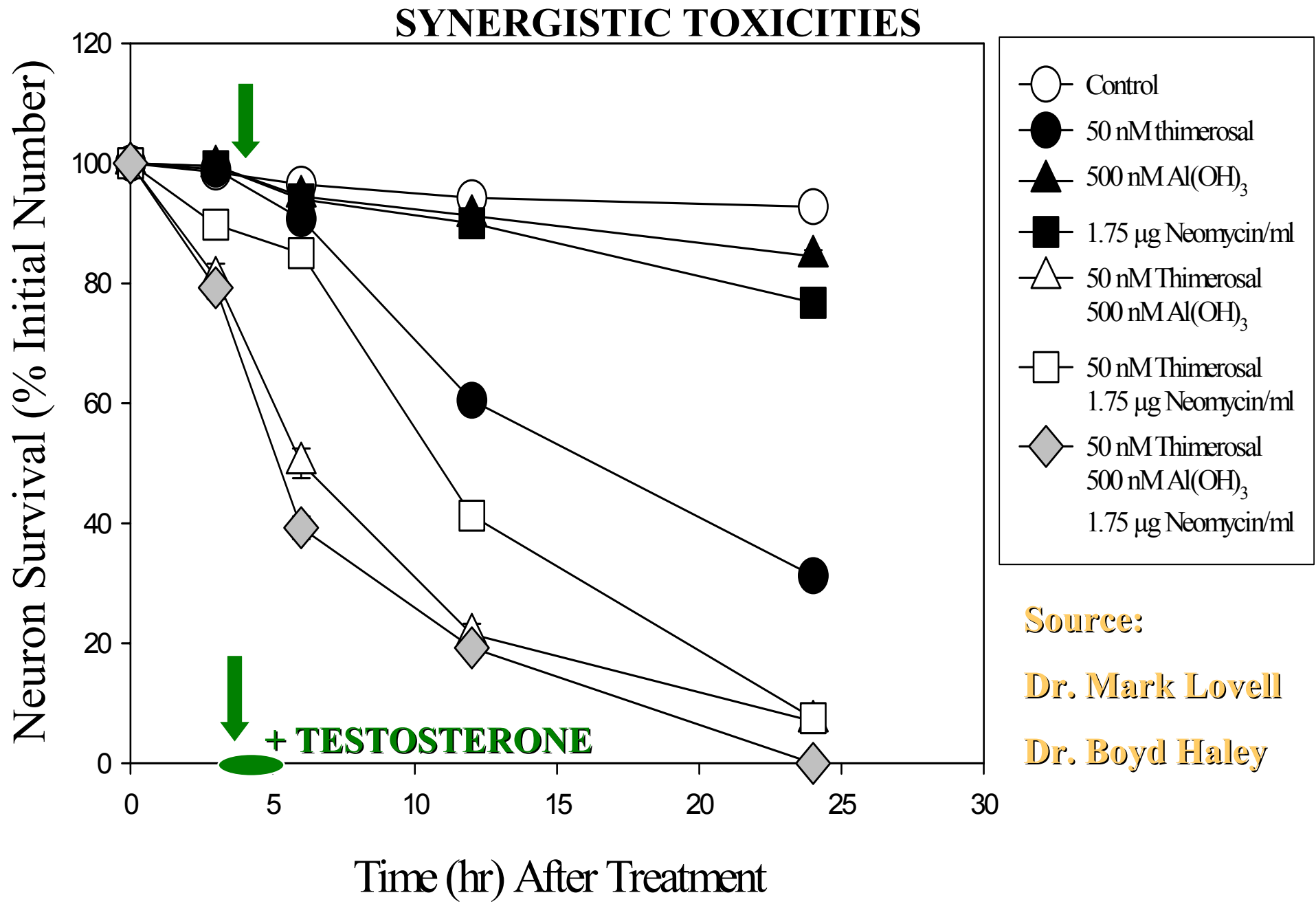
with other

Substances

Publications I:

- Haley, Lovell. Synergistic toxicities. [unpublished material].
- Czlonkoska A, Ciesielska A, Joniec I. Influence of estrogens on neurodegenerative processes. Med Sci Monit 2003;9:RA-247-RA256.
- Waly M, Olteanu H, Banerjee R, et al. Activation of methionine synthase by insulin-like growth factor-1 and dopamine: a target for neurodevelopmental toxins and thimerosal. Mol Pschiatry 2004;1-13.
- Crook TG, Freeman JJ. Reactions induced by the concurrent use of thimerosal and tetracycline. Am J Optometry & Physioloogical Optics 1983;60:759-761.
- Clarkson TW. Metal toxicity in the Central Nervous System. Environ Health Perspectives 1987;75:59-64.

Statements I:



Source:

Dr. Mark Lovell

Dr. Boyd Haley

Molecular Evaluations

of the

Effects of Mercury

on

Specific Sites of Neuron Degeneration

Publications I:

- Li S, Thompson SA, Woods JS. Localization of sigma-glutamylcysteine synthase mRNA expression in mouse brain following methylmercury treatment using reverse transcription in Situ PCR amplification. Toxicology & Applied Pharmacology 1996;140:180-187.

- Ueha-Ishibashi T, Oyama Y, Nakao H, et al. Effect of thimerosal, a preservative in vaccines, on intracellular Ca2+ concentrations of rat cerebellar neurons. Toxicology 2004;195:77-84.

- Gustafsson J, Pousette A, Svensson E. Sex-specific occurrence of androgen receptors in rat brain. J Biol Chem 1976;251:4047-4054.

Metabolic/Perfusion Imagining

In

Autistic Children

Publications I:

- Ryu YH, Lee JD, Yoon PH, et al. Perfussion impairments in infantile autism on technetium-99m ethyl cysinate dimer brain single-photon emission tomography: comparison with findings with magnetic resonance imaging. European J Nuclear Med 1999;26:253-259.

- Starkstein SE, Vazquiz S, Vrancic D, et al. SPECT findings in mentally retarded autistic individuals. J Neuropsychiatry Clin Neurosci 2000;12:370-375.

These metabolic/perfusion scans of children with autistic spectrum disorders showed damage in similar areas to those areas that have been shown to be damaged by mercury, are those areas in which the brain is afforded minimal protection against the effects of mercury (i.e. they produce minimal glutathione levels), are areas that have been demonstrated to have testosterone receptors resulting in the buildup of significant testosterone concentrations (i.e. testosterone has been shown to potentiate thimerosal neuronal toxicity, whereas estrogen has been shown to reduce thimerosal neuronal toxicity), and the damage observed is consistent with that observed in neuron tissue culture systems following extremely low dose mercury exposure (i.e. neuron functional abnormalities, as apposed to complete structural neuron obliteration).

Articles Recommending the Removal of Thimerosal from Vaccines

&

The Continued Presence of Thimerosal in Vaccines

Publications I:

- Kravchenko AT, Dzagurov SG, Chervonskaia GP. Evaluation of the toxic action of prophylactic and therapeutic preparations on cell cultures. Paper III: The detection of toxic properties in medical biological preparations by degree of cell damage in in the L-132 continuous cell line. Zh Mikrobiol Epidemiol Immunobiol 1983;3:87-92.
- Cox NH, Forsyth A. Thiomersal allergy and vaccination reactions. Contact Dermatitis 1988;18:229-233.
- Forstrom L, Hannuksela M, Kousa M, et al. Merthiolate hypersensitivity and vaccination. Contact Dermatitis 1980;6:241-245.
- Seal D, Ficker L, Wright P, et al. The case against thimerosal. Lancet 1991;338:315-316.

Publications II:

- Heyworth MF, Truelove SC. Problems associated with the use of merthiolate as a preservative in anti-lymphocytic globulin. Toxicology 1979;12:325-333.

- Schumm WR, Reppert E, Jurich AP, et al. Self-reported changes in subjective health and anthrax vaccination as reported by over 900 Persian Gulf War ear veterans. Psychological Reports 2002;90:639-653.

- Winship KA. Organic mercury compounds and their toxicity. Adv Drug React Ac Pois Rev 1986;3:141-180.

Statements I:

Kravchenko et al.

"Thus thimerosal, commonly used as a preservative, has been found not only to render its primary toxic effect, but also capable of changing the properties of cells. This fact suggests that the use of thimerosal for the preservation of medical biological preparations, especially those intended for children, is inadmissible."

Pediatric Diphtheria-Tetanus (DT)

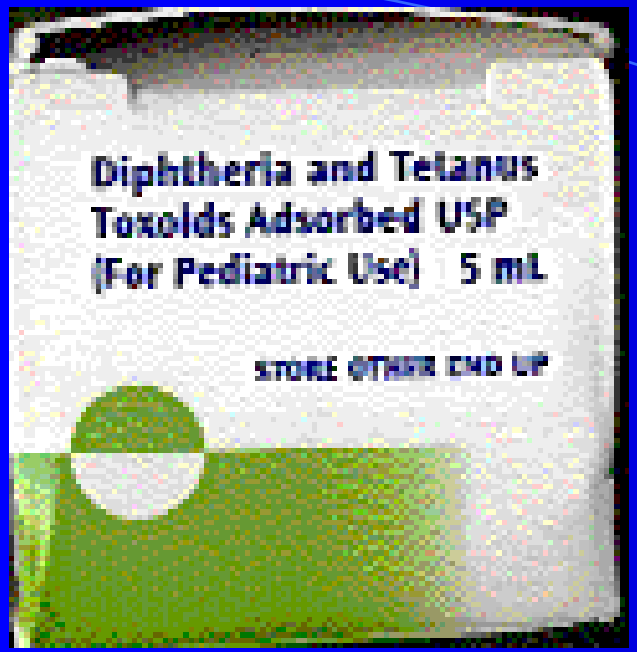
Vaccine

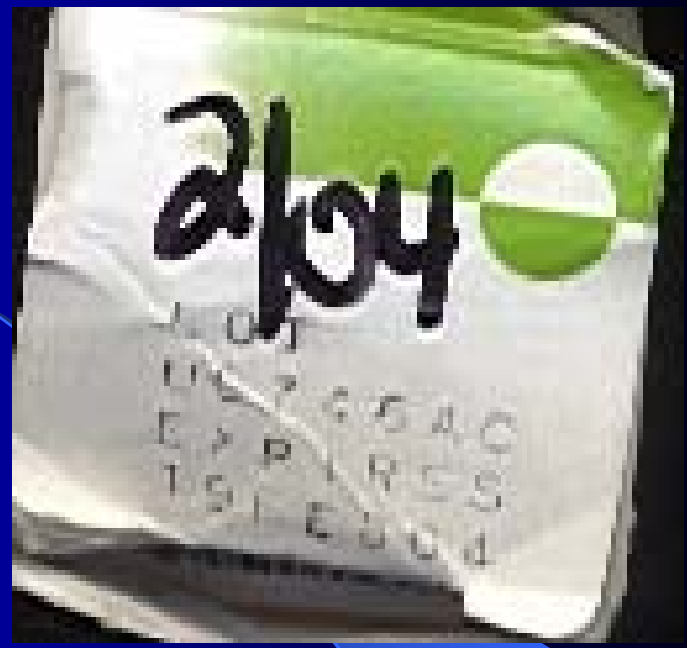
Aventis Pasteur

5 mL Vial - 0.5 mL Dose

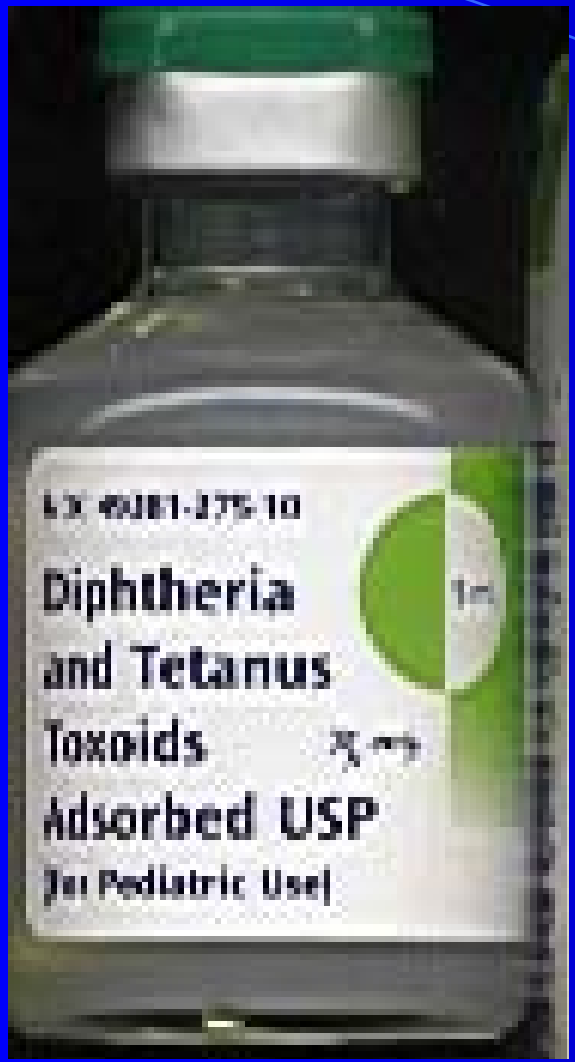
Expires 19 February 2004

1:10,000 [25 Micrograms Mercury] Thimerosal





DO NOT FREEZE. Store between 2° – 8°C (35° – 46°F). FOR INTRAMUSCULAR INJECTION. SHAKE WELL. Dosage: For infants 2 – 12 months, three 0.5 mL doses at least 4 weeks apart; a reinforcing dose is given 6 – 12 months after the third dose. For children 1 – 6 years, two 0.5 mL doses at least 4 weeks apart; a reinforcing dose is given 6 – 12 months after the second dose. For indications and directions see package insert. Thimerosal (mercury derivative) 1:10,000 added as preservative.


Diphtheria
and Tetanus
Toxoids
Adsorbed USP
(for Pediatric Use)


LOT U074AC
EXP 19FEB04
4223

Tetanus-Diphtheria (Td) Vaccine

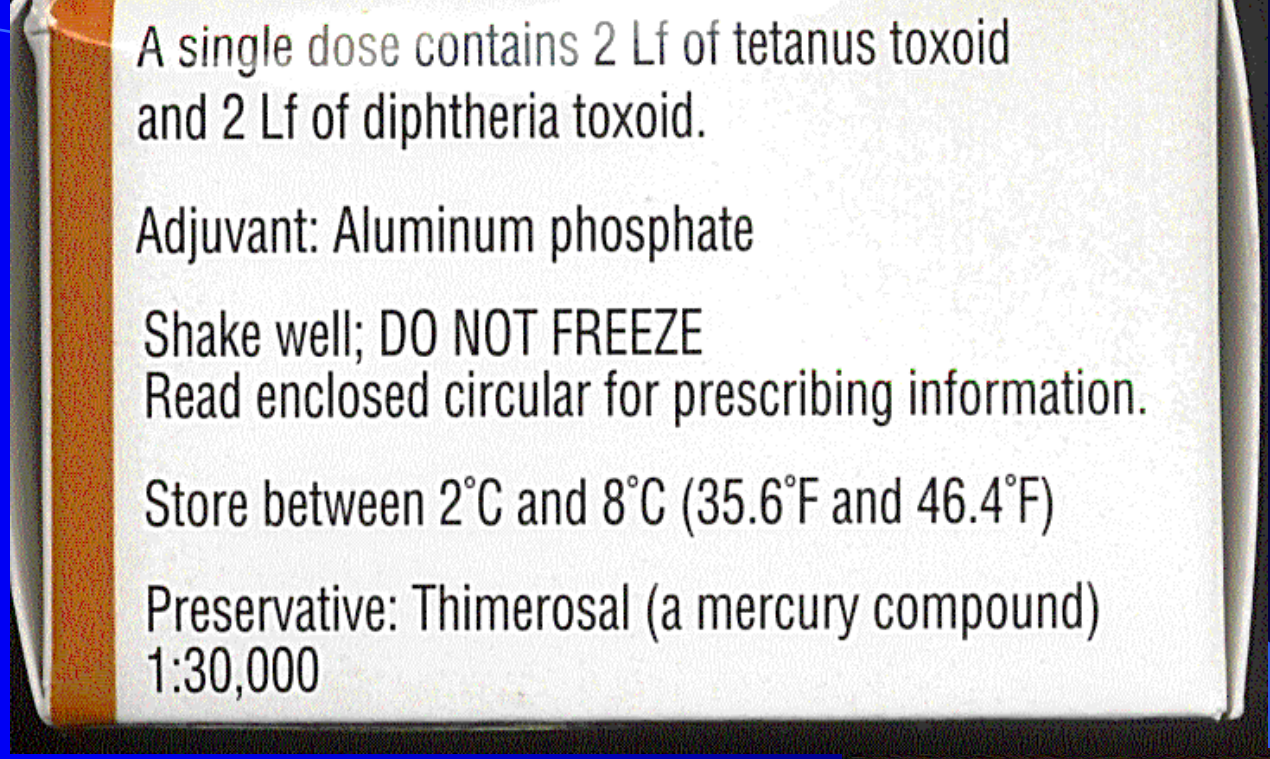
Massachusetts Public Health Biological Laboratories

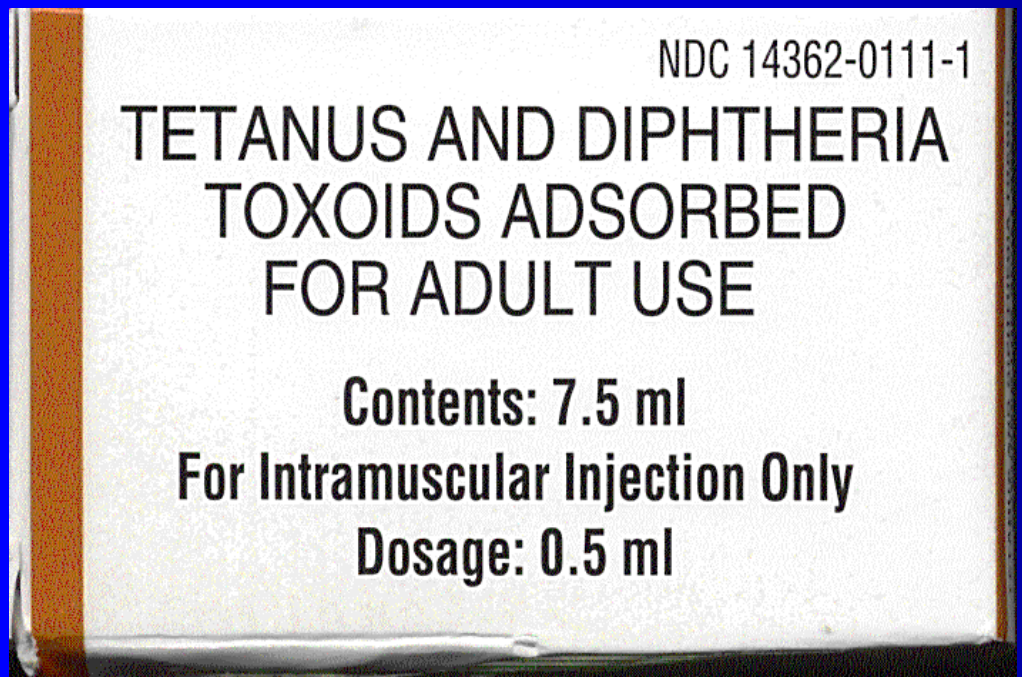
For Children > 7 years-old

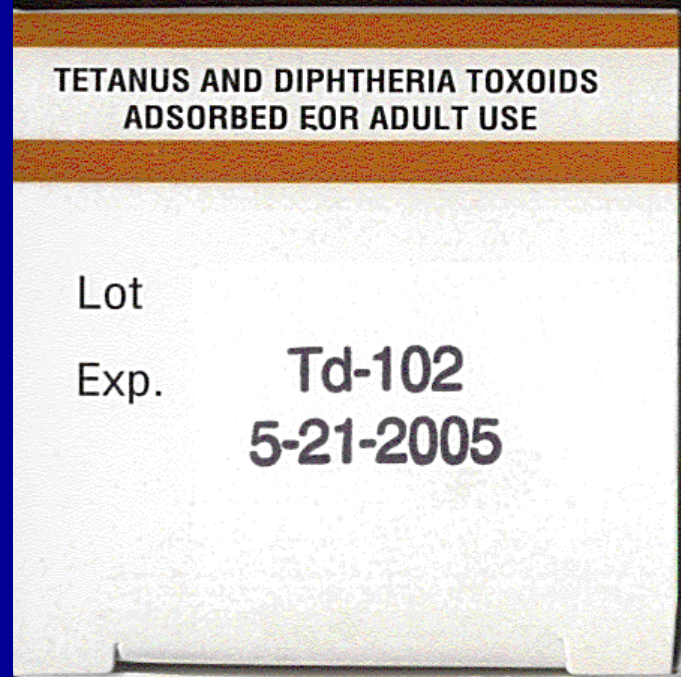
7.5 mL Vial – 0.5 mL Dose

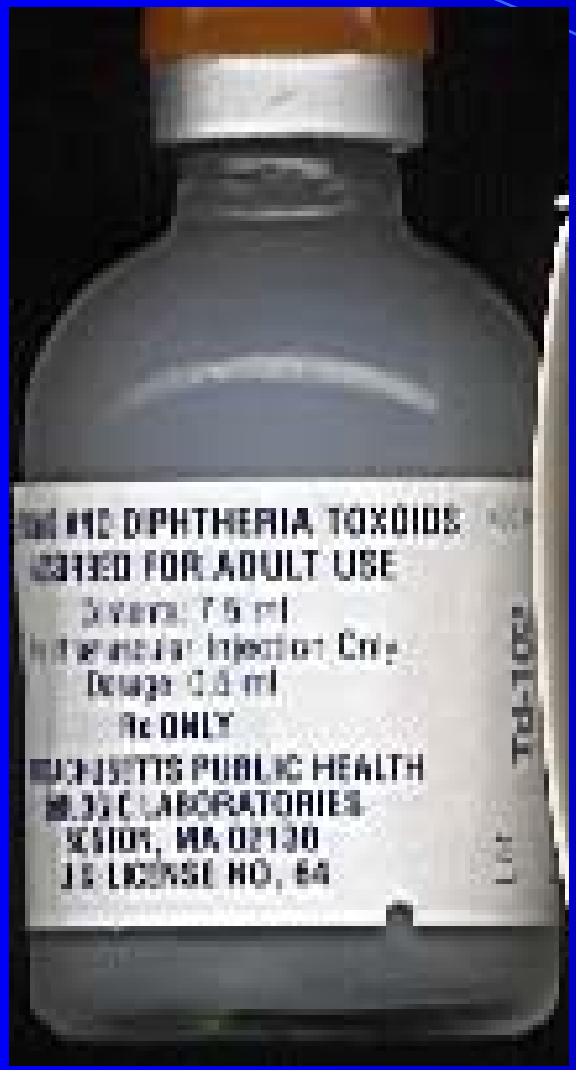
Expires 21 May 2005

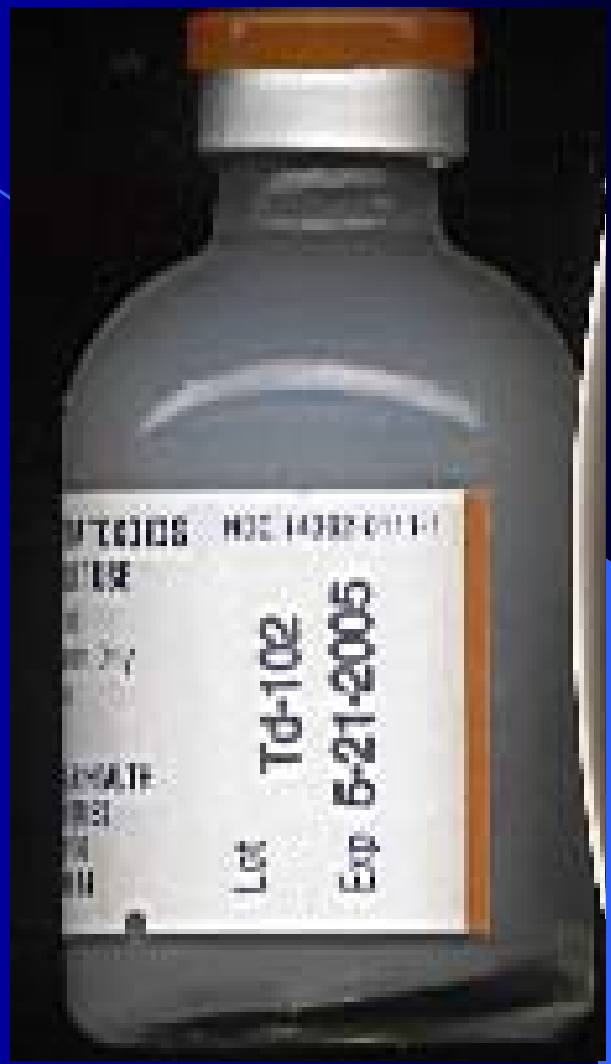
1:30,000 [8.3 Micrograms Mercury] Thimerosal


A single dose contains 2 Lf of tetanus toxoid
and 2 Lf of diphtheria toxoid.
Adjuvant: Aluminum phosphate
Shake well; DO NOT FREEZE
Read enclosed circular for prescribing information.
Store between 2°C and 8°C (35.6°F and 46.4°F)
Preservative: Thimerosal (a mercury compound)
1:30,000


NDC 14362-0111-1
TETANUS AND DIPHTHERIA
TOXOIDS ADSORBED
FOR ADULT USE
Contents: 7.5 ml
For Intramuscular Injection Only
Dosage: 0.5 ml


TETANUS AND DIPHTHERIA TOXOIDS
ADSORBED FOR ADULT USE
Lot
Exp.
Td-102
5-21-2005


DIPHTHERIA TOXOIDS
FOR ADULT USE
Rx ONLY
Td-102


Lot Td-102
Exp 6-21-2005

Influenza Virus Vaccine

Fluzone

Aventis Pasteur

5 mL Vial

Expires 30 June 2004

1:10,000 [25 Micrograms Mercury] Thimerosal

Dosage: Not for use in infants under 6 months of age. For intramuscular injection. Persons 9 years of age and older, one 0.5 mL injection; persons 3 through 8 years of age, two 0.5 mL injections, given one month apart; persons 6 months through 35 months, two 0.25 mL injections, given one month apart. For indications and directions see package insert. Prepared from influenza viruses propagated in chicken embryos and inactivated with formaldehyde. A nonionic surfactant (Triton® X-100*) is added during manufacture. Each dose contains the preservative thimerosal [(mercury derivative), 25 µg mercury/dose].

*Triton® X-100 – Registered trademark of Union Carbide, Co., USA.


Influenza
Virus
Vaccine
Fluzone®


4842
LOT U113044
EXP 30JUN04

Japanese Encephalitis Virus Vaccine

JE-VAX

Aventis Pasteur

3 x 1 mL Vial

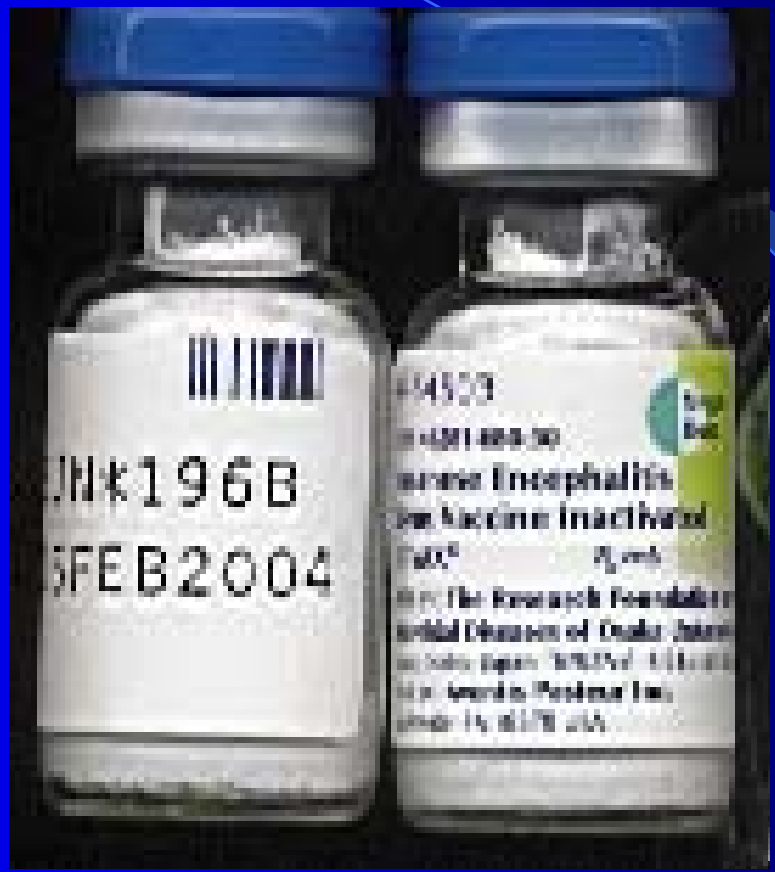
Expires 15 February 2004

0.007% [35.7 Micrograms Mercury] Thimerosal

Store between 2° – 8°C (35° – 46°F). **DO NOT FREEZE.** Reconstitute contents of vial with 1.3 mL of Sterile Diluent provided. After reconstitution, the vaccine should be used within 8 hours and must not be stored. **SHAKE WELL after reconstitution.**

Dosage: Immunization consists of a series of three 1 mL subcutaneous injections. For indications and directions see enclosed circular. The vaccine is prepared from mouse brains infected with Japanese encephalitis (JE) virus, "Nakayama-NIH" strain and is inactivated with formaldehyde. Thimerosal (mercury derivative) is added as a preservative to a final concentration of 0.007%. Diluent contains no preservatives.

Vaccine Lot No	EJN*196B
Expiration Date	15FEB2004
Diluent Lot No	D013*126


JN*196B
5FEB2004

Additional Vaccines Still Containing Thimerosal

** Meningococcal Polysaccharide Vaccine

Aventis Pasteur, 10 Dose Vial (25 Micrograms of Mercury per Dose), Lot UB505AA - Expires 17 Jun 05

** Td Vaccine

Aventis Pasteur, 10 Dose Vial (25 Micrograms of Mercury per Dose), Lot U1014AA - Expires 2 Sept 05

** Tetanus Toxoid Absorbed Vaccine

Aventis Pasteur, 10 Dose Vial (25 Micrograms of Mercury per Dose), Lot U1048BA - Expires 8 Sept 05

** Tetanus Toxoid Vaccine

Aventis Pasteur, 15 Dose Vial, (25 Micrograms of Mercury per Dose), Lot U0775AA - Expires 19 Mar 05

Conclusion

Therefore, if a certain segment of the population has a decreased ability to excrete mercury, as has been demonstrated for several different genotypes, there can be little doubt that mercury concentrations once administered to children as part of the childhood routine vaccination schedule resulted in a significant number of children developing neurodevelopmental disorders. This is especially true when a sudden shift in the amount of mercury administered, as occurred in the United States when the amount of mercury administered to children more than doubled as part of the routine childhood immunization schedule in the first six months of life (i.e. from 75 micrograms of mercury generated as a result of three DTwP immunizations to a minimum of 187.5 micrograms from three DTwP, three Hib, and three hepatitis B immunizations), since the gene pool will contain many susceptible individuals that under previous environmental conditions would have been normal, but under the new environmental conditions are unable to thrive.

Studies Missing the Link

Between

Thimerosal

&

Neurodevelopmental Disorders

Offit PA, Jew RK. Addressing parents' concerns: Do vaccines contain harmful preservatives, adjuvants, or residuals? Pediatrics 2003;112:1394-1401.

Authors state, "Although no published studies to date have compared the incidence of neurodevelopmental delay in children who received thimerosal-free or thimerosal-containing vaccine…"

We have authored three peer-reviewed scientific publications that have examined children receiving thimerosal-containing childhood vaccines in comparison to thimerosal-free childhood vaccines.

Authors state, "However, no data exist on the capacity of low-dose, chronic exposure to ethylmercury to harm the developing nervous system."

We have presented in the previous slides extensive evidence from the peer-reviewed literature showing in various systems, including humans that chronic low-dose exposure to ethylmercury can cause damage to the developing nervous system.

Authors state, "However, the pharmacokinetics of ethylmercury and methylmercury are not the same."

We have presented in the previous slides extensive evidence from the peer-reviewed literature (i.e. from a total of 16 studies, including one by the FDA) concluding that ethylmercury and methylmercury are similar.

Verstraeten T, Davis RL, DeStefano F, et al. Safety of thimerosal-containing vaccines: A two-phased study of computerized health maintenance organization databases. Pediatrics 2003;112:1039-1048.

Halsey NA [served for three years with the CDC in the Immunization Division], Salmon DA, Moulton LH. Comments on Verstraeten et al, safety of Thimerosal-containing vaccines from Nov 5, 2003 Pediatrics

- Comment that the results have changed from the Institute of Medicine presentation, where a statistically significant dose-response association was observed between thimerosal exposure and neurodevelopomental exposure by three months.
- Raised questions of whether the authors accurately accounted for the mercury children were exposed to from thimerosal-containing childhood vaccines.
- The authors comment that by separating HMOs and diagnoses the authors potentially diluted-out statistically significant results.
- The authors call for an independent review of the data concerning the relationship between thimerosal and neurodevelopmetnal disorders.

Additional Serious Comments:

- Thomas Verstraeten, the head author of the study, failed to disclose to Pediatrics as per the journal's requirements that he is employed by GlaxoSmithKline a vaccine manufacture that produced thimerosal-containing vaccines.

- The authors appeared to fail to take into account that a significant proportion of children in some of the HMOs examined by Verstraeten et al were administered thimerosal-free DTaP vaccine. This can be demonstrated by analyzing Table 1 from study, where thimerosal-free DTaP intermediate mercury exposure values are absent.

- The authors also have a potential source of confounding because whole-cell DTP and acellular DTaP vaccines were included in the study, and a gradual transition was made from whole-cell DTP vaccine to acellular DTaP vaccine during the study period. It has been established by the Institute of Medicine that the evidence is compatible with a causal relationship between whole-cell DTP vaccination and acute and chronic encephalopathy.

Thimerosal:

Beyond the Science

The Public Health Service and the American Academy of Pediatrics issued a statement in July 1999 “urging” vaccine makers to reduce or eliminate thimerosal because of “theoretical potential for neurotoxicity.”

In an internal email written 29 June 1999, by former FDA scientist Peter Patriarca offered his colleagues a "pros and cons" assessment of thimerosal statement shortly before its release:

"Will raise questions about FDA being 'asleep at the switch' for decades, by allowing a potentially hazardous compound to remain in many childhood vaccines, and not forcing manufacturers to exclude it from new products. Will also raise questions about various advisory bodies about aggressive recommendations for use. We must keep in mind that the dose of ethyl mercury was not generated by 'rocket science': conversion of the % of thimerosal to actual ug [micrograms] of mercury involves 9th grade algebra. What took the FDA so long to do the calculations? Why didn't CDC and the advisory bodies do these calculations while rapidly expanding the childhood immunization schedule?"

Source: Annette Fuentes. Autism in a needle? A toxic tale of vaccinations and mercury poisoning. In These Times, November 11, 2003. The email was obtained by Rep. Dan Burton (R-Ind.).

Roger Brenier, of the CDC's national immunization program, received the email. In a recent interview he explained why the cumulative amount of mercury was never figured.

"Vaccines tend to be evaluated on an individual basis, the requirements for safety and efficacy on an individual basis," Brenier said. "This holistic view of safety was not part of the review."

Source: Annette Fuentes. Autism in a needle? A toxic tale of vaccinations and mercury poisoning. In These Times, November 11, 2003.

Simpsonwood Meeting (7-8 June 2000) in Norcross, GA where the findings of the Vaccine Safety Datalink (VSD) analysis showing a link between Thimerosal-containing vaccines and neurodevelopmental outcomes were discussed in a closed meeting by a panel of experts.

Dr. Johnston: Page 198: “This association leads me to favor a recommendation that infants up to two years old not be immunized with thimerosal containing vaccines if suitable alternative preparations are available.“ “Forgive this personal comment, but I got called out a eight o’clock 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.”

Dr. Weil: Page 207: “The number of dose related relationships are linear and statistically significant. You can play with this all you want. They are linear. They are statistically significant.”

Dr. Brent: Page 229: “The medical legal findings in this study, causal or not, are horrendous…If an allegation was made that a child’s neurobehavioral findings were caused by thimerosal, you could readily find a junk scientist who would support the claim with ‘a reasonable degree of certainty.’ But you will not find a scientist with any integrity who would say the reverse with data that is available. And that is true. So we are in a bad position from the standpoint of defending lawsuits if they were initiated and I am concerned.”

Dr. Clements: Page 247: “I am really concerned that we have taken off like a boat going down one arm of the mangrove swamp at high speed, when in fact there was not enough discussion really early on about which way the boat should go at all. And I really don’t want to risk offending everyone in the room by saying that perhaps this study should not have been done at all, because the outcome of it could have to some extent, been predicted, and we have all reached this point now where we are left hanging…I know how we handle it from here is extremely problematic.” “But nonetheless, we know from many experiences in history that the pure scientist has done research because of pure science. But that pure science has resulted in splitting the atom or some other process which is completely beyond the power of the scientists who did the research to control it. And what we have here is people who have, for every best reason in the world, pursued a direction of research. But there is now the point at which the research results have to be handled, and even if this committee decides that there is no association and that information gets out, the work that has been done and through the freedom of information that will be taken by others and will be used in ways beyond the control of this group. An I am very concerned about that as I suspect it is already too late to do anything regardless of any professional body and what they say…”

Mercury in Medicine
–
Taking Unnecessary Risks

A report prepared by the staff of the Subcommittee on Human Rights and Wellness, Committee on Government Reform

Unites States House of Representatives

Chairman Dan Burton

May 2003

"There's no question that mercury does not belong in vaccines. There are other compounds that could be used as preservatives. And everything we know about childhood susceptibility, neurotoxicity of mercury at the fetus and infant level, points out that we should not have these fetuses and infants exposed to mercury. There's no need of it in the vaccines."

"Mercury is hazardous to humans. Its use in medicinal products is undesirable, unnecessary and should be minimized or eliminated entirely."

"Manufacturers of vaccines and thimerosal (an ethylmercury compound used in vaccines), have never conducted adequate testing on the safety of thimerosal. The FDA has never required manufacturers to conduct adequate safety testing on thimerosal and ethylmercury compounds."

"Studies and papers documenting the hypoallergenicity and toxicity of thimerosal (ethylmercury) have existed for decades."

"The amount of ethylmercury to which children were exposed through vaccines prior to the 1999 announcement exceeded two safety thresholds established by the Federal Government for a closely related substance – methylmercury. While the Federal Government has established no safety threshold for ethylmercury, experts agree that the methylmercury guidelines are a good substitute."

"The FDA and CDC failed in their duty to be vigilant as new vaccines containing thimerosal were approved and added to the immunization schedule. When hepatitis B and Haempohilus Influenza Type B vaccines were added to the recommended schedule of childhood immunizations, the cumulative amount of ethylmercury to which children were exposed nearly tripled."

"The CDC in general and the National Immunization Program in particular are conflicted in their duties to monitor the safety of vaccines, while also charged with the responsibility of purchasing vaccines for resale as well as promoting increased immunization rates."

"To date, studies conducted or funded by the CDC that purportedly dispute any correlation between autism and vaccine injury have been of poor design, under-powered, and fatally flawed. The CDC's rush to support and promote such research is reflective of a philosophical conflict in looking fairly at emerging theories and clinical data related to adverse reactions from vaccinations."

Kelly Patricia O'Meara. Vaccines may fuel autism epidemic. Insight on the News, 24 June – 7 July, 2003, Volume 19, pgs 24-27.

"According to Len Lavenda, a spokesman for Aventis Pasteur, 'The current package insert does not accurately reflect what is being marketed.'"

"The Indian Congressman [Dan Burton] continues, 'One reason this isn't getting the attention it needs is that the Food and Drug Administration has very close ties to the pharmaceutical companies, as does the Department of Health and Human Services [HHS] and the Centers for Disease Control and Prevention. I've said in the past that in some cases it appears that it's a revolving door and people leave government health agencies and go to work for the pharmaceuticals, which I think have undue influence on our health agencies. Of course, they may not want to look at this because there's a possibility that large claims would be filed and the pharmaceutical companies would have to cough up the money to take care of these kids who have been damaged.'"

Rep. Dr. Dave Weldon (Fla-R)'s letter of 31 October 2003 To Dr. Julie Gerberding, Director, CDC

"I have read the upcoming Pediatrics study and several earlier versions of this study dating back to February 2000. I have read various emails from Dr. Verstraeten and coauthors. I have reviewed the transcripts of a discussion at Simpsonwood, GA between the author, various CDc employees, and vaccine industry representatives. I found a disturbing pattern which merits a thorough, open, timely, and independent review by researchers outside of the CDC, HHS, the vaccine industry, and others with a conflict of interest in vaccine related issues (including many in University settings who may have conflicts."

"A review of these documents leaves me very concerned that rather than seeking to understand whether or not some children were exposed to harmful levels of mercury in childhood vaccines in the 1990s, there may have been a selective use of data to make the associations in the earliest study disappear."

"This study increases speculation of an association between TCVs [Thimerosal-containing vaccines] and neurodevelopmental outcomes. I cannot say it was the author's intent to eliminate the earlier findings of an association. Nonetheless, the elimination of this association is exactly what happened and the manner in which this was achieved raises speculation. The dialogue at the Simpsonwood meeting clearly indicates how easily the authors could manipulate the data and have reasonable sounding justifications for many of their decisions."

The End