

Facility Automation Management Engineering (FAME) Systems

33 Hoffman Avenue, Lake Hiawatha, NJ 07034

Wednesday, 5 October 2005

To Whom It May Concern:

The review that follows this introductory letter is a critical assessment of the information published by the Centers for Disease Control and Prevention (CDC) published at <http://www.cdc.gov/flu/about/qa/thimerosal.htm> on 22 September 2005, which I visited as a part of my research in this area on 25 September 2005.

In general, to clearly differentiate between my assessment comments and those of the CDC, the CDC's printed statements are quoted in a "Times New Roman" font followed by this reviewer's remarks in an indented "Nimrod" font.

In cases where there is an important spelling or grammatical error, that error is noted by using a parenthesized "sic; *correction*" text "(sic; xxxx)" insertion placed immediately after the error.

Quotes from general reference articles and documents will be presented in an "Arial" font; and federal laws and statutes will be quoted in a "Lydian" font.

~~For those who have access to a color printer, this reviewer's comments are made in a blue color with text needing correction in red. [Revised 12 Oct. 2005]~~

Should anyone find any factual misrepresentations in this reviewer's remarks, then this reviewer requests that the factual error along with the scientifically sound and appropriate documents that prove your point to this reviewer so that this reviewer can learn from you, incorporate that new knowledge into his understanding, and, where indicated, appropriately correct this document.

Respectfully,



Paul G. King, PhD, MS, BA
Founder, **F.A.M.E. Systems**

“Questions & Answers: Thimerosal-Containing Influenza Vaccine

September 22, 2005”

“Updated: September 22, 2005

What is thimerosal?

Thimerosal is a very effective preservative that has been used since the 1930s to prevent contamination in some multi-dose vials of vaccines (preservatives are not required for vaccines in single dose vials).”

Thimerosal is not *per se* a preservative.

Thimerosal is a highly toxic, organic mercury compound¹ that: a) is a systemic poison and b) has, since 1968 if not before, been illegally² used as a preservative in some vaccines.

Its illegal use as a preservative in vaccines is explicitly the case because the scientifically sound and appropriate toxicology studies required to prove “Any preservative used shall be sufficiently nontoxic so that the amount present in the recommended dose of the product will not be toxic to the recipient” (added to the Federal Food, Drug, and Cosmetic Act in the 1968 amendments thereto), have, as the FDA admits and the record demonstrates³, never been conducted.

Moreover, in a 1948 Journal of the American Medical Association (JAMA) paper, Harry E. Morton et al.⁴ clearly established that Thimerosal was not suitable for use as a vaccine preservative, but this definitive finding has been knowingly ignored by both the vaccine makers and the FDA from the day it was published until the present.

Considering Dr. Morton’s findings, CDC, why is Thimerosal still allowed to be used in any vaccine manufacturing process?

“Thimerosal contains approximately 49% ethylmercury.”

The CDC is again mistaken.

¹ See APPENDIX A: “Abbreviated Material Safety Data Sheet” for Thimerosal.

² Thimerosal has been illegally used as a preservative since 1968 when the FDA enacted regulations requiring a compound to be proven safe, (21 CFR 610.15(a):

“TITLE 21 --FOOD AND DRUGS. CHAPTER I--FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH AND HUMAN SERVICES PART 610--GENERAL BIOLOGICAL PRODUCTS STANDARDS Subpart B--General Provisions
Sec. 610.15 Constituent materials.

(a) Ingredients, preservatives, diluents, adjuvants. All ingredients used in a licensed product, and any diluent provided as an aid in the administration of the product, shall meet generally accepted standards of purity and quality. **Any preservative used shall be sufficiently nontoxic so that the amount present in the recommended dose of the product will not be toxic to the recipient**, and in the combination used it shall not denature the specific substances in the product to result in a decrease below the minimum acceptable potency within the dating period when stored at the recommended temperature. ...” before use as a preservative.

³ According to the web page <http://cerhr.niehs.nih.gov/CERHRchems/index.html>, contains Thimerosal, CAS 54-64-8, was not nominated by the FDA to have its toxicity appropriately studied until “11/99.” However, that proposed study’s status was changed to “Nomination Deferred” in “7/00” because there were “Chemicals with higher priorities” for, given the studies that were allowed to proceed, no scientifically sound reason.

⁴ Harry E. Morton, Leon L. North and Frank D. Engley, “THE BACTERIOSTATIC AND BACTERIOCIDAL ACTIONS OF SOME MERCURIAL COMPOUNDS ON HEMOLYTIC STREPTOCOCCI In Vivo and in Vitro Studies,” *JAMA* 136(1), pp 37-41 (1948).

Factually, Thimerosal contains, by weight, 49.55% mercury⁵ and about 56.73% “ethylmercury.”

“There is no convincing evidence of harm caused by the low doses of thimerosal in vaccines, except for minor reactions like redness and swelling at the injection site.”

Yet again, the CDC is mistaken.

First, Thimerosal, at the levels found in today’s Thimerosal-containing vaccines, has been documented to cause severe adverse reactions, including, but not limited to, anaphylactic shock and death in “sensitive” individuals^{6,7} – apparently the CDC conveniently overlooked these major reactions.

In addition, contrary to the CDC’s statements, the “convincing evidence of harm caused by the low doses of” Thimerosal in Thimerosal-preserved vaccines is extensive⁸ and growing⁹

“However, in July 1999 the Public Health Service (PHS) agencies, the American Academy of Pediatrics (AAP), and vaccine manufacturers agreed that thimerosal should be reduced or eliminated in vaccines as a precautionary measure.”

This reviewer finds that the CDC’s statement here is almost correct.

Factually the “9 July 1999” joint statement said: (with bolding added for emphasis)

“Nevertheless, **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.

PHS and AAP are working collaboratively to assure that the replacement of thimerosal-containing vaccines takes place as expeditiously as possible while at the same time ensuring that our high vaccination coverage levels and their associated low disease levels throughout our entire childhood population are maintained.”

In spite of the phrases, “as soon as possible” and “as expeditiously as possible,” as well as a commitment to remove all “thimerosal-containing vaccines” in these expedited time frames, more than six (6) years later, at least eight (8) “Thimerosal Preserved” vaccines and nine (9) “Reduced Thimerosal” vaccines are still FDA-licensed to be manufactured and distributed for use in the U.S. today.

⁵ 12th Edition of the **Merck Index, 9451** [col. 1, pg. 1590] (1996)).

⁶ Lars Forstrom, M. Hannuksela, Merja Kousa and E. Lehmuskallio, “Merthiolate hypersensitivity and vaccination,” **Contact Dermatitis, 6**, pages 241-245 (1980).

⁷ Cox NH, Forsyth A. Thimerosal allergy and vaccination reactions. *Contact Dermatitis* 1988;18:229-33.

⁸ The supporting references for Thimerosal toxicity in the Citizen Petition, **2004P-0349**, published by the FDA in their Public Dockets on Wednesday, 4 August 2004.

⁹ “Updated Publications List That Supports The Proposition: Thimerosal Causes Mercury Poisoning,” published, located or revisited since June 2004, are listed in **Appendix B**.

What is the CDC's justification for these realities?

As of 6 September 2005, CDER Vaccine Thimerosal web page¹⁰ shows that the vaccine manufacturers are now shipping seven (7) "Thimerosal Preserved" vaccine products into the North American market:

- All of the multi-dose vials of Aventis Pasteur, Incorporated's "Meningococcal" vaccine, Menomune®,
- Aventis Pasteur, Limited's multi-dose "DT" vaccine,
- Mass Public Health's "Td" vaccine
- Aventis Pasteur, Incorporated's "TT" vaccine,
- Most lots of Aventis Pasteur, Incorporated's "Influenza" vaccine, Fluzone,
- Most lots of Chiron/Evans' "Influenza" vaccine, Fluvirin, and
- BIKEN's, "Japanese Encephalitis" vaccine, JE-VAX, which is distributed by Aventis Pasteur, Incorporated,

along with eight (8) "Trace Thimerosal"¹¹ and one (1) "Near-Trace"¹² Thimerosal" vaccine products:

- Aventis Pasteur, Incorporated's "DTaP" vaccine, Tripedia,
- Aventis Pasteur, Incorporated's "DTaP-Hib" vaccine, Trihibit,
- GlaxoSmithKline's "DTaP-HepB-IPV" vaccine, Pediarix,
- Aventis Pasteur, Incorporated's single-dose "DT" vaccine,
- Aventis Pasteur, Incorporated's "Td" vaccine, Decavac,
- GlaxoSmithKline's "Hepatitis B" vaccine, Engerix-B,
- GlaxoSmithKline's "HepA/HepB" vaccine, Twinrix,
- GlaxoSmithKline's "Near Trace Influenza" vaccine, Fluarix, and
- The "Preservative Free" lots of Chiron/Evans' "Influenza" vaccine, Fluvirin.

Based on the preceding realities and the time elapsed, this reviewer finds that seemingly none of the parties to this notice have made a serious attempt to honor the "as soon as possible" and "as expeditiously as possible" commitments they made.

"Today, all routinely recommended licensed pediatric vaccines that are currently being manufactured for the U.S. market, with the exception of influenza vaccine, contain no thimerosal or only trace amounts."

¹⁰ <http://www.fda.gov/cber/vaccine/thimerosal.htm>

¹¹ According to the FDA's 2000 definition, a "Trace Thimerosal" vaccine is any vaccine that nominally contains *not more than* 1 µg/0.5-mL dose.

¹² A "Near-Trace Thimerosal" vaccine is any vaccine that nominally contains **not** more than 1.25 µg/0.5-mL dose (this reviewer's definition).

This reviewer finds, while this statement is almost¹³ true, the CDC's statement is an attempt to draw the reader away from the reality that not only are at least eight "Thimerosal Preserved" vaccines still licensed for use in the U.S. but there are also some in-date lots in the U.S. distribution chain for various previously licensed, but now "discontinued (in the U.S., at least), "Thimerosal Preserved" vaccines, which, based on the commitment made in 1999 and the continuing stream of pronouncements by CDC and FDA officials, officials, should not be available for administration in the U.S. today, but still are being administered because they are within their expiration dating period.

Five (5) of the eight (8) FDA-licensed "Thimerosal Preserved" vaccines are routinely administered to children under the age of eighteen years of age.

Furthermore, though all vaccine manufacturers have been required by law, since 1968, to prove, *using appropriate scientifically sound toxicology studies*, Thimerosal is safe for use as a preservative before putting it in any vaccine², neither the vaccine makers nor the federal government has, to date¹⁴, conducted and published the requisite studies, rendering all "Thimerosal Preserved" vaccines adulterated by statute (21 U.S.C. 351(a)(2)(B)) and illegal to be sold to and/or administered to humans or animals – an issue to which the government has obviously turned a "blind eye."

That the Public Health Service, CDC and the FDA have no latitude in complying with this statutory mandate, law or binding policy was clearly established in a unanimous 1988 Supreme Court case, *Kevan BERKOVITZ, et al., v. USA* [108 S.Ct. 1954, 100 L.Ed.2d 531, 56 USL W 4549 (Cite as: 486 U.S. 531, 108 S.Ct. 1954)], where the Court held that an federal administrator has no discretion in complying with any statute, regulation, or policy that specifically prescribes a course of action for a federal employee to follow.

Furthermore, it has been recently reported on the electronic media that, in the 1970's, Eli Lilly personnel found that Thimerosal in vaccine formulations was toxic at the "1 ppm level."

Given this report, how does the CDC continue to claim that "Thimerosal Preserved" and vaccines containing 1ppm or more Thimerosal are safe?

"Thimerosal preservative-free influenza vaccines are available, but in limited quantities. The total amount of inactivated influenza vaccine available without thimerosal as a preservative will continue to increase as manufacturing capabilities are expanded."

This reviewer can attest to the limited availability of "Thimerosal preservative-free influenza vaccines."

¹³ Technically, GlaxoSmithKline's recently licensed Influenza vaccine, Fluarix™, nominally contains more than a "trace amount"¹⁰ of Thimerosal but meets the definition (**Footnote 11**) that this reviewer has generated.

¹⁴ According to the web page <http://cerhr.niehs.nih.gov/CERHRchems/index.html>, of mid-September 2005, containing Thimerosal, CAS 54-64-8, was not nominated by the FDA to have its toxicity appropriately studied until "11/99." However, that proposed study's status was changed to "Nomination Deferred" in "7/00" because there were "Chemicals with higher priorities" for, given the studies that were allowed to proceed, no scientifically sound reason.

However, this reviewer finds the CDC's "will continue to increase as manufacturing capabilities are expanded" clearly confirms the knowing failure of the "vaccine manufacturers" to honor the commitment they made in 1999.

"Updated: September 14, 2004

Does the influenza vaccine contain thimerosal?

Yes, the majority of influenza vaccines distributed in the United States currently contain thimerosal as a preservative."

Again, this reviewer notes that, under law, all such vaccines are adulterated under 21 U.S.C. 351(a)(2)(B) and are, thus, illegal to be sold to or administered to humans or animals.

Can the CDC explain to the American public why they support administering adulterated vaccines to humans and animals?

"However, some contain only trace amounts of thimerosal and are considered by the Food and Drug Administration (FDA) to be preservative-free."

The decision of the FDA to allow the use of the obviously deceptive term, "preservative-free," which they knew, or should have known, would be perceived by the public to be the same as "Thimerosal-free," because of the CDC's and FDA's knowingly misleading statement, used in this document and others, "Thimerosal is a ... preservative ..." [Note: The preceding statement is misleading because Thimerosal is not a preservative – it has only been misused⁴ as a preservative since 1935.]

Furthermore, proof of long-term toxicological safety is also required under 21 U.S.C. 351(a)(2)(B) for any drug, including vaccine, formulations that contain any level of the highly toxic¹, bio-accumulative systemic poison, Thimerosal (49.55% mercury by weight) in such formulations and, as far as this reviewer has been able to ascertain, the requisite proofs of safety have not provided.

Finally, any vaccine that contains less than 0.003% Thimerosal is "preservative-free" because 0.003% is the lowest nominal Thimerosal level that the FDA recognizes for the Thimerosal present in the vaccine formulation to qualify that formulation as being "Thimerosal Preserved." [Note: Because of recognized mercury toxicity at 0.1%¹⁵, 0.01% Thimerosal is the nominal maximum amount that can be added to a formulation. However, a test result of up to 125% of that level is allowed for a given multi-dose or single-dose container.]

"Manufacturers of preservative-free flu vaccine use thimerosal early in the manufacturing process. The thimerosal gets diluted as the vaccine goes through the steps in processing. By the end of the manufacturing process there is not enough thimerosal left in the vaccine to act as a preservative and the vaccine is labeled 'preservative-free'."

¹⁵ D. G. Fagan, J. S. Pritchard, Thomas W. Clarkson and M. R. Greenwood, "Organ mercury levels in infants with omphaloceles treated with organic mercurial antiseptic," *Archives of Disease in Childhood*, 52, pages 962-964 (1977).

While this reviewer understands the CDC's rationale here, this reviewer is compelled to again ask, why is a vaccine containing any level of a highly toxic¹, bio-accumulative systemic poison, Thimerosal (49.55% mercury by weight) being introduced into commerce without proving that such vaccines do not mercury poison those who receive them every year for 75 to 80-plus years, in appropriate, scientifically sound, long-term, toxicology studies, at a level 10,000 times (an appropriate safety level for an unnecessary¹⁶ component that remains in such reduced-Thimerosal vaccines)?

Why, CDC, aren't such vaccines also "adulterated" within the meaning of that term as expressed in 21 U.S.C. 351(a)(2)(B)?

"Updated: September 22, 2005

Is influenza vaccine that does not contain thimerosal as a preservative available this flu season (2005-2006)?

For the 2005-06 flu season, a limited amount of influenza vaccine that does not contain thimerosal as a preservative is available. Sanofi pasteur estimates that they will produce 6-8 million doses of thimerosal-free vaccine this year."

Thus, practically speaking, less than 8 million doses will be available to vaccinate the babies 6 months to 4 years because only the Sanofi-pasteur vaccine is approved for this age group.

Since there are more than 16 million children in this group and the first vaccination is supposed to be dosed twice with a 30-day interval between doses, the need for the 6-months-to-4-years group is more than 20 million doses.

Based on the preceding, even if the use of this vaccine could be restricted to that age group, less than 20 % of the most at risk children could be vaccinated with this Thimerosal-free vaccine.

Since some of the more than 52 million in the 4-to-18-year age group, or the parents of children in this age group, and some of the more than 210 million in the 18-and-older age group will want a Thimerosal-free influenza vaccination, and, therefore, these groups will compete with the 6-months-to-4-years age group for this vaccine, the actual percentage of the total group that could be vaccinated with this Thimerosal-free sanofi-pasteur vaccine will probably be less than 3% of the number who could be inoculated with this Thimerosal-free vaccine.

Moreover, given the recently published review article¹⁷, that established that the influenza vaccination is no more effective than a placebo vaccination in preventing a child 2 years and under from getting the flu, what is the CDC's justification for recommending vaccinating such children when the vaccine will not effectively prevent them from getting the flu?

¹⁶ There are other compounds that are not highly toxic, bio-accumulative systemic poisons that can be, have been, and are being, successfully used as preservatives in vaccines (e.g., 2-phenoxyethanol).

¹⁷ Jefferson T, Smith S, Demicheli V, Harnden A, Rivetti A, Di Pietrantonj C. Assessment of the efficacy and effectiveness of influenza vaccines in healthy children: systematic review. Lancet 2005;365:773-80.

Does the CDC really want to mercury poison all the children 2 and under who get a “Thimerosal Preserved” flu shot?

Doesn't giving children 2 years and under a single flu vaccine (12.5 micrograms of mercury from Thimerosal) exceed the daily intake on that day for such children (0.1 microgram per kilogram of body weight per day¹⁸) unless the child weighs more than 125 kg (276 pounds)?

How many children 2 and under weigh 125-kg?

What about those two and under who get 2 doses of a Thimerosal-preserved flu vaccine, how many of these weigh more than 250 kg (551 pounds)?

“GlaxoSmithKline projects that they will produce 8 million doses of preservative-free vaccine for use in people 18 years of age and over. A minimal number of preservative-free vaccine may be available from Chiron late in the influenza season.”

Since there are more than 210 million in the 18-and-over age group, less than 4 % of this age group will be able to get this “preservative-free” vaccine even if they wanted it.

This means that about 200 million Americans in the 18-and-over age group will be either not getting vaccinated or being injected with 25 micrograms of mercury from Thimerosal.

Unless these people weigh more than 250 kg (551 pounds) and have had no previous mercury exposure risk (from air, water, food, dental amalgams, and prior vaccinations), these people will be similarly exceeding the 0.1 microgram of mercury per kilogram of body weight per day¹⁸ on the day they are vaccinated.

Also, the nasal-spray influenza vaccine (sold commercially as FluMist®) does not contain any thimerosal and can be given to healthy people 5 to 49 years of age who are not pregnant.

While this reviewer recognizes that the FluMist flu vaccine is as described.

However, this reviewer has serious reservations about giving anyone this vaccine.

This is the case because, according to the “Information for Vaccine Recipients or Parents/Guardians” section of the package insert¹⁹, after the vaccine is administered, the recipients or their parents/guardians are “advised that vaccine recipients should avoid close contact (e.g., within the same household) with immunocompromised individuals for at least 21 days.”

¹⁸ Based on the published work of Burbacher et al (Thomas M. Burbacher, Danny D. Shen, Noelle Liberato, Kimberly S. Grant, Elsa Cernichiari, and Thomas Clarkson, “Comparison of Blood and Brain Mercury Levels in Infant Monkeys Exposed to Methylmercury or Vaccines Containing Thimerosal,” *Environ Health Perspect* **113**, pages 1015-1021 (2005)) [see also Appendix B, B-24], if anything, Thimerosal is significantly more than twice as toxic, long-term, as “methyl mercury” ingested in the form of methylmercurihydroxide in the Burbacher study.

¹⁹ In the proposed 2005-2006 package insert (booklet) that is published at: <http://www.flumist.com/pdf/prescribinginfo.pdf>; on page 10, lines 302-304.

Thus, after being administered FluMist, the recipient “should avoid close contact with” anyone for at least 21 days lest that contact person be an “immunocompromised individual” and get the flu from the person who has been treated with FluMist.

Thus, for 21 days, the recipient is a “Typhoid Mary” spreading the FluMist flu to those with whom he or she comes into “close contact.”

Since, outside of the recipient’s immediate family, the recipient does not know the immune status of those with whom he or she might may come into “close contact,” the recipient should voluntarily enter a three-week quarantine period where he or she does not go to school or work or play with any one else.

Since most recipients cannot afford to miss school or work for three weeks, it is absurd to expect voluntary compliance by all the recipients.

Thus, the manufacturer, with the blessing of the CDC and the FDA, is marketing a vaccine that, in immunizing the recipient, not only gives the recipient the flu, but, like the live polio vaccine, also puts the public at risk of being given the flu by the recipient for some time (21 days in this case).

Is the increasing use of this vaccine, perhaps, one of the reasons that the influenza rates have been increasing since FluMist was introduced?

Is it really a good idea, CDC, to create hundreds of thousands of “Typhoid Mary” carriers who, because the majority will ignore the quarantine recommendation, may then infect some of those they come into contact with in any crowded environment?

Won’t those so infected then infect some others?

Is the CDC, as it appears, trying to increase the incidence of flu by supporting the use of a live-virus vaccine, FluMist, which gives the people a “mild flu” to “protect” them from getting a “worse” flu?

Moreover, this reviewer is concerned about the risk that a person treated with FluMist, which (based on the need for quarantine) is easily transmitted from person to person, will be, in turn, exposed to the “bird flu” that currently is hard to transmit to humans and a mutated strain will be formed that has the virulence of the “bird flu” and the “person to person” transmissibility of FluMist.

CDC and FDA, is that what you two are trying to do – increase the risk of the formation of a strain of “bird flu” that is easily transmitted from person to person?

If not, the license for this live-virus vaccine should be revoked until the manufacturer can prove that the live strains cannot, under any circumstances, interact with the “bird flu” in the manner suggested by this reviewer. [Note: To the extent that this reviewer understands what is currently doable in the area of the genetic manipulation of the flu viruses, the alterations required to effect the desired blocks to triggering such a mutation are at the cutting edge of the applicable science, if not outside of that edge, and, *even if they are possible*, the costs would render this already significantly more expensive vaccine cost prohibitive.]

Why has the government again allowed such an inherently risky vaccine to be licensed?

Didn't the harm caused (to those who came into close contact with inoculated individuals, their wastes, or sewage containing their wastes) by the live poliovirus vaccine teach the CDC and the FDA anything about the risks inherent to vaccines containing strains of a live-virus that is inherently more than capable of mutating?

“Updated: September 22, 2005

Is it safe for children to receive an influenza vaccine that contains thimerosal?

Yes. There is no convincing evidence of harm caused by the small amount of thimerosal in vaccines, except for minor effects like swelling and redness at the injection site due to sensitivity to thimerosal.”

This reviewer finds the CDC's answer not only patently false but also deliberately misleading.

As previously stated, Thimerosal has long been known to trigger immediate Thimerosal-triggered severe adverse reactions, including anaphylaxis and death, in some persons inoculated with a Thimerosal-containing vaccine^{6,7}.

In addition, Thimerosal has been confirmed to be toxic at the “parts-per-billion level” ($\leq 0.00001\%$ Thimerosal) by S. Makani et al (2004)²⁰, and Mostafa Waly et al (2004)²¹ (at 10 nanomoles per liter [4 ng per mL {0.0000004%}] or, in other words, below 200 ng of mercury from Thimerosal per milliliter of solution [or gram of tissue]).

Since nominally an additional 12.5, 25, or, worst case (a child who has never been vaccinated for flu and is old enough to get two, 25-microgram/0.5mL doses within 30 days of each other), 50 micrograms of Thimerosal mercury are injected each time a “Thimerosal Preserved” vaccine is administered to a some individuals who, because mercury bio-accumulates, may already have a significant mercury load and, for whatever reasons, a reduced excretion ability, why isn't it obvious, CDC, that this vaccination schedule is, to varying degrees, clinically mercury poisoning some of those so treated and sub-clinically poisoning all of the others whenever a “Thimerosal Preserved” flu vaccine is administered?

“Most importantly, since 1999, newly formulated thimerosal preservative-free childhood vaccines (Hepatitis B, Hib, and DTaP) have been licensed. With the newly formulated childhood vaccines, the maximum total exposure during the first six months of life will now be less than three micrograms of mercury.

²⁰ S. Makani, Sastry Gollapudi, Leman Yel, Shubpa Chiplunkar and Sudhir Gupta, “Biochemical and molecular basis of thimerosal-induced apoptosis in T Cells: a major mole of mitochondrial pathway,” *Genes and Immunity*, 3(5), pages 270-278 (2002).

²¹ Mostafa Waly, Horatiu Olteanu, Ruma Banerjee, Sang-Woon Choi, Joel B. Mason, Belinda S. Parker, Saraswati Sukumar, S. Shim, Alok Sharma, Jorge M. Benzecry, V.-A. Power-Charnitsky and Richard C. Deth, **IMMEDIATE COMMUNICATION**, “Activation of methionine synthase by insulin-like growth factor-1 and dopamine: a target for neurodevelopmental toxins and thimerosal,” *Molecular Psychiatry*, pages 1-13 (January 27, 2004). [Confirmation of Thimerosal Effects at Parts per Billion]

When the “Thimerosal Preserved” flu shot is added, as the CDC’s guidelines suggest at 6 months and the maximum total exposure computed with this flu shot, the maximum total is nominally less than 15.5 micrograms of Thimerosal mercury, an amount that, *on the day a “Thimerosal Preserved” flu shot is given*, will exceed 12.5 micrograms – an amount that is only “safe,” on that day, for a 125-plus kilogram child.

Since the body’s capacity to intercept Thimerosal and its “ethyl mercury” metabolite, and excrete them before they or their breakdown products can be non-reversible incorporated into the body’s various tissues as “bound inorganic mercury” is a finite unknown, the larger the bolus dose relative to the guessed-at “safe” level, the greater the risk to the child for to be clinically mercury poisoned.

This is the case because, *based on other studies*, the half-life of this bound inorganic mercury is on the order of two to three decades.

Thus, not only will the mercury poisoning persist but, once the child’s mercury elimination mechanisms are compromised by the initial mercury poisoning, the body’s capacity to excrete mercury and other heavy metals is also further impaired.

“Based on guidelines established by the FDA, the Environmental Protection Agency (EPA) and the Agency for Toxic Substances and Disease Registry (ATSDR), no child will receive excessive mercury from childhood vaccines regardless of whether or not their flu shot contains thimerosal as a preservative.”

This reviewer gain notes that none of these guideline values, “established by the FDA, the Environmental Protection Agency (EPA) and the Agency for Toxic Substances and Disease Registry (ATSDR),” are, as required by law, based on appropriate, scientifically sound, rigorous, long-term, repeated-annual-bolus dosing of a “Thimerosal Preserved” flu vaccine.

Further, these guideline values seem to be mostly, or completely, based on studies of the levels of mercury exposure and residual post-putative-exposure mercury levels in adults.

Because: a) the bioaccumulative “inorganic mercury” that forms from the Thimerosal injected has a half-life in the brain that exceeds the childhood (> 18 years) of the children being injected with Thimerosal-containing vaccines, b) Thimerosal (see Appendix B, reference B-1) and Thimerosal’s end-stage “inorganic mercury” (see Footnote 8’s Reference 9) have been shown to be toxic to living human brain and/or skin cells at levels below or at 20 parts per billion (20 micrograms per kilogram), and c) the CDC does not know what each child’s background mercury burden is, the CDC has no proof to substantiate their claim, “no child will receive excessive mercury from childhood vaccines regardless of whether or not their flu shot contains thimerosal as a preservative.”

Furthermore, since there are young children who have been medically diagnosed with mercury intoxication (poisoning) who were not breast fed nor consumers of fish but were injected with “Thimerosal Preserved” vaccines while their non-injected counterparts, raised in the same environment do not exhibit any of the symptoms of mercury poisoning, the reality must be that

these were poisoned by the mercury in their “Thimerosal Preserved” vaccines.

Since: a) these have been proven to be so poisoned, b) the requisite scientifically sound and appropriate toxicological studies, including bolus-dosing to determine the safe level for Thimerosal in individuals having a normal background dietary and environmental exposure to mercury, with a safety margin of at least 10X at the preservative level, have not been published and c) the scheduled government-funded studies have been blocked (see Footnote 14), how can the CDC know, unless they are omniscient, that administering a “Thimerosal Preserved” vaccine to children will mercury poison “no child”?

“Recent research suggests that healthy children under the age of 2 are more likely than older children and as likely as people over the age of 65 to be hospitalized with flu complications. Therefore, vaccination with reduced or standard thimerosal-content flu vaccine is encouraged when feasible in children, including those that are 6-23 months of age.”

Since previous (see Footnote 16) and recent²² published research has shown that the influenza vaccine provides marginal or no protection from contracting the flu, what has hospitalization rates to do with protecting the inoculee from getting and/or transmitting the disease, flu in this case, which is supposed to be the justification for administering the vaccine to any one?

If a vaccine is not truly effective, for those 2 and under or those over 65 and, as the CDC admits, each vaccination carries with it dangers (including, in this case, mercury poisoning from up to 25 micrograms of mercury from Thimerosal), then how can the CDC justify their administration recommendation?

Or is the CDC’s goal, as it seems to this reviewer, simply to further poison Americans with Thimerosal (49.55% mercury) since that is all the vaccine appears to do for those 2 and under, and, apparently, for those over 65?

“Updated: September 14, 2004

Is it safe for pregnant women to receive an influenza vaccine that contains thimerosal?
Yes.”

This reviewer cannot agree with the CDC because:

- After a thorough review of the body of scientific data and reconsideration of that data when a pharmaceutical manufacturer appealed the state’s finding, California found Thimerosal to be a reproductive hazard falling under California’s Proposition 65 statutes.
- The U.S. Registry of the Toxic Effects of Chemical Substances (RTECS) contains the following entries that bear on the toxicity of Thimerosal
 - “EFFECTS ON FERTILITY (POST-IMPLANTATION MORTALITY)”;
 - “EFFECTS ON FERTILITY (ABORTION)”;
 - “EFFECTS ON EMBRYO OR FETUS (FETAL DEATH)”;

²² Jefferson T, Rivetti D, Rivetti A, Rudin M, Di Pietrantonj C, Demicheli V. Efficacy and effectiveness of influenza vaccines in elderly people: A systemic review. *Lancet*. 2005 Sep 22; Early Online Publication.

- “TUMORIGENIC EFFECTS (UTERINE TUMORS)”;
 - “TUMORIGENIC (NEOPLASTIC BY RTECS CRITERIA)”;
 - “TUMORIGENIC (TUMORS AT SITE OF APPLICATION).”
- **In a 1987 article titled, “LEATHALITY AND TERATOGENICITY OF ORGANIC MERCURY (THIMEROSAL) ON THE CHICK EMBRYO,” Asima Digar et al (see APPENDIX B, Reference B-3) found that 100 micrograms of Thimerosal per egg injected into 254 fertile eggs at days 1, 2, 3, 4, 10 and 11 of incubation and harvested at day 19 was sufficient to kill “46.46%” (118) of the treated embryos and induce gross visible malformations in apparently “36.03%” (49) of the ones that survived to the harvest date. These data clearly indicate that Thimerosal is a teratogen (mutation-causing) agent at the “2 ppm” level. This is the case because, based on weight data for eggs in the U.S.²³, the content of the eggs weighed between 50 and 70 grams and 100 micrograms of Thimerosal were injected into this closed system. Unfortunately, no microscopic examination data are available to examine changes at the cellular level. Based on the content weight information for American eggs, one may presume that the concentration of the Thimerosal in this closed system was between 1.4 and 2.0 micrograms per gram (ppm) Thimerosal (0.7 to 1 ppm mercury) – levels that could be reached on the developing fetus whenever the mother’s circulating organic mercury level exceeds 1 ppm (1 µg per gram). For women with a significant circulating background mercury level from their diet, Rho shots (about 50% of children with DSM IV “autism” are born to Rh-negative mothers) and their dental amalgam fillings, a significant number of pregnant women injected with an additional 25 micrograms of Thimerosal mercury from a “Thimerosal Preserved” influenza vaccination will, for some period of time, have circulating levels of mercury which exceed the 0.3 ppm level.**
 - **In addition, a published review²⁴ of the information on the influenza vaccine reported:**
 - “In fact, for the 2003-04 flu season, the CDC reported ‘only 3 to 14% of those who got vaccinated were protected against the flu.’”
 - “Few doctors realize that most flu vaccines contain 25 micrograms of mercury per dose. Both the EPA and FDA’s allowable daily exposure limits are 0.1 microgram per kg, meaning that recipients of a flu vaccine must weigh at least 551 pounds to meet federal exposure guidelines. Therefore, by injecting the mother, the fetus would receive a dose of mercury that exceeds the federal limits by several hundred-fold. Furthermore, ..., all federal guidelines are based upon studies of exposure tolerances in adults, not a fetus.”
 - “Manufacturers of the flu vaccine themselves, include package inserts that admit adequate studies have not been conducted on this vaccine. For example, the Fluzone insert stated: ‘Animal reproduction studies have not been conducted with Influenza Virus Vaccine. It is not known whether Influenza Virus Vaccine can

²³ http://www.sizes.com/food/chicken_eggs.htm

²⁴ <http://www.scoop.co.nz/stories/HL0503/S00089.htm>

cause fetal harm when administered to a pregnant woman or can affect reproduction capacity.’”

Based on: a) the preceding findings, b) the confirmation that Thimerosal-derived mercury readily crosses the placental barrier (see Reference B-4 in APPENDIX B) and seems to build up in fetal tissues, c) the absence of scientifically sound and appropriate animal reproduction studies on Thimerosal or the vaccines, normally required for drugs administered to women and d) in light of the build up of protein-bound “inorganic mercury” in the brains of baby monkeys found by Thomas Burbacher et al (see Footnote 18), how can the CDC, in good conscience, continue to recommend giving the “Thimerosal Preserved” influenza vaccine unless the CDC does not care that, *to some degree*, the 25-micrograms of Thimerosal injected will contribute to the long-term mercury poisoning of that fetus?

“A study of influenza vaccination examining over 2,000 pregnant women demonstrated no adverse fetal effects associated with influenza vaccine.”

Citing the referenced study, “Heinonen OP, Shapiro S, Monson RR, Hartz SC, Rosenberg L, Slone D. Immunization during pregnancy against poliomyelitis and influenza in relation to childhood malignancy. Int J Epidemiol 1973;2:229–35,” is problematic because that epidemiological study was primarily concerned with addressing the issues of childhood malignancy and not mercury poisoning.

On this basis and in the absence of appropriate animal reproduction studies, how is the failure to elicit excess childhood malignancies pertinent to the issue of mercury poisoning of the brain and other organs?

“Case reports and limited studies indicate that pregnancy can increase the risk for serious medical complications of influenza.

One study found that out of every 10,000 women in their third trimester of pregnancy during an average flu season, 25 will be hospitalized for flu related complications.”

While these findings are factual, they ignore the following realities:

- **There is no proof that these 25 “out of every 10,000 women in their third trimester of pregnancy during an average flu season” had, or will actually have, influenza**
- **Anecdotal “case reports and limited studies” are insufficient to reach any population conclusion, including “pregnancy can increase the risk for serious medical complications of influenza,” because, given the numbers of cases and the size of the studies, the findings reported may have occurred by chance.**
- **Vaccination with the influenza vaccine is not nearly 100% effective in protecting the person vaccinated from getting influenza.**

Given: a) the preceding realities, b) the fact that most doses of the influenza vaccine are “Thimerosal Preserved,” c) in the absence of the requisite animal reproductive studies, and d) the proven reproductive toxicity of Thimerosal, this reviewer must again ask, how can the CDC recommend giving the “Thimerosal Preserved” influenza vaccine to pregnant women?

“Additionally, influenza-associated excess deaths among pregnant women have been documented during influenza pandemics.”

Since there is no proof that these “influenza-associated excess deaths among pregnant women” were caused by influenza or that, absent the influenza, these deaths would not have occurred, this reviewer must reject the CDC’s assertions as more “wishful thinking” than anything else.

“Because pregnant women are at increased risk for influenza-related complications and because a substantial safety margin has been incorporated into the health guidance values for organic mercury exposure, the benefits of influenza vaccine with reduced or standard thimerosal content outweighs the theoretical risk, if any, of thimerosal.

First, this reviewer finds that the CDC has failed to provide any scientifically sound proof, *not speculation*, that “pregnant women are at increased risk for influenza-related complications” or, more importantly, that influenza-vaccinated pregnant women have significantly less risk of “influenza-related complications” than their unvaccinated counterparts.

Second, based on recent evidence and the reported 1971 findings by Eli Lilly that Thimerosal was toxic at the 1-ppm level, the level of Thimerosal in a “Thimerosal Preserved” vaccine, 100 ppm, is 100 times that putative toxic level indicating that no real “safety margin has been incorporated into the health guidance values for organic mercury exposure.”

Since there are no proven “benefits of influenza vaccine with reduced or standard thimerosal content,” these unproven benefits cannot be used to overcome the proven mercury poisoning risk to the mother and her fetus associated with Thimerosal.

Finally, if nothing else, until the requisite scientifically sound and appropriate (21 CFR 610.15(a)) Thimerosal toxicity studies, including the appropriate multi-year long-term toxicity studies, and animal reproductive studies have been conducted and it has been proven that removing the Thimerosal from the influenza vaccine does not reduce the severity of adverse reactions observed (as required by 42 U.S.C. 300aa-27), the CDC’s recommendation that an adulterated drug be given to pregnant women, or for that matter, anyone seems to be an illegal act on their part.

CONCLUDING COMMENT

Hopefully, the CDC will provide this reviewer, and the readers of this review, with scientifically sound and factual studies that address the toxicity and risk issues as well as the court case citations that establish that the CDC, FDA and/or the vaccine manufacturers are not bound by the U.S. policies, laws and statutes governing vaccines, in specific, and drugs, in general.

APPENDIX A

“Abbreviated Material Safety Data Sheet”

SECTION 1. CHEMICAL IDENTIFICATION

NAME: THIMEROSAL

SECTION 2. COMPOSITION/INFORMATION ON INGREDIENTS

CAS #: 54-64-8 Molecular Formula: C₉H₉HGNAO₂S EC NO: 200-210-4

SYNONYMS:

((O-CARBOXYPHENYL)THIO)ETHYLMERCURY SODIUM SALT, ETHYLMERCURITHIOSALICYLIC ACID SODIUM SALT, MERTHIOLATE SODIUM, MERTORGAN, MERZONIN, MERZONIN SODIUM, SODIUM ETHYLMERCURIC THIOSALICYLATE, SODIUM O-(ETHYLMERCURITHIO) BENZOATE, SODIUM ETHYLMERCURITHIOSALICYLATE, SODIUM MERTHIOLATE, THIMEROSAL, THIMEROSALATE, THIOMERSAL, THIOMERSALATE *

SECTION 3. HAZARDS IDENTIFICATION

LABEL PRECAUTIONARY STATEMENTS

HIGHLY TOXIC (USA); VERY TOXIC (EU); VERY TOXIC BY INHALATION, IN CONTACT WITH SKIN AND IF SWALLOWED; DANGER OF CUMULATIVE EFFECTS; MAY CAUSE SENSITIZATION BY INHALATION AND SKIN CONTACT, IRRITATING TO EYES; RESPIRATORY SYSTEM AND SKIN; CALIF. PROP. 65 REPRODUCTIVE HAZARD.

TARGET ORGAN(S): NERVES, KIDNEYS, *GUT, SKIN, LIVER, PANCREAS, SPLEEN, GLANDS, ETC.*

SENSITIZER; CAUSES IRRITATION.

KEEP AWAY FROM FOOD, DRINK AND ANIMAL FEEDINGSTUFFS.

AFTER CONTACT WITH SKIN, WASH IMMEDIATELY WITH PLENTY OF WATER.

IN CASE OF CONTACT WITH EYES, RINSE IMMEDIATELY WITH PLENTY OF WATER AND SEEK MEDICAL ADVICE.

WEAR SUITABLE PROTECTIVE CLOTHING.

IN CASE OF ACCIDENT OR IF YOU FEEL UNWELL, SEEK MEDICAL ADVICE IMMEDIATELY (SHOW THE LABEL WHERE POSSIBLE).

SECTION 4. FIRST-AID MEASURES

IF SWALLOWED, WASH OUT MOUTH WITH WATER PROVIDED PERSON IS CONSCIOUS.

CALL A PHYSICIAN IMMEDIATELY.

IF INHALED, REMOVE TO FRESH AIR. IF NOT BREATHING GIVE ARTIFICIAL RESPIRATION; IF BREATHING IS DIFFICULT, GIVE OXYGEN.

IN CASE OF SKIN CONTACT, FLUSH WITH COPIOUS AMOUNTS OF WATER FOR AT LEAST 15 MINUTES. REMOVE CONTAMINATED CLOTHING AND SHOES. CALL A PHYSICIAN.

IN CASE OF CONTACT WITH EYES, FLUSH WITH COPIOUS AMOUNTS OF WATER FOR AT LEAST 15 MINUTES. ASSURE ADEQUATE FLUSHING BY SEPARATING THE EYELIDS WITH FINGERS. CALL A PHYSICIAN.

SECTION 5. FIRE FIGHTING MEASURES

...

SECTION 6. ACCIDENTAL RELEASE MEASURES

WEAR SELF-CONTAINED BREATHING APPARATUS, RUBBER BOOTS AND HEAVY RUBBER GLOVES. SWEEP UP, PLACE IN A BAG AND HOLD FOR WASTE DISPOSAL. AVOID RAISING DUST. VENTILATE AREA AND WASH SPILL SITE AFTER MATERIAL PICKUP IS COMPLETE. EVACUATE AREA.

SECTION 7. HANDLING AND STORAGE

REFER TO SECTION 8.

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

SAFETY SHOWER AND EYE BATH. USE ONLY IN A CHEMICAL FUME HOOD. WASH CONTAMINATED CLOTHING BEFORE REUSE. WASH THOROUGHLY AFTER HANDLING. DO NOT BREATHE DUST. DO NOT GET IN EYES, ON SKIN, ON CLOTHING. AVOID PROLONGED OR REPEATED EXPOSURE. NIOSH/MSHA-APPROVED RESPIRATOR. COMPATIBLE CHEMICAL-RESISTANT GLOVES. CHEMICAL SAFETY GOGGLES. KEEP TIGHTLY CLOSED. STORE IN A COOL DRY PLACE.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AND ODOR: SOLID.

PHYSICAL PROPERTIES: MELTING POINT: 234 C, FLASHPOINT >482F (>250C)

SOLUBILITY: 1g in mL of water; 8 mL of ethanol; **SPECIFIC GRAVITY:** 0.5 G

APPENDIX A

"Abbreviated Material Safety Data Sheet"

SECTION 10. STABILITY AND REACTIVITY

STABILITY: STABLE.

CONDITIONS TO AVOID: MAY DISCOLOR ON EXPOSURE TO LIGHT.

INCOMPATIBILITIES: STRONG OXIDIZING AGENTS, STRONG ACIDS, STRONG BASES.

HAZARDOUS COMBUSTION OR DECOMPOSITION PRODUCTS: CARBON MONOXIDE, CARBON DIOXIDE, MERCURY, MERCURY OXIDES, AND SULFUR OXIDES.

HAZARDOUS POLYMERIZATION: WILL NOT OCCUR.

SECTION 11. TOXICOLOGICAL INFORMATION

ACUTE EFFECTS:

CAUSES SKIN IRRITATION.

MAY BE FATAL IF ABSORBED THROUGH SKIN.

CAUSES EYE IRRITATION.

MAY BE FATAL IF INHALED.

MATERIAL IS IRRITATING TO MUCOUS MEMBRANES AND UPPER RESPIRATORY TRACT.

MAY BE FATAL IF SWALLOWED.

POSSIBLE ALLERGIC REACTION TO DUST IF INHALED, INGESTED OR IN CONTACT WITH THE SKIN. HYPERSENSITIVITY REACTIONS MANIFESTED BY ERYTHEMA, PAPULAR OR VESICULAR ERUPTIONS OCCUR OCCASIONALLY. ALLERGIC CONJUNCTIVITIS HAS BEEN REPORTED.

TO THE BEST OF OUR KNOWLEDGE, THE CHEMICAL, PHYSICAL, AND TOXICOLOGICAL PROPERTIES HAVE NOT BEEN THOROUGHLY INVESTIGATED.

CHRONIC EFFECTS:

TARGET ORGAN(S): NERVES, KIDNEYS, ETC.

RTECS #: OV8400000 MERCURY, ((O-CARBOXYPHENYL)THIO)ETHYL-, SODIUM SALT

IRRITATION DATA: EYE-RABBIT: 8 µg mild AJOPAA 78,98,1974

TOXICITY DATA:

IAL-CHD LDLO:	60 mg/kg/4W-I	JOPDAB	104,311,1984
ORL-RAT LD50:	75 mg/kg	PCOC**	-,1130,1966
SCU-RAT LD50:	98 mg/kg	CTOXAO	4,185,1971
UNR-RAT LD50:	40 mg/kg	30ZDA9	-,290,1971
ORL-MUS LD50:	91 mg/kg	NYKZAU	58,235,1962
IPR-MUS LD50:	54 mg/kg	NYKZAU	58,235,1962
SCU-MUS LD50:	66 mg/kg	QJPPAL	12,212,1939
IVN-MUS LD50:	45 mg/kg	QJPPAL	12,212,1939

TARGET ORGAN DATA:

BRAIN AND COVERINGS (OTHER DEGENERATIVE CHANGES); BEHAVIORAL (ANOREXIA, HUMAN); BEHAVIORAL (CHANGE IN MOTOR ACTIVITY); BEHAVIORAL (ATAXIA); BEHAVIORAL (COMA); LUNGS, THORAX OR RESPIRATION (OTHER CHANGES); GASTROINTESTINAL (NAUSEA OR VOMITING); KIDNEY, URETER, BLADDER (CHANGES IN TUBULES); EFFECTS ON FERTILITY (POST-IMPLANTATION MORTALITY); EFFECTS ON FERTILITY (ABORTION); EFFECTS ON EMBRYO OR FETUS (FETAL DEATH); TUMORIGENIC EFFECTS (UTERINE TUMORS); NUTRITIONAL AND GROSS METABOLIC (CHANGES IN: METABOLIC ACIDOSIS); TUMORIGENIC (NEOPLASTIC BY RTECS CRITERIA); TUMORIGENIC (TUMORS AT SITE OF APPLICATION).

[NOTE: Note: ONLY SELECTED REGISTRY OF TOXIC EFFECTS OF CHEMICAL SUBSTANCES (RTECS) DATA IS PRESENTED HERE. SEE ACTUAL ENTRY IN RTECS FOR COMPLETE INFORMATION.]

SECTION 12. ECOLOGICAL INFORMATION: DATA NOT YET AVAILABLE.

SECTION 13. DISPOSAL CONSIDERATIONS

CONTACT A LICENSED PROFESSIONAL WASTE DISPOSAL SERVICE TO DISPOSE OF THIS MATERIAL.

DISSOLVE OR MIX THE MATERIAL WITH A COMBUSTIBLE SOLVENT AND BURN IN A CHEMICAL INCINERATOR EQUIPPED WITH AN AFTERBURNER AND SCRUBBER.

OBSERVE ALL FEDERAL, STATE AND LOCAL ENVIRONMENTAL REGULATIONS.

APPENDIX A

“Abbreviated Material Safety Data Sheet”

SECTION 14. TRANSPORT INFORMATION

...

SECTION 15. REGULATORY INFORMATION

EUROPEAN INFORMATION

EC INDEX NO: 080-004-00-7

VERY TOXIC

R 26/27/28 VERY TOXIC BY INHALATION, IN CONTACT WITH SKIN AND IF SWALLOWED.

R 33 DANGER OF CUMULATIVE EFFECTS.

R 50/53 VERY TOXIC TO AQUATIC ORGANISMS, MAY CAUSE LONG-TERM ADVERSE EFFECTS IN THE AQUATIC ENVIRONMENT.

S 13 KEEP AWAY FROM FOOD, DRINK AND ANIMAL FEEDINGSTUFFS.

S 28 AFTER CONTACT WITH SKIN, WASH IMMEDIATELY WITH PLENTY OF SOAP SUDS.

S 36 WEAR SUITABLE PROTECTIVE CLOTHING.

S 45 IN CASE OF ACCIDENT OR IF YOU FEEL UNWELL, SEEK MEDICAL ADVICE IMMEDIATELY (SHOW THE LABEL WHERE POSSIBLE).

S 60 THIS MATERIAL AND ITS CONTAINER MUST BE DISPOSED OF AS HAZARDOUS WASTE.

S 61 AVOID RELEASE TO THE ENVIRONMENT. REFER TO SPECIAL INSTRUCTIONS/SAFETY DATA SHEETS.

REVIEWS, STANDARDS, AND REGULATIONS

ACGIH TLV-TWA 0.1 MG(HG)/M3 (SKIN)

MSHA STANDARD-AIR:TWA 0.05 MG(HG)/M3

OSHA PEL (GEN INDU):8H TWA 0.01 MG(HG)/M3

OSHA PEL (CONSTRUC):8H TWA 0.01 MG(HG)/M3 (SKIN)

OSHA PEL (SHIPYARD):8H TWA 0.01 MG(HG)/M3 (SKIN)

OSHA PEL (FED CONT):8H TWA 0.01 MG(HG)/M3 (SKIN)

OEL-AUSTRALIA: TWA 0.05 MG(HG)/M3, SKIN, JAN1993

OEL-BELGIUM: TWA 0.05 MG(HG)/M3, SKIN, JAN1993

OEL-DENMARK: TWA 0.05 MG(HG)/M3, SKIN, JAN1999

OEL-FINLAND: TWA 1 MG(HG)/M3, JAN1999

OEL-FRANCE: VME 0.1 MG(HG)/M3, JAN1999

OEL-GERMANY: MAK 0.01 PPM (0.1 MG(HG)/M3), JAN1999

OEL-HUNGARY: TWA 0.02 MG(HG)/M3, STEL 0.04 MG(HG)/M3, JAN1993

OEL-JAPAN: OEL 0.05 MG(HG)/M3, JAN1999

OEL-THE NETHERLANDS: MAC-TGG 0.05 MG(HG)/M3, MAC-K 0.15 MG(HG)/M3, SKIN, JAN1999

OEL-NORWAY: TWA 0.05 MG(HG)/M3, JAN1999

OEL-THE PHILIPPINES: TWA 0.05 MG(HG)/M3, JAN1993

OEL-POLAND: MAC(TWA) 0.05 MG(HG)/M3, MAC(STEL) 0.15 MG(HG)/M3, JAN1999

OEL-RUSSIA: TWA 0.05 MG(HG)/M3, STEL 0.01 MG(HG)/M3, JAN1993

OEL-SWEDEN: NGV 0.05 MG(HG)/M3, SKIN, JAN1999

OEL-THAILAND: STEL 0.05 MG(HG)/M3, JAN1993

OEL-UNITED KINGDOM: LTEL 0.05 MG(HG)/M3, STEL 0.15 MG(HG)/M3, JAN1993

OEL IN ARGENTINA, BULGARIA, COLOMBIA, JORDAN, KOREA CHECK ACGIH TLV;

OEL IN NEW ZEALAND, SINGAPORE, VIETNAM CHECK ACGIH TLV

NIOSH REL TO MERCURY, ARYL AND INORGANIC-AIR:CL 0.1 MG/M3 (SK)

NIOSH* DHHS #92-100,1992

NOHS 1974: HZD 84569; NIS 83; TNF 5617; NOS 30; TNE 242717

NOES 1983: HZD 84569; NIS 32; TNF 3695; NOS 41; TNE 152997; TFE 114190

EPA GENETOX PROGRAM 1988, POSITIVE: S CEREVISIAE GENE CONVERSION

EPA TSCA SECTION 8(B) CHEMICAL INVENTORY

EPA TSCA TEST SUBMISSION (TSCATS) DATA BASE, JANUARY 2001

U.S. INFORMATION

THIS PRODUCT IS SUBJECT TO SARA SECTION 313 REPORTING REQUIREMENTS - MERCURY COMPOUNDS.

THIS PRODUCT IS A CHEMICAL KNOWN TO THE STATE OF CALIFORNIA TO CAUSE DEVELOPMENTAL TOXICITY.

SECTION 16. OTHER INFORMATION

APPENDIX B

“Updated Publications List That Supports The Proposition: Thimerosal Causes Mercury Poisoning”

Part A: Important Publications Including Those Found After July 2004

- B-1** Frank B. Engley, Jr. Mercurials as Disinfectants Evaluation of mercurial antimicrobial action and comparative toxicity. Soap and Chemical Specialties, 1956 Dec.:200, 201, 203, 205, 223, 224 and 225.

[Note: This was an excellent article that was fashioned from a presentation at the Chemical Specialties Manufacturing Association Meeting by Dr. Frank Engley earlier in 1956.] In the published paper, Dr. Engley comments:

"The problems involving the use of chemicals as anti-bacterial agents have been of particular interest to me as a bacteriologist ... Some ten years or more ago with Morton and North we were asked to carry out a study on mercurials for the Council on Pharmacy and Chemistry of the American Medical Association which was published in its journal in 1948. This report suggested that mercurials did not fulfill all the conditions expected of antiseptics...Unlike the theatrical or political figure who once said that it didn't matter what was written about him so long as they wrote something and spelled his name correctly-we in the field of scientific investigation would rather be quoted correctly than not at all. In this regard the report might not be the most misquoted or maligned report from certain quarters but it is in there with the best or the worst depending upon your point of view or the source of your income."

Then, he proceeds to describe the ineffectiveness of Thimerosal as a preservative in vaccines and other pharmaceutical products by stating:

"The use of mercurials as preservatives in vaccines and antisera is of considerable interest. These chemicals are added to protect against the introduction of organisms in multi-use containers in particular. We have always wondered about their efficacy in that both vaccines and antisera contain reactive groups to tie up these compounds. In a series of continuing experiments over the past several years we have begun to evaluate various preservatives in serum and vaccines under conditions of use. Employing stock vaccines and serum with and without preservatives and stored at varying lengths of time a contaminating dose of representative sporeformer (Bacillus subtilis) in the spore stage gram negative rod (E. coli) and gram positive coccus (S. aureus) were added. While the mercurial preservatives had good activity on initial addition, after storage of three, six or more months decreasingly less to negligible residual activity appeared to be left, indicating that the chemical was tied up by the protein of the biological of otherwise inactivated. A check on a series of over one thousand bottles of various biologicals from clinics obtained after use revealed that up to five percent contained micro-organisms. This would suggest that once these biologicals are in the hands of users a problem still exists. Regarding preservatives, one of the real problems existing in hospitals and clinics is the need for good preservatives in the routine eye dilators and nasal preparations of the decongestant type. Routine checks of these indicate a high percentage of contaminated solutions. In one instance we had direct evidence of upper respiratory cross-infection from the use of a common nasal dropper preparation in a clinic."

Dr. Engley then comments about the toxicity of mercurials such as Thimerosal by stating:

"The toxicity of chemicals used as drugs on or in the body has been of considerable interest since man first began exposing himself to various chemicals many years ago. Unfortunately there have not been good techniques for toxicity determinations of certain types of chemicals which might be really indicate of toxicity for humans...Graph 15 compares mercurial compounds and shows how they fit in with other compounds in toxicity...Mercurochrome appears to be the least toxic ranging down through Merthiolate" **(Merthiolate is another name for Thimerosal)** "...One point should be made here. Bichloride of mercury has always been pointed out as an extremely toxic mercurial and the organic mercurials were supposed to be much less toxic, but according to these data, we find bichloride right in the middle of the organic mercurials in regard to cell toxicity...mercurial antiseptics proved to be more toxic than the antibiotics in common usage..."

Also, Dr. Engley observed (see Graph 15) toxic effects for Thimerosal in his human tissue skin culture cell system at levels from 1 ppm of Thimerosal down to less than 15 parts-per-billion of Thimerosal. Specifically, he was able to show toxicity from Thimerosal at levels comparable to those in recent studies that have shown low parts-per-billion levels of Thimerosal are toxic (at 10 to 20 parts-per-billion of Thimerosal) to human cells almost 50 years before many of the current studies were published. Furthermore, the low parts-per-billion levels of Thimerosal that Dr. Engley observed to be toxic to human tissue culture cells are many-fold lower than the levels recently demonstrated by Burbacher et al (see reference B-24) to be present in the brain following injection of Thimerosal-containing

APPENDIX B

“Updated Publications List That Supports The Proposition: Thimerosal Causes Mercury Poisoning”

vaccines (age- and weight-adjusted) mirroring the US childhood vaccines schedule). One additional important point is that in Graph 16, Dr. Engley compares the relative toxicity of mercurials to various organs in the body including: cord, heart, spleen, and skin. He found that, among the organs of the body he tested, the cord (i.e. nervous system tissue) is, as we know, most sensitive organ to mercury (i.e. mercury was more toxic for the cord than for heart or spleen), and that the skin had a similar sensitivity to mercury intoxication as the cord.

- B-2** Undated, 7-page 1991 Merck memo: From: “Maurice R. Hilleman WP 26-200B”; To: “DR. DAVID GORDON RY 33-76”; Regarding: “VACCINE TASKFORCE ASSIGNMENT THIMEROSAL (MERTHIOLATE) PRESERVATIVE – PROBLEMS, ANALYSIS, SUGGESTIONS FOR RESOLUTION,” which: **a)** was discovered in a recent court case and **b)** clearly indicates that Merck had been aware of the excessive level of mercury being injected into babies for some time. This memo ends with the following two telling paragraphs in the postscript:
- “The seasoned conclusion Wigzell gives is, “Our opinion, however, is that the problems associated with the spread of mercury via vaccination are so minor that there is no reason to push a hastened solution.
- Note, however, that Wigzell mentions only Thimerosal-reserved DTP or DT given in at least 3 doses since the 1950s. Even with such small exposures, Sweden is moving as expeditiously as feasible to achieve a zero input of mercury from Thimerosal.”
- B-3** Digar A, Sensharma GC, Samal S. Lethality and teratogenicity of organic mercury (Thimerosal) on the chick embryo. *J Anat Soc India* 1987;36:153-9.
- B-4** Gasset AR, Itoi M, Ishii Y, Ramer RM. Teratogenicities of Ophthalmic Drugs II. Teratogenicities and Tissue Accumulation. *Arch Ophthalmol.* 1975 Jan;93:52-55.
- B-5** Oliver WT, Platonow N. Studies on the pharmacology of N-(ethylmercuri)-p-toluenesulfonanilide. *Am J Vet Res.* 1960 Sep;21:906-16.
- “This article shows dose dependent and outcomes specific to dosing level and repetition frequency. The apparent lack of clinical symptoms and non-lethality (within the 38-day period these animals were monitored) of a single 140 µg/Kg dose coupled with the rapid appearance of clinical symptoms and swift lethality (6 hours) after a single 224 µg/Kg dose indicates to this informed reviewer that humans and animals have varying abilities to intercept and protect critical systems from the clinical mercury poisoning and lethal effects of N-(ethylmercuri)-p-toluenesulfonanilide, which, when exceeded, lead to observable mercury-poisoning symptoms and animal death within 6 hours of dosing. Finally, this article clearly establishes that, outside of the “medical profession,” where various terms are used to disguise the disease, these researchers clearly recognized the disease as mercury poisoning.
- Another key finding was that, though the gross effects are the same, mercury poisoning, each compound has a slightly different modus operandi with respect to its specific pattern of poisoning.”
- B-6** Withrow TJ, Brown NT, Hitchins VM, Strickland AG. Cytotoxicity and Mutagenicity of Ophthalmic Solution Preservatives and UVA Radiation in L5178Y Cells. *Photochem Photobiol.* 1989 Sep;50(3):385-9.
- B-7** Westphal GA, Asgari S, Schulz TG, Bungler J, Muller M, Hallier E. Thimerosal induces micronuclei in the cytochalasin B block micronucleus test with human lymphocytes. *Arch Toxicol.* 2003 Jan;77(1):50-5.
- B-8** 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). *Mutat Res.* 2003 Jun 6;537(2):151-68.

APPENDIX B

“Updated Publications List That Supports The Proposition: Thimerosal Causes Mercury Poisoning”

Part B: Additional Key Publications From Mid-2004 To Mid-September 2005

- B-9** Gosselin NH, Brunet RC, Carrier G, LeBouchard M, Feeley M. Reconstruction of methylmercury intakes in indigenous populations from biomarker data, *J. Exposure Analysis and Environmental Epidemiology*. 2005 Jun 29;advance online publication: 1-11.

“Significant amounts of methylmercury (MeHg) can bioaccumulate in fish and sea mammals. To monitor MeHg exposure in individuals, organic and inorganic mercury are often measured in blood samples or in hair strands, the latter being by far the best integrator of past exposure. With knowledge of the MeHg kinetics in humans, the levels of both biomarkers can be related to MeHg body burden and intakes. In the present study, we use the toxicokinetic model of Carrier et al. (2001) describing the distribution and excretion of MeHg in humans, to reconstruct the history of MeHg intakes of indigenous women of the Inuvik region in Canada starting from total mercury concentrations in hair segments. From these reconstructed MeHg intakes, the corresponding simulated mercury blood concentrations are found to be good predictors of the concentrations actually measured in blood samples. **An important conclusion of this study is that, for almost all subjects, the reconstructed history of their MeHg intakes provides much lower intake values than intakes estimated from questionnaires on food consumption and estimated MeHg levels in these foods; the mean value of the reconstructed MeHg intakes is 0.03 mg/kg/day compared with the mean value of 0.20 mg/kg/day obtained from questionnaires.** The model was also used to back-calculate the MeHg intakes from concentrations in hair strands collected from aboriginals of the Amazon region in Brazil, a population significantly more exposed than the population of the Inuvik region.”

- B-10** Havarinasab S, Haggqvist B, Bjorn E, Pollard KM, Hultman P. Immunosuppressive and autoimmune effects of thimerosal in mice. *Toxicol Appl Pharmacol*. 2005 Apr 15;204(2):109-21.

This paper reports:

“With regard to the fraction of total mercury present as inorganic mercury after thimerosal treatment, Suzuki et al. (1973) reported 17–21% Hg²⁺ in the kidneys 6 days after a single injection of thimerosal. A similar fraction of Hg²⁺ was seen in the kidneys of our mice after 6 days continuous peroral treatment. **We found a maximum fraction of inorganic mercury (41%) after 14 days thimerosal treatment.** A comparable dose of Hg given as MeHg for up to 30 days caused a continuous increase in the fraction of inorganic mercury, which however reached only 22% after 30 days treatment (Haggqvist et al, unpublished observations). Finally, when equipotent doses of Hg were given as thimerosal or MeHg for up to 30 days, the maximum total kidney Hg concentration was higher after thimerosal as compared with MeHg treatment. **The presence of a substantial fraction of inorganic mercury in the tissues of thimerosal-treated mice, and the many similarities between the immunostimulation which develops after thimerosal treatment and primary treatment with inorganic mercury (Pollard and Hultman, 1997), indicates that inorganic Hg may be responsible for the immunostimulatory effect. The threshold for induction of HgIA using inorganic Hg is around 4 µg/g tissue (Hultman and Nielsen, 2001), a threshold which was rapidly reached in thimerosal-treated mice. However, this observation does not exclude the possibility that EtHg also contributed to the stimulatory effect.**

In conclusion, treatment of genetically metal-susceptible mice with the organic mercury compound thimerosal (EtHg) has initially a similar suppressive effect on the immune system as MeHg. However, **thimerosal treatment subsequently leads to strong immunostimulation and autoimmunity, which is at variance with only a weak autoimmune response after MeHg treatment.**

Suzuki, T., Takemoto, T.I., Kashiwazki, H., Miyama, T., 1973. Metabolic fate of ethylmercury salts in man and animal. In: Miller, M., Clarkson, T. (Eds.), *Mercury, Mercurials and Mercaptans*. Charles C. Thomas, Springfield, IL, pp. 209–232.

Pollard, K.M., Hultman, P., 1997. Effects of mercury on the immune system. In: Sigel, H., Sigel, A. (Eds.), *Mercury and Its Effects on Environment and Biology*. Marcel Dekker, Basel, pp. 421–440.

Hultman, P., Nielsen, J.B., 2001. The effect of dose, gender, and non-H-2 genes in murine mercury-induced autoimmunity. *J. Autoimmun.* 17, 27–37.”

Reviewer’s Observation:

This article clearly establishes that, unlike “MeHg” mercury poisoning, Thimerosal mercury poisoning includes a “strong immunostimulation and autoimmunity” component making it much less safe to use Thimerosal in drugs than it would be to use a “methylmercury”-releasing component in a drug formulation.

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- B-11** A Two-Phased Population Epidemiological Study of the Safety of Thimerosal-Containing Vaccines1.pdf in Adobe Acrobat Format Geier DA, Geier MR. A two-phased population epidemiological study of the safety of thimerosal-containing vaccines: a follow-up analysis. Med Sci Monit. 2005 Apr;11(4):CR160-70.

“Summary

Background: Thimerosal is an ethylmercury-containing preservative in vaccines. Toxicokinetic studies have shown children received doses of mercury from thimerosal-containing vaccines (TCVs) that were in excess of safety guidelines. Previously, an ecological study showing a significant association between TCVs and neurodevelopmental disorders (NDs) in the US was published in this journal.

Material/Methods: A two phased population-based epidemiological study was undertaken. Phase one evaluated reported NDs to the Vaccine Adverse Event Reporting System (VAERS) following thimerosal-containing Diphtheria-Tetanus-acellular-Pertussis (DTaP) vaccines in comparison to thimerosal-free DTaP vaccines administered from 1997 through 2001. Phase two evaluated the automated Vaccine Safety Datalink (VSD) for cumulative exposures to mercury from TCVs at 1-, 2-, 3-, and 6-months of-age for infants born from 1992 through 1997 and the eventual risk of developing NDs.

Results: Phase one showed significantly increased risks for autism, speech disorders, mental retardation, personality disorders, and thinking abnormalities reported to VAERS following thimerosal-containing DTaP vaccines in comparison to thimerosal-free DTaP vaccines. Phase two showed significant associations between cumulative exposures to thimerosal and the following types of NDs: unspecified developmental delay, tics, attention deficit disorder (ADD), language delay, speech delay, and neurodevelopmental delays in general.

Conclusions: This study showed that exposure to mercury from TCVs administered in the US was a consistent significant risk factor for the development of NDs. **It is clear from these data and other recent publications linking TCVs with NDs that additional ND research should be undertaken in the context of evaluating mercury-associated exposures and thimerosal-free vaccines should be made available.”**

Reviewer’s Observation:

Given the clear central-nervous-system-related mercury poisoning effects found for a single 50-microgram dose of Thimerosal, it should be obvious that the mercury-poisoning effects are stronger and more systemic when, as is the case, multiple 25- and 50- microgram doses were administered in the period from the late 1980’s to, for some U.S. children and most children in some developing countries, the present (mid-2000’s).

- B-12** Geier DA, Geier MR. Neurodevelopmental disorders following thimerosal-containing childhood immunizations: a follow-up analysis. Int J Toxicol. 2004 Nov-Dec;23(6):369-76.

“CONCLUSIONS

The present study provides additional epidemiological evidence linking thimerosal with neurodevelopmental disorders. From the late 1980s to the late 1990s, the level of thimerosal in childhood vaccinations based on the recommended vaccination schedule within the first 6 months of life increased from 75 μ grams of ethylmercury starting at 2 months (3 DTP vaccines at 25 μ grams of ethylmercury each) to approximately 200 μ grams of ethylmercury (three DTP vaccines [25 μ grams of ethylmercury each], three Hib vaccines [25 μ grams of ethylmercury each], three hepatitis B vaccines [12.5 μ grams of ethylmercury each], and in many children influenza vaccine [12.5 μ grams of ethylmercury]). ... It is clear that the results of the present study mandate that additional research should be undertaken, not only for autism, but (sic; but also) other childhood neurodevelopmental disorders, by evaluating childhood mercury-associated exposures, especially from thimerosal-containing childhood vaccines.”

Reviewer’s Observation:

Like the CDC, the author’s repeat the oft-made mistake of confusing the percentage of mercury by weight in Thimerosal, 49.55% (see Footnote 5), with the weight percentage of ethylmercury in Thimerosal, which is actually 56.73%. Otherwise, the authors’ conclusions as to the need for clinical research is right n the mark because a) the evidence of harm is clear and b) the requisite appropriate scientifically sound toxicology studies required by law (21 CFR 610.15(a)) have, as yet, not been conducted and/or published.

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B-13 James SJ, Cutler P, Melnyk S, Jernigan S, Janak L, Gaylor DW, Neubrandner JA. Metabolic biomarkers of increased oxidative stress and impaired methylation capacity in children with autism. *Am J Clin Nutr.* 2004 Dec;80(6):1611-7.

“ABSTRACT

Background: Autism is a complex neurodevelopmental disorder that usually presents in early childhood and that is thought to be influenced by genetic and environmental factors. Although abnormal metabolism of methionine and homocysteine has been associated with other neurologic diseases, these pathways have not been evaluated in persons with autism.

Objective: The purpose of this study was to evaluate plasma concentrations of metabolites in the methionine transmethylation and transsulfuration pathways in children diagnosed with autism.

Design: Plasma concentrations of methionine, S-adenosylmethionine (SAM), S-adenosylhomocysteine (SAH), adenosine, homocysteine, cystathionine, cysteine, and oxidized and reduced glutathione were measured in 20 children with autism and in 33 control children. On the basis of the abnormal metabolic profile, a targeted nutritional intervention trial with folinic acid, betaine, and methylcobalamin was initiated in a subset of the autistic children.

Results: Relative to the control children, the children with autism had significantly lower baseline plasma concentrations of methionine, SAM, homocysteine, cystathionine, cysteine, and total glutathione and significantly higher concentrations of SAH, adenosine, and oxidized glutathione. This metabolic profile is consistent with impaired capacity for methylation (significantly lower ratio of SAM to SAH) and increased oxidative stress (significantly lower redox ratio of reduced glutathione to oxidized glutathione) in children with autism. The intervention trial was effective in normalizing the metabolic imbalance in the autistic children.

Conclusions: An increased vulnerability to oxidative stress and a decreased capacity for methylation may contribute to the development and clinical manifestation of autism. ...

TABLE 1

Comparison of methionine cycle and transsulfuration metabolites between autistic children and control children¹

	Control Children (n = 33)	Autistic Children (n = 20)
Methionine (µmol/L)	31.5 ± 5.7 (23–48)	19.3 ± 9.7 (15–25) ²
SAM (nmol/L)	96.9 ± 12 (77–127)	75.8 ± 16.2 (68–100) ³
SAH (nmol/L)	19.4 ± 3.4 (16–27)	28.9 ± 7.2 (14–41) ²
SAM:SAH	5.2 ± 1.3 (4–8)	2.9 ± 0.8 (2–4) ²
Adenosine (µmol/L)	0.27 ± 0.1 (0.1–0.4)	0.39 ± 0.2 (0.17–0.83) ⁴
Homocysteine (µmol/L)	6.4 ± 1.3 (4.3–9.0)	5.8 ± 1.0 (4.0–5.8) ³
Cystathionine (µmol/L)	0.17 ± 0.05 (0.1–0.27)	0.14 ± 0.06 (0.04–0.2) ⁵
Cysteine (µmol/L)	202 ± 17 (172–252)	163 ± 15 (133–189) ²
tGSH (µmol/L)	7.6 ± 1.4 (3.8–9.2)	4.1 ± 0.5 (3.3–5.2) ²
Oxidized glutathione (nmol/L)	0.32 ± 0.1 (0.11–0.43)	0.55 ± 0.2 (0.29–0.97) ²
tGSH:GSSG	25.5 ± 8.9 (13–49)	8.6 ± 3.5 (4–11) ²

¹ All values are $\bar{x} \pm SD$; range in parentheses. SAM, S-adenosylmethionine;

SAH, S-adenosylhomocysteine; tGSH, total glutathione; GSSG, oxidized glutathione.

^{2–5} Significantly different from control children: ² P < 0.001, ³ P < 0.01, ⁴ P < 0.05, ⁵ P < 0.002.”

Reviewer’s Observations:

While this article points out the effects observed, it does not address the specific causal agent for the outcomes observed choosing instead to characterize it broadly as “oxidative stress.” Based on what this reviewer understands, the major cause of this “oxidative stress” is mercury poisoning of the enzymatic pathways that regulate the production and utilization of these key biochemicals.

B-14 Boris M, Goldblatt A, Galanko J, James SJ. Association of MTHFR gene variants with autism. *J Am Phys Surg* 2004;9:106-8.

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“ABSTRACT

Autism is a complex neurodevelopment disorder with numerous possible genetic and environmental influences.

We retrospectively examined the laboratory data of 168 children sequentially referred to our facility with a confirmed diagnosis of autism or pervasive developmental disabilities (PDD). Since folate and methylation (single carbon metabolism) are vital in neurological development, we routinely screened children for the common mutations of the methylenetetrahydrofolate reductase gene (MTHFR), which regulates this pathway. All children had polymerase chain reaction (PCR) DNA evaluation to determine the frequency of the 677 and 1298 common polymorphisms in the MTHFR gene.

We observed a significantly increased frequency of the homozygous mutation 677CT allele (TT): 23% in the autistic children compared to 11% in the control population ($P < 0.0001$). Additionally, the heterozygous 677CT allele (CT) was present in 56% of the autistic children compared to 41% in the control population ($P < 0.0001$). Somewhat paradoxically, the normal 1298AA allele was significantly higher in the autistic group, 55%, compared to the controls, 44% ($P < 0.05$). Despite the increased frequency of normal 1298AA alleles, the compound 677CT/1298AC heterozygous mutations were more prevalent in the autistic population, 25%, than in controls, 15% ($P = 0.01$).

Overall, the data show an increased risk of autism spectrum disorder (ASD) associated with common mutations affecting the folate/methylation cycle. These associations by themselves may provide a partial explanation for a subgroup of children genomically at risk for ASD disorders. Increased folic acid during pregnancy and early development may offset the genomic risk factors, and this deserves further study. Further, since folate-dependent methylation provides, in part, the methyl group for inactivation of monoamine neurotransmitters via the catecholamine-O-methyltransferase (COMT) system, this observation may help to further differentiate subtypes within the broad phenotype of ASD. A search for additional genomic and environmental risk factors should be undertaken. In particular, the methylation/transsulfation and COMT pathways should be investigated.”

Reviewer’s Observations:

While this article points out the genomic variabilities that may have some association with the causeless symptoms currently diagnosed as “autism,” it does not address the specific causal agent for the “autism.” Based on what this reviewer understands, the unstated cause of the “causeless” disorder, “autism,” is mercury poisoning and the correlations point to differences in the ability to resist being poisoned by the Thimerosal mercury in the vaccines injected into them from the day they were born.

- B-15** Environmental Working Group. Overloaded? New Science, New Insights about Mercury and Autism in Susceptible Children. Washington, DC: EWG Action Fund; Issued 13 December 2004. Published to the Internet on 3 march 2005 at:
http://www.ewg.org/reports/autism/execsumm.php?print_version=1

“Findings

An eighteen-month investigation by Environmental Working Group concludes that scientists have identified a signature metabolic profile or “biomarker” in autistic children that may indeed characterize a “small subset” of susceptible children. These findings represent a potential milestone in our understanding of individual vulnerability to toxic substances, including, but not limited to, mercury. This science turns on its head the IOM’s judgment that research into the thimerosal/autism link be abandoned, and instead strengthens significantly the case for additional research in this area. We found that:

- Newly published research and follow-up testing by former FDA senior research scientist Dr. Jill James, now of the University of Arkansas for Medical Sciences, has uncovered a unique and consistent metabolic imbalance in autistic children when compared to normal healthy children... This impairment manifests as a severe deficit in the body’s most important antioxidant and metals detoxifier, glutathione. When compared to normal health children, autistic children showed a significant impairment in every one of five measurements of the body’s ability to maintain a healthy glutathione defense. These findings are strong evidence that if these children were exposed to a potentially toxic dose of mercury or other compound they would be much less able to mount an effective defense...
- The finding of a significant glutathione deficit in autistic children provides a biological basis for integrating many facets of autism that have baffled researchers attempting to pin the autism epidemic on a single gene or chemical exposure.
- The implications of these findings extend well beyond thimerosal and autism. Reduced antioxidant defense may characterize a group of individuals who are demonstrably more sensitive to the effects of a

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range of toxic chemical exposures, and shed light on increasing rates of related learning and behavioral disorders.

- These findings raise serious concerns about the studies that have allegedly proven the safety of mercury in vaccines. While Dr. James' results do not prove that mercury causes autism, they significantly strengthen this possibility. The epidemiologic studies used to dismiss a causal relationship between mercury and autism assumed that all children have the same resistance to chemical exposure. Given James' finding that autistic children would be much more sensitive to certain chemical contaminants, studies that do not acknowledge these vulnerabilities cannot be used to dismiss the relationship between environmental chemicals, including mercury, and the disease.
- When James' results are considered together with the existing body of science, including other recently published research, the weight of the evidence now strongly supports increased research into the relationship between thimerosal and autism as well as other neurodevelopmental and neurodegenerative disorders.

Recommendations

Research

The findings by James significantly strengthen the science supporting a connection between mercury and autism. Contrary to the recommendation of the Institute of Medicine, that research on the relationship between mercury and autism essentially be abandoned, the weight of the evidence in the basic biological sciences now supports accelerated funding and research into the biological pathways and genetic mechanisms that may make some individuals more vulnerable to mercury and a host of other environmental toxins. We recommend increased federal support for research in this area.

A small follow-up group of children in this study have benefited markedly when their impaired antioxidant defense was restored. This provides important clues about treatments that could derive from increased funding for research in this area...

Several studies are underway to explore the relationship between thimerosal-containing vaccines and autism in greater detail—including a follow-up study underway by the CDC ... The power of these studies would be dramatically enhanced if they included Dr. James' simple blood test to examine the antioxidant capacity of autistic and healthy children as a factor that modifies an individual's sensitivity to mercury toxicity.

Policy Reform: Environmental Health

James' findings also have major implications for public health protections and pollution control. They potentially identify a subgroup of people with dramatically increased risk of harm from industrial chemicals, and provide important new evidence that policies designed to protect the average person, or even the average child, from chemical exposure, are insufficient to fully protect the public health. Children with the metabolic profile James has identified may be more susceptible to a vast number of common pollutants, from arsenic in drinking water and pressure-treated wood, to air pollution from cars and power plants. Environmental and health officials must evaluate the adequacy of current laws and policies to protect individuals with a heightened sensitivity to chemicals exposure.

Policy Reform: Immunizations

The Environmental Working Group strongly supports the standard battery of childhood immunizations recommended by the American Academy of Pediatrics and the CDC. Clearly, vaccinations have led to many major advances in public health. At the same time, EWG recommends the removal of thimerosal and all mercury-based preservatives from all

vaccines in the United States, as is currently required by law in California and Iowa.

As individual states and many industrialized countries have phased out or banned the use of the mercury-based preservative in vaccines, the use of immunizations preserved with thimerosal continues unabated in the developing world. Precisely because of the clear public health benefits of vaccinations, the limited access to refrigeration, and the need to deliver vaccines in multiple dose containers in these countries, we urge the World Health Organization and multinational drug companies to move quickly to develop and adopt an alternative, low cost, effective preservative that is safer than mercury-based thimerosal.”

Reviewer's Observation:

In general, this reviewer agrees with the findings and recommendations except that the long-term relationship that needs to be studied is the “relationship between Thimerosal-containing vaccines” and the mercury intoxication (poisoning) of all of those who are administered any such Thimerosal-containing vaccines.

B-16 McGinnis WR. Oxidative stress in autism. *Altern Ther Health Med.* 2004 Nov-Dec;10(6):22-36.

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“If we learn that oxidative stress is an important mechanism in autism, then our search for the genetic and environmental causes becomes much more focused. From the oxidative wounds, our science may more rapidly deduce the cause, treatment and prevention of autism.”

Reviewer’s Observations:

When these researchers recognize that mercury poisoning is the major cause of this “oxidative stress,” then perhaps, like this reviewer, they will understand that mercury poisoning is the “disease” and start studying all of the metabolic pathways damaged or corrupted by mercury. Hopefully, that day will come soon.

- B-17** Vojdani A, Pangborn JB, Vojdani E, Cooper EL. Infections, toxic chemicals and dietary peptides binding to lymphocyte receptors and tissue enzymes are major instigators of autoimmunity in autism. *Int J Immunopathol Pharmacol.* 2003 Sep-Dec;16(3):189-99. DG-IV-1

“Similar to many complex autoimmune diseases, genetic and environmental factors including diet, infection and xenobiotics play a critical role in the development of autism. In this study, we postulated that infectious agent antigens such as streptokinase, dietary peptides (gliadin and casein) and ethyl mercury (xenobiotic) bind to different lymphocyte receptors and tissue enzyme (DPP IV or CD26). We assessed this hypothesis first by measuring IgG, IgM and IgA antibodies against CD26, CD69, streptokinase (SK), gliadin and casein peptides and against ethyl mercury bound to human serum albumin in patients with autism. A significant percentage of children with autism developed anti-SK, anti-gliadin and casein peptides and anti-ethyl mercury antibodies, concomitant with the appearance of anti-CD26 and anti-CD69 autoantibodies. These antibodies are synthesized as a result of SK, gliadin, casein and ethyl mercury binding to CD26 and CD69, indicating that they are specific. Immune absorption demonstrated that only specific antigens, like CD26, were capable of significantly reducing serum anti-CD26 levels. However, for direct demonstration of SK, gliadin, casein and ethyl mercury to CD26 or CD69, microtiter wells were coated with CD26 or CD69 alone or in combination with SK, gliadin, casein or ethyl mercury and then reacted with enzyme labeled rabbit anti-CD26 or anti-CD69. Adding these molecules to CD26 or CD69 resulted in 28-86% inhibition of CD26 or CD69 binding to anti-CD26 or anti-CD69 antibodies. The highest % binding of these antigens or peptides to CD26 or CD69 was attributed to SK and the lowest to casein peptides. We, therefore, propose that bacterial antigens (SK), dietary peptides (gliadin, casein) and Thimerosal (ethyl mercury) in individuals with pre-disposing HLA molecules, bind to CD26 or CD69 and induce antibodies against these molecules. In conclusion, this study is apparently the first to demonstrate that dietary peptides, bacterial toxins and xenobiotics bind to lymphocyte receptors and/or tissue enzymes, resulting in autoimmune reaction in children with autism.”

Reviewer’s Observations:

While this reviewer understands the validity of the researchers’ findings, he hopes that, in future studies, these researchers will do similar studies on: a) a matched group of comparably Thimerosal-containing-vaccine vaccinated children that are not children with autism, and b) a matched control group of unvaccinated children to separate out the issues as to which is the major causative factor or factors for the immune responses observed. Based on the existing body of evidence, Thimerosal in Thimerosal-containing vaccines seems to be the primary immune/autoimmune triggering agent.

- B-18** Parran DK, Barker A, Ehrich M. Effects of Thimerosal on NGF Signal Transduction and Cell Death in Neuroblastoma Cells. *Toxicol Sci.* 2005 Jul;86(1):132-40.

“Signaling through neurotrophic receptors is necessary for differentiation and survival of the developing nervous system. The present study examined the effects of the organic mercury compound thimerosal on nerve growth factor signal transduction and cell death in a human neuroblastoma cell line (SH-SY5Y cells). Following exposure to 100 ng/ml NGF and increasing concentrations of thimerosal (1 nM–10 mM), we measured the activation of TrkA, MAPK, and PKC-d. In controls, the activation of TrkA MAPK and PKC-d peaked after 5 min of exposure to NGF and then decreased but was still detectable at 60 min. Concurrent exposure to increasing concentrations of thimerosal and NGF for 5 min resulted in a concentration-dependent decrease in TrkA and MAPK phosphorylation, which was evident at 50 nM for TrkA and 100 nM for MAPK. Cell viability was assessed by the LDH assay. Following 24-h exposure to increasing concentrations of thimerosal, the EC₅₀ for cell death in the presence or absence of NGF was 596 nM and 38.7 nM, respectively. **Following 48-h exposure to increasing concentrations of thimerosal, the EC₅₀ for cell death in the presence and absence of NGF was 105 nM and 4.35 nM, respectively.** This suggests that NGF provides protection against thimerosal cytotoxicity. To determine if apoptotic versus necrotic cell death was occurring, oligonucleosomal fragmented DNA was quantified by ELISA. Control levels of

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fragmented DNA were similar in both the presence and absence of NGF. With and without NGF, thimerosal caused elevated levels of fragmented DNA appearing at 0.01 mM (apoptosis) to decrease at concentrations >1 mM (necrosis). These data demonstrate that thimerosal could alter NGF-induced signaling in neurotrophin-treated cells at concentrations lower than those responsible for cell death. ...

In light of the proclivity of thimerosal to bind any protein containing sulfhydryl groups, it is likely that the effects of thimerosal on differentiation are the result of multiple sites of action. A comparison of the effective concentration at these various sites will be necessary to determine the critical actions of thimerosal, which ultimately result in the disruption of differentiation.”

Reviewer’s Observations:

While this reviewer supports the validity of the researchers’ findings here, this reviewer finds that to put things in perspective, the researchers could have also expressed their findings in terms of that relate the level at which significant toxicity were found to the level of Thimerosal in “Thimerosal Preserved” vaccines so that the average reader could more easily see the relative toxicity levels for the experiments to the vaccine levels. Since, in the absence of added nerve growth factor (NFG), the researchers reported, *after 48-hours of incubation*, a calculated “EC50 for cell death” Thimerosal concentration of “4.35 nM” or 4.35×10^{-9} moles of Thimerosal per liter of solution [4.35×10^{-12} moles of Thimerosal (x 404.82 g of Thimerosal per mole of Thimerosal) per milliliter (mL) of solution] or 1.76×10^{-9} g of Thimerosal per mL [1.76 parts-per-billion Thimerosal or 0.872 ppb mercury from Thimerosal. Thus, these researchers have established a 48-hour toxicity to the cell system for levels less than (<) 2 ppb Thimerosal or less than (<) 1 ppb mercury. Since, in ng per mL (ppb), the nominal level of Thimerosal in a “Thimerosal Preserved” vaccine containing 0.01% Thimerosal is 100,000 ppb, the level in such vaccines is > 56,800 times the toxic level found by these researchers. For a 0.5-mL dose, 50,000 ng of Thimerosal are injected into each person. Even assuming a uniform distribution in the person receiving the vaccine, to reduce the dose to below the toxic level found here, the recipient would have to weigh more than 28.4 kg (62.6 pounds). In the real-world case where the Thimerosal injected accumulates in brain and other lipid-rich cells, the probable minimum recipient weight for a 50,000 ng bolus of Thimerosal to be safe is at least 5 times the modeled level or 142 kg (313 pounds). In any case, injecting 25,000 ng (in the 0.25-mL dose given to babies 6-months and younger) into young children only begins to be truly safe when their weight significantly exceeds 14.2 kg (31.3 pounds) and most 6-month-old and younger children weigh less than half this value – clearly indicating that a single 0.25-mL injection of a Thimerosal-preserved vaccine significantly mercury poisons those to whom it is given. Based on this data, at birth, where babies weighing as little as 1 kg (2.2 pounds), the safe level of Thimerosal, setting a 10-x safety factor, in such vaccines would be less than 0.17 microgram of Thimerosal in a 0.5-mL dose of vaccine or, < 0.3 ppm Thimerosal (< 0.15 ppm mercury).

- B-19** Humphrey ML, Cole MP, Pendergrass JC, Kiningham KK. Mitochondrial Mediated Thimerosal-induced Apoptosis in a Human Neuroblastoma Cell Line (SK-N-SH). *Neurotoxicology*. 2005 Jun;26(3):407-16.

“Environmental exposure to mercurials continues to be a public health issue due to their deleterious effects on immune, renal and neurological function. Recently the safety of thimerosal, an ethyl mercury-containing preservative used in vaccines, has been questioned due to exposure of infants during immunization. Mercurials have been reported to cause apoptosis in cultured neurons; however, the signaling pathways resulting in cell death have not been well characterized.

Therefore, the objective of this study was to identify the mode of cell death in an in vitro model of thimerosal-induced neurotoxicity, and more specifically, to elucidate signaling pathways which might serve as pharmacological targets.

Within 2 h of thimerosal exposure (5 μ M) to the human neuroblastoma cell line, SK-N-SH, morphological changes, including membrane alterations and cell shrinkage, were observed. Cell viability, assessed by measurement of lactate dehydrogenase (LDH) activity in the medium, as well as the 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide (MTT) assay, showed a time- and concentration-dependent decrease in cell survival upon thimerosal exposure. In cells treated for 24 h with thimerosal, fluorescence microscopy indicated cells undergoing both apoptosis and oncosis/necrosis. To identify the apoptotic pathway associated with thimerosal-mediated cell death, we first evaluated the mitochondrial cascade, as both

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inorganic and organic mercurials have been reported to accumulate in the organelle. Cytochrome c was shown to leak from the mitochondria, followed by caspase 9 cleavage within 8 h of treatment. In addition, poly(ADP-ribose) polymerase (PARP) was cleaved to form a 85 kDa fragment following maximal caspase 3 activation at 24 h. Taken together these findings suggest deleterious effects on the cytoarchitecture by thimerosal and initiation of mitochondrial-mediated apoptosis. ...

In summary, we have shown that thimerosal can cause mitochondrial-mediated apoptosis in a human neuroblastoma cell line. To our knowledge, this is the first study to chronologically show the mitochondrial, cytosolic and nuclear events associated with thimerosal-mediated toxicity in a non-differentiated neuronal system. Although thimerosal has been shown to alter redox status, further evaluation will be required to determine the effect, if any, these alterations have on the cascade of events reported in this study.”

Reviewer’s Observation:

This article has shed more light on the cellular pathways by which this systemic mercury poison, Thimerosal, poisons intracellular components and reinforces how insidious mercury poisoning is at the cellular level.

- B-20** James SJ, Slikker W 3rd, Melnyk S, New E, Pogribna M, Jernigan S. Thimerosal Neurotoxicity is Associated with Glutathione Depletion: Protection with Glutathione Precursors. *Neurotoxicology*. 2005 Jan;26(1):1-8.

“Thimerosal is an antiseptic containing 49.5% ethyl mercury that has been used for years as a preservative in many infant vaccines and in flu vaccines. Environmental methyl mercury has been shown to be highly neurotoxic, especially to the developing brain. Because mercury has a high affinity for thiol (sulfhydryl (–SH)) groups, the thiol-containing antioxidant, glutathione (GSH), provides the major intracellular defense against mercury-induced neurotoxicity. Cultured neuroblastoma cells were found to have lower levels of GSH and increased sensitivity to thimerosal toxicity compared to glioblastoma cells that have higher basal levels of intracellular GSH. Thimerosal-induced cytotoxicity was associated with depletion of intracellular GSH in both cell lines. Pretreatment with 100 mM glutathione ethyl ester or Nacetylcysteine (NAC), but not methionine, resulted in a significant increase in intracellular GSH in both cell types. Further, pretreatment of the cells with glutathione ethyl ester or NAC prevented cytotoxicity with exposure to 15 µM Thimerosal. Although Thimerosal has been recently removed from most children’s vaccines, it is still present in flu vaccines given to pregnant women, the elderly, and to children in developing countries. The potential protective effect of GSH or NAC against mercury toxicity warrants further research as possible adjunct therapy to individuals still receiving Thimerosal-containing vaccinations. ...

In summary, we have shown that human glioblastoma cells are more resistant to Thimerosal cytotoxicity than neuroblastoma cells at doses in the low micromolar range and that the resistance is correlated with higher intracellular levels of intracellular glutathione. The significant protection by NAC and glutathione ethyl ester against Thimerosal cytotoxicity suggests the possibility that supplementation with glutathione precursors might be protective against mercury exposures in vivo. Numerous clinical studies have demonstrated the efficacy of NAC in increasing intracellular glutathione levels and reducing oxidative stress in humans ... Since cytotoxicity with both ethyl- and methylmercury have been shown to be mediated by glutathione depletion, dietary supplements that increase intracellular glutathione could be envisioned as an effective intervention to reduce previous or anticipated exposure to mercury. This approach would be especially valuable in the elderly and in pregnant women before receiving flu vaccinations, in pregnant women receiving Rho D immunoglobulin shots, and individuals who regularly consume mercury-containing fish.”

Reviewer’s Observations:

This reviewer supports the scientific conclusions reached by the authors with respect to Thimerosal cytotoxicity and immediate protection by glutathione and glutathione precursors. This reviewer has reservations about the supplementation strategy unless it is long term and coupled with supplements that promote the “sequestering” and “elimination” of the protein-bound inorganic mercury that forms from the metabolism of the “ethylmercurihydroxide” metabolite of Thimerosal and, to a lesser extent, from the metabolism of the methylmercury compound present in fish and other ingested foods. Furthermore, this reviewer finds the authors’ statement, “Although Thimerosal has been recently removed from most children’s vaccines, it is still present in flu vaccines given to pregnant women, the elderly, and to children in developing countries,” to be inaccurate because it fails to note that Thimerosal, at some level, is present in most of the doses of the flu vaccine that given to children as well as more than a half-dozen other in-date U.S.-licensed vaccines that are or

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may be administered to children under the age of 18 on the US, including at least three (3) “Thimerosal Preserved” vaccines.

- B-21** Mutkus L, Aschner JL, Syversen T, Shanker G, Sonnewald U, Aschner M. In Vitro Uptake of Glutamate in GLAST- and GLT-1-Transfected Mutant CHO-K1 Cells Is Inhibited by the Ethylmercury-Containing Preservative Thimerosal. *Biol Trace Elem Res.* 2005 Summer;105(1-3):71-86.

“In summary, we detail the effects of thimerosal on mRNA and protein expression of the predominately astrocytic glutamate transporters GLAST and GLT-1 in a transfected mutant CHO-K1 cell line DdB7. The results indicate that thimerosal is a potent inhibitor of transport activity as measured by D-aspartate uptake. This effect is more pronounced in GLT-1-transfected cells, and it occurs in the presence of selective changes in mRNA and protein expression of GLAST and GLT-1. Given the differential effects on transporter expression, the most likely explanation for the potent inhibitory effects of thimerosal on glutamate transport in CHO cells is a direct inhibitory effect of ethylmercury on transporter activity. Overall, the study provides direct evidence for the potential of thimerosal to alter glutamate homeostasis ...”

Reviewer’s Observation:

The importance of this article is that it again shows that “Thimerosal” is disruptive to processes in the central nervous system.

- B-22** Morita M, Higuchi C, Moto T, Kozuka N, Susuki J, Itofusa R, Yamashita J, Kudo Y. Dual Regulation of Calcium Oscillation in Astrocytes by Growth Factors and Pro-Inflammatory Cytokines via the Mitogen-Activated Protein Kinase Cascade. *J Neurosci.* 2003 Nov 26;23(34):10944-52.

“In response to neurotransmitters, astrocytes show various types of calcium increase (transient, oscillatory, and complex), the physiological significance of which is still controversial. To explore this variability, we examined factors affecting the calcium increase pattern in cultured astrocytes and investigated the consequences of the astrocytic calcium response in slice preparations. We found that growth factors (GFs) (EGF plus basic FGF) promoted calcium oscillation in response to glutamate, ATP, or thimerosal (which directly activates the inositol-1,4,5 triphosphate receptor) and that this effect was suppressed by pro-inflammatory cytokines (interleukin-1 β or tumor necrosis factor- α), lipopolysaccharide, or a MEK (mitogen-activated protein kinase) inhibitor, suggesting dual regulation of calcium oscillation in astrocytes by factors affecting brain function and pathology via the mitogen-activated protein kinase (MAPK) cascade. The calcium oscillation was accompanied by enlargement of the calcium store, cell proliferation, and the development of a hypertrophic morphology. The cytokines suppressed GF-induced MAPK-dependent immediate early gene promoter activation, but not phosphorylation of extracellular signal-regulated kinase (ERK), showing that they affected gene regulation by acting on the MAPK cascade downstream of ERK. In slice preparations, a metabotropic glutamate receptor agonist converted the spontaneous neuronal calcium increase, attributable to synaptic transmission, to an oscillatory response similar to that seen in astrocytes in culture, indicating that the calcium response in astrocytes acted as a feedback mechanism on the activity of neighboring neurons. This is the first evidence for a dual regulation of calcium oscillation by physiological factors and for the control of calcium dynamics actually being used in physiological processes.

...

It is reasonable to assume that the response of neurons to glutamate released by astrocytes is dependent on the subtype of glutamate receptor, which can vary outside synapses, and that the inhibitory effects are caused by inhibitory mGluRs (groups II and III). If this were the case, the physiological role of the calcium response and glutamate release by the astrocyte would vary, depending on the structure and topology of the glutamate release site on the astrocyte and the glutamate-receptive site on the neuron. In conclusion, we propose that the soluble factor-mediated regulation of astrocyte calcium dynamics is a novel mechanism for sensing the state of the CNS environment and responding to it by altering the physiology and pathology of the CNS. Additional studies on this regulatory mechanism should provide significant information on how the brain works.”

Reviewer’s Observations:

The importance of this article is that it shows that “Thimerosal” directly interferes with calcium-regulated neural processes by binding a key receptor site.

- B-23** Jin Y, Kim DK, Khil LY, Oh U, Kim J, Kwak J. Thimerosal decreases TRPV1 activity by oxidation of extracellular sulfhydryl residues. *Neurosci Lett.* 2004 Oct 21;369(3):250-5.

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“TRPV1, a receptor for capsaicin, plays a key role in mediating thermal and inflammatory pain. Because the modulation of ion channels by the cellular redox state is a significant determinant of channel function, we investigated the effects of sulfhydryl modification on the activity of TRPV1. Thimerosal, which oxidizes sulfhydryls, blocked the capsaicin-activated inward current (I_{cap}) in cultured sensory neurons, in a reversible and dose-dependent manner, which was prevented by the co-application of the reducing agent, dithiothreitol. Among the three cysteine residues of TRPV1 that are exposed to the extracellular space, the oxidation-induced effect of thimerosal on I_{cap} was blocked only by a point mutation at Cys621. These results suggest that the modification of an extracellular thiol group can alter the activity of TRPV1. Consequently, we propose that such a modulation of the redox state might regulate the physiological activity of TRPV1. ...

In summary, because TRPV1 has been implicated in the transmission of pain, and serves as a sensor for multimodal noxious stimuli ..., the modulation of I_{cap} by extracellular oxidizing agents reported here will contribute to revealing the mechanisms that regulate the activity of TRPV1 during pathologic conditions ...”

Reviewer’s Observation:

The importance of this article is that it shows that “Thimerosal” directly interferes with calcium transport and neural transmission by oxidizing sulfhydryls important to the activity of the TRPV1.

- B-24** Burbacher TM, Shen DD, Liberato N, Grant KS, Cernichiari E, Clarkson T. Comparison of Blood and Brain Mercury Levels in Infant Monkeys Exposed to Methylmercury or Vaccines Containing Thimerosal. “,” Environ Health Perspect. 2005;113:1015-21.

“Thimerosal is a preservative that has been used in manufacturing vaccines since the 1930s. Reports have indicated that infants can receive ethylmercury (in the form of thimerosal) at or above the Environmental Protection Agency (EPA) guidelines for methylmercury (MeHg) exposure, depending on the exact vaccinations, schedule, and size of the infant. This study compared the systemic disposition and brain distribution of total and inorganic mercury in infant monkeys following thimerosal exposure with infants exposed to MeHg. Monkeys were exposed to MeHg (via oral gavage) or vaccines containing thimerosal (via i.m. injection) at birth and 1, 2, and 3 weeks of age. Total blood mercury (Hg) levels were determined 2, 4 and 7 days after each exposure. Total and inorganic brain Hg levels were assessed 2, 4, 7 or 28 days after the last exposure. The initial and terminal half-life of Hg in blood following thimerosal exposure was 2.1 and 8.6 days, which are significantly shorter than the elimination half-life of Hg following MeHg exposure at 21.5 days. Brain concentrations of total Hg were significantly lower by ~3-fold for the thimerosal-exposed infants when compared to the MeHg infants, while the average brain-to-blood concentration ratio was slightly higher for the thimerosal-exposed infants (3.5 ± 1.0 vs. 2.5 ± 0.6). A higher percentage of the total Hg in the brain was in the form of inorganic mercury for the thimerosal-exposed infants (34% vs 7%). The current study indicates that MeHg is not a suitable reference for risk assessment from exposure to thimerosal derived Hg. Knowledge of the toxicokinetics and developmental toxicity of thimerosal is needed to afford a meaningful assessment of the developmental effects of thimerosal-containing vaccines. ...

The key findings of the current study are the differences in the disposition kinetics and demethylation rates of thimerosal and MeHg. Consequently, MeHg is not a suitable reference for risk assessment from exposure to thimerosal derived Hg. Knowledge of the biotransformation of thimerosal, the chemical identity of the Hg-containing species in the blood and brain, and the neurotoxic potential of intact thimerosal and its various biotransformation products, including ethylmercury are urgently needed to afford a meaningful interpretation of the potential developmental effects of immunization with thimerosal-containing vaccines in newborns and infants. This information is critical if we are to respond to public concerns regarding the safety of childhood immunizations.”

Reviewer’s Observations:

The importance of this article is that it confirms that, in the timeframe of the study, the level of long-term mercury poison, bound “inorganic mercury,” accumulating in the Thimerosal-injected baby monkeys’ brains was, on average, more than twice the average level of found in the brain of the baby monkeys fed the same level of methylmercurihydroxide. In addition, the variability of the level of this “inorganic mercury” in the brains of the Thimerosal-injected monkeys (from 1 to >20 ng/g) clearly indicates a variation in the excretion and metabolism of the monkeys in this treatment group in spite of the “sameness” of their treatment.