A Toxicologist’s View of Thimerosal and Autism

H. Vasken Aposhian, Ph.D.
Professor of Molecular and Cellular Biology
Professor of Pharmacology
The University of Arizona
IOM Meeting
February 9, 2004
1- Review of mercury toxicology.
2- Significance of recent papers.
3- Why pharmacokinetics of thimerosal in most infants are not applicable to “pre-autistic” children.
4- Need for new data.
5- Epidemiology data??
6- Summary.

I believe in the use of vaccines.
Forms of Mercury

1. Elemental Mercury
   • "Liquid silver"
   • Mercury vapor

2. Organic Mercury
   (Delayed Response)
   • Methylmercury
   • Thimerosal
   • Dimethylmercury

3. Mercuric Mercury

4. Mercurous Mercury
Target Organs

1. Mercury vapor → brain
2. Methylmercury → brain
3. Thimerosal → brain
4. Mercuric mercury → kidney
Sources and Forms of Brain Mercury

Brain

- Mercury Vapor
- Methyl Mercury
- Methyl Mercury
- Mercury Vapor
- Thimerosal
- Thimerosal

Sources:
- Mercury Vapor
- Thimerosal
- Vaccine
- Methyl Mercury

Forms:
- Mercury Vapor
- Methyl Mercury
- Thimerosal
AMERICAN ACADEMY OF PEDIATRICS

Lynn R. Goldman, MD, MPH; Michael W. Shannon, MD, MPH; and the Committee on Environmental Health


Is Autism an Efflux Disorder?
Wilson’s Disease as a Model of an Efflux Disease

1- Mutation in ATP7B gene.

2- ATP7B (copper transport protein) expressed primarily in the liver is deficient/lacking.

3- Hepatic and CNS copper accumulation and toxicity.

4- Hepatic and CNS signs and symptoms.

5- Treatable genetic disorder.
Reduced Levels of Mercury in First Baby Haircuts of Autistic Children

Amy S. Holmes,¹ Mark F. Blaxill,² and Boyd E. Haley³

¹Baton Rouge, Louisiana, USA
²SafeMinds, Cambridge, Massachusetts, USA
³Chemistry Department, University of Kentucky, Lexington, Kentucky, USA
<table>
<thead>
<tr>
<th>Exposure differences in autistic group as compared to controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Autistic group \hline</td>
</tr>
<tr>
<td>((N = 94)) \hline</td>
</tr>
<tr>
<td>Control group \hline</td>
</tr>
<tr>
<td>((N = 45)) \hline</td>
</tr>
<tr>
<td>Mercury levels in first baby haircut (ppm, mean (\pm SD))</td>
</tr>
<tr>
<td>0.47 ((\pm 0.28))^a</td>
</tr>
</tbody>
</table>

^a Indicates a significant difference between groups.
A Case-Control Study of Mercury Burden in Children with Autistic Spectrum Disorders

Jeff Bradstreet, M.D.
David A. Geier, B.A.
Jerold J. Kartzinel, M.D.
James B. Adams, Ph.D.
Mark R. Geier, M.D., Ph.D.

Autistic children have a greater burden of mercury.
Significance of these two papers:

It appears that autistic children lack an effective mercury efflux system.
Ethyl Mercury Efflux From Tissue Appears To Be Inhibited

Non Autistic

Tissue → Blood → Hair

Autistic

Tissue → Blood (Efflux Inhibited) → Hair
It appears that autistic children lack an effective mercury efflux system.
Estimated Daily Intake and Retention (µGrams/Day) of Mercury in the General Population Not Occupationally Exposed to Mercury

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Elem. Hg Vapor</th>
<th>Inorg.Hg Compds</th>
<th>MethylHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air</td>
<td>0.030 (0.024)</td>
<td>0.002 (0.001)</td>
<td>0.008 (0.0064)</td>
</tr>
<tr>
<td>Food Sources:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fish</td>
<td>0</td>
<td>0.600 (0.042)</td>
<td>1-6</td>
</tr>
<tr>
<td>Non-Fish</td>
<td>0</td>
<td>3.6 (0.25)</td>
<td>0</td>
</tr>
<tr>
<td>Drinking Water</td>
<td>0</td>
<td>0.050 (0.0035)</td>
<td>0</td>
</tr>
<tr>
<td>Dental Amalgam</td>
<td>3.8-21 (3-17)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>3.9-21 (3.1-17)</td>
<td>4.3 (0.3)</td>
<td>1-6 (1-6)</td>
</tr>
</tbody>
</table>

Numbers in parenthesis = retention amounts.
Possible Different Responses to IM Thimerosal

1- Excreted ➔ no autism.

2- Efflux impaired ➔ thimerosal final insult (trigger) ➔ autism.

3- Efflux impaired.

Thimerosal adds to mercury burden.

Eventually toxic level of Hg exceeded.

Autism.

Much research needed.
Mercury concentrations and metabolism in infants receiving vaccines containing thiomersal: a descriptive study

Michael E Pichichero, Elsa Cernichiari, Joseph Lopreiato, John Treanor
Thimerosal pharmacokinetics obtained using non-autistic children are not the same as those expected for autistic children. The latter appear to have different efflux kinetics.
Epidemiology ??

Was the right question asked?
Epidemiological studies cannot prove cause and effect. Rather, they reveal statistical correlations.
Results of research using thimerosal in non-human primates may not be applicable to autistic children and should be viewed and used with caution.
Summary

1- Organic mercury compounds have a delayed response.

2- Holmes paper and Bradstreet paper together indicate that autistic children have a mercury efflux disorder.

3- Pharmacokinetics in non-autistic children may not be applicable to autistic children.
Summary (cont.)

4- Results of some research using non-human primates may not be meaningful when extrapolated to autistic children because of a possible efflux disorder.

5- It is this toxicologist’s view that the link between thimerosal and neurodevelopmental disorders in children has become more plausible. Thimerosal appears to add organic mercury to the mercury burden of children with an Hg efflux disorder.