Genetics, Environment, Autism, and the Law

Dr. James Lyons-Weiler, PhD
REDUCING HUMAN PAIN AND SUFFERING THROUGH KNOWLEDGE
Who Am I?

• Biologist, Evolutionary Biologist, Systems Biology Expert, Cancer Biomarkers Research Expert, Bioinformatics Expert

• CEO, Director, Scientist @ The Institute for Pure and Applied Knowledge, a pure public charity research institute that conducts research in the public interest.
Three books (2014-2016)
Potential COI Disclosure

• I do not receive income from the manufacture, sale, or distribution of vaccines (or any other medical product)
• In 2016, I was compensated for consulting effort on two vaccine injury litigations, <$10,000 total
• I do receive payment from IPAK from donations from the public, incl. vaccine risk aware individuals.
• IPAK Employees are not allowed to personally profit from any intellectual property we generate
• Book proceeds are donations to IPAK
Mish Michaels loses WGBBH science job — because she doesn’t believe in vaccines
Autism

Source: US Centers for Disease Control and Prevention
http://www.cdc.gov/ncbddd/autism/data.html

2001 Vaccine makers begin to phase thimerosal out of vaccines

1986 Congress passes liability protection for vaccine makers and vaccine schedule begins to rapidly expand

Autism rate by birth year

- 1 in 10,000 (1970s)
- 1 in 500 (1980s)
- 1 in 150 (1990s)
- 1 in 125 (1996)
- 1 in 110 (1998)
- 1 in 88 (2000)
- 1 in 68 (2004)
and PDD-NOS. These conditions differ from each other in degree of severity of symptoms in two core domains.

In DSM-5, three domains of ASD were recognized; in DSM, two have been combined, and thus DSM-5 identifies two domains, as shown in Table 2.

**TABLE 2. DOMAINS OF AUTISM SPECTRUM DISORDER**

<table>
<thead>
<tr>
<th>DSM-IV</th>
<th>DSM-5</th>
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<tbody>
<tr>
<td>Social domain</td>
<td>Social/Communication domain</td>
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<td>Communication domain</td>
<td>Restrictive, repetitive behaviors</td>
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<tr>
<td>Restrictive, repetitive behaviors</td>
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</table>


A. Persistent deficits in social communication and social interaction across contexts, not accounted for by general developmental delays and manifest by all three of the following:
   1. Deficits in social-emotional reciprocity
   2. Deficits in nonverbal communicative behaviors used for social interaction
   3. Deficits in developing and maintaining relationships

B. Restricted, repetitive patterns of behavior, interests, or activities as manifested by at least two of the following:
   1. Stereotyped or repetitive speech, motor movements, or use of objects.
   2. Excessive adherence to routines, ritualized patterns of verbal or nonverbal behavior, or excessive resistance to change.
   3. Highly restricted, fixated interests that are abnormal in intensity or focus.
4. Hyper- or hyporeactivity to sensory input or unusual interest in sensory aspects of environment.

C. Symptoms must be present in early childhood* but may not become fully manifest until social demands exceed limited capacities.

D. Symptoms together limit and impair everyday functioning.

*This condition is contradicted elsewhere within DSM-5.

Under DSM-5, if no restrictive, repetitive behaviors are present, social communication disorder may be diagnosed.

A major assumption was made in DSM-5 with a merger of social and communication phenotypes: that the bulk of a lack of social reciprocity is due to deficits in communication skills and not to a domain (of its own). Thus, the loss of speech is technically judged toward CDD. Because the loss of speech after
Parental Refusal of Childhood Vaccines and Medical Neglect Laws

Efihamios Panidis, JD, MBioethics, and Douglas J. Opel, MD, MPH

**Objectives.** To examine the relation of vaccine refusal and medical neglect under child welfare laws.

**Methods.** We used the Westlaw legal database to search court opinions from 1905 to 2016 and identified cases in which vaccine refusal was the sole or a primary reason in a neglect proceeding. We also delineated if religious or philosophical exemptions from required school immunizations were available at the time of adjudication.

**Results.** Our search yielded 9 cases from 5 states. Most courts (7 of 9) considered vaccine refusal to constitute neglect. In the 4 cases decided in jurisdictions that permitted religious exemptions, courts either found that vaccine refusal did not constitute neglect or considered it neglect only in the absence of a sincere religious objection to vaccination.

**Conclusions.** Some states have a legal precedent for considering parental vaccine refusal as medical neglect, but this is based on a small number of cases. Each state should clarify whether, under its laws, vaccine refusal constitutes medical neglect. (Am J Public Health. 2017;107:68–71. doi:10.2105/AJPH.2016.303500)

Parental refusal of childhood vaccines is a contentious issue in pediatrics and result in harm to the child constitute child maltreatment.
Genetics

• >850 genes “involved” in Autism
• No individual gene accounts for >1% of ASD
• **20% of autistics have >> Copy Number Variations (CNVs)**
• de Novo variants more common in sporadic vs. familial cases
• **regulatory genes in early development**
• **synaptogenesis throughout life**
• Familial vs. Genetic Risk
• Every mode of inheritance (dominant, recessive, complex)
• Pinto >2-3 affected genes > ASD risk
1. Identical, monozygotic (MZ) twins show a significantly higher concordance of autism diagnosis than fraternal, dizygotic twins for autism, even though siblings grew up together, sharing many environmental influences.

2. No single gene has been found to have a large effect, and studies have resulted in the discovery of numerous genes, clustered in specific pathways, each explaining a minor percentage of cases of autism ASD.

3. First-degree relatives of affected individuals are often found with sub-threshold autism or ASD symptoms, indicating that autism and ASD is a heterogeneous, variegated set of conditions, as opposed to a discrete (all/none) genetic disease.

In the terminology of genetics, these observations led to the conclusion that a simple autosomal or X-linked dominant model, or even a recessive mode of monogenic inheritance, was insufficient to describe the patterns of inheritance of risk of autism. They pointed to autism risk as a complex trait, involving many loci and many genes, with likely interactions among genes (epistasis). However,
Heritability, >2,000,000 estimates (any human traits): 1958-2012 (Polderman et al.)
Phenomimicry: Some cases disrupted mutations, others by environmental exposure

- CHD7, CHD8 – neural crest, early development
  - LOF mutations vs. Valproaic acid
- Mutations in ER genes, Thimerosal inhibition of ERAP1
- Mitochondrial mutations vs. Glyphosate-induced mitopathy
- Microglial cell modulation of MAO-A, LoF mutations in MAO-A
- LOF mutation ANY protein-encoding gene, autoimmunity

**Finding mutations does not rule out environment**
Functional Groups by Age

• -9 mo to 0 years
  Early (pre-natal) regulatory genes
  CHD7, CHD8 (neural crest, neurogenesis)

• 0- 2 years
  Peri/post-natal brain development
  Synaptogenesis, PRUNING

• 2-4 years
  PRUNING, MYELINATION

• Lifetime
  Synaptic proteins
  Glutamate receptors
  Serotonin receptors (e.g., SCN1A)
  Cellular detox proteins (ERAP1)
  Mitochondrial genes (ROS)
Transcriptional Programs Increased for ASD Genetic Risk during Human Neocortical Development

M2, M3: Early fetal development, transcriptional regulators upregulated.

M13, M16, M17: Late fetal into early postnatal development, upregulated synaptic genes.

Integrative Functional Genomic Analyses Implicate Specific Molecular Pathways and Circuits in Autism

Vaccines given at 0, 2, 4, 6, 12, and 15-18 months
Figure 2. Percent “genetic” liability contributed by mutation class type (estimates from Gaugler et al., 2014). Pure “genetic” ASD and de novo variation represent the least amount of liability. Common variants set the stage and are thus not “autism” genes;
Pinto et al
Largest Genetic Studies (Hallmayer, 2011; Sandin, 2014)

• Did not measure any environmental factors

• Did not estimate G x E interactions

• Both concluded around 50% E, 50% G
MZ, DZ, G%, E%, missing%

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<thead>
<tr>
<th>Source</th>
<th>MZ</th>
<th>DZ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tick 5%</td>
<td>98%</td>
<td>53%</td>
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<tr>
<td>Tick 1%</td>
<td>98%</td>
<td>67%</td>
</tr>
</tbody>
</table>

Broad-sense heritability 67-94%, shared E, 7-35%

<table>
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<tr>
<th>Source</th>
<th>%G</th>
<th>%E</th>
<th>%missing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hallmayer</td>
<td>38(h2)</td>
<td>58</td>
<td>4</td>
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<tr>
<td>Sandin</td>
<td>46</td>
<td>54</td>
<td>0</td>
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<tr>
<td>Colvert</td>
<td>56</td>
<td>30</td>
<td>8</td>
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</table>
Implies low narrow-sense heritability h2 (approx. h2 = 0)
New Studies

• People who self-identify as being on the spectrum tend to have kids w/ASD traits – regardless of diagnosis.


Gaugler T et al.
Most genetic risk for autism resides with common variation.
“Reproducibility of Environment Effects in Twins” Shared Environment Interpretation

Environmental susceptibility will look like common variation if the correct environmental factors are not studied.
“Reproducibility of Environment Effects in Twins” Unique Environment Studies Needed

Environmental susceptibility will look like **common variation** if the correct environmental factors are not studied.
G x E Interactions
Bowers & Erickson (2014) Review

• Organophosphates <- $PON1$ gene
• Pregnancy-related stress <- $ADRB2$ gene
• Traffic-related particulate matter (pollution) <- $MET$ gene

• Periconceptional maternal prenatal vitamin <- $(MTHFR, CBS, COMT)$

Additional evidence of G x E

• **Rose et al.** Mercury damage in autism may be mediated via mitochondrial dysfunction in some

• **Choi et al.** Maternal immune activation leads to (IL-17a) activation -> abnormal cortical phenotype

• **Hadley et al., 2014.** Glutamate receptors and transporters (mGlur gene network > 270 genes) – autistics have more CNV’s than neurotypicals

• **Nayak et al. 2002.** Protein malnutrition may influence the specific manifestation of aluminum-induced neurotoxicity

• **Numerous studies** – Lifelong microglial activation
Evidence of Specific G x E in Vaccines

- Sodium channel gene SCN1A variation associated with sensitivity to vaccine-induced encephalopathy (O’Roak et al. 2011)

- MTHFR mutations Thimerosal susceptibility (Austin, 2014)
Phenomimicry: Some cases disrupted mutations, others by environmental exposure

• CHD7, CHD8 – neural crest, early development
  • LOF mutations vs. Valproaic acid
• Mutations in ER genes, Thimerosal inhibition of ERAP1
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• LOF mutation ANY protein-encoding gene, autoimmunity
Individual Genes

• **ASD Risk Genes (< 1%)**
  - Synaptic proteins (>70), GABA-B3 receptor, Shank2/3  TSC1/2  MECP2  PTEN  dup(16p11), **CNTNAP2**

• **Environmental Susceptibility Genes (40-60%)**
  - Glutamate receptors, endoplasmic reticulum proteins, cellular detoxification pathway proteins

• **Autism Phenotype Modifier Genes (40%; communication skills, intellect)**
  - FoxP1, serotonin transporters
Schasfma et al. 2017

- Genetics: CNTAP2
- Gender: (M/F)
- MIA (LPS + Bacterial infection)

**Abstract**

The male bias in the incidence of autism spectrum disorders (ASDs) is one of the most notable characteristics of this group of neurodevelopmental disorders. The etiology of this sex bias is far from known, but pivotal for understanding autism, the three hit categories of gene environment interactions have been proposed. In this study, we examined the role of the sex-specific gene CNTAP2 and the environment of LPS + bacterial infection on the behavior. The results showed that CNTAP2 was associated with vocalizations, social recognition, habituation, dishabituation, CRH expression, and H3K4me3. The *p* values were less than 0.001 for vocalizations and less than 0.047 for social recognition.
Glutamate released from hippocampal astrocytes induces neuronal synchrony through the activation of extrasynaptic NR2B-containing NMDA receptors: in the hippocampus, besides activating ionotropic glutamate receptors in the postsynaptic terminals. glutamate...
SPEECH, MICROGLIA, AND NERVE CELL EXTENSION 
ROLES IN LOSS-OF-FUNCTION MUTATIONS

Loss-of-function (LoF) driven pathway analysis revealed three major clusters of 
functionally aggregate gene modules in ASD (Liu et al., 2014), reflecting func-
tional groups involved in the following:

- Speech and language, clustering around the gene FOXP2.
- Microglial activation, clustering around the gene PTEN.
- Microtubule-processes in nerve cell function, clustering around the 
gene SPAST.

The importance of FOXP2 and PTEN in ASD has been discussed previously in 
this book. The SPAST cluster found by Liu et al. (2014) may indicate the impor-
tance of a microtubule reorganization, which is important for both cell shape 
development (neurite extension and neuronal arborization) and microglial and 
astrocyte functioning. Another effect could be disruption of the modulation of 
the endoplasmic reticulum, important for cellular waste transport and detoxi-
fication. Mutations in genes in this cluster could lead to sequestration of toxins 
in cells such as astrocytes (disrupting glutamate uptake) and microglia, which 
hinder proper mediation of synapses and autophagy.
Genes Organized by Contribution to ASD Phenotype (examples)

• **“ASD”**
  - CHD8, KATNAL2, 5-HT2A receptor, 16p11.2 dup/del,

• **“Autism severity”**
  - MOA-B

• **Neural development**
  - CHD7

• **Macrocephaly**
  - PTEN

• **Language ability**
  - 16p11.2 CNVs, 5-HT2RA, FOXP1
  - mitochondrial dysfunction

• **Intellectual ability**
  - SHANK genes, Glutamate receptor genes, BDNF, MAO-A, 5-HT2A serotonin receptor

• **Social Function/Affective Knowledge**
  - OXTR, DD4R

• **Repetitive behaviors**
  - SLC25A12

• **Hypersensitivity to sound**
  - CNTN5, CNTN6

• **Aggression**
  - MOA-A
  - CD13

• **Severity of Depression**
  - rs6311
Environmental Factor (Known and Suspected)

• Congenital Rubella Inf.
• Aluminum
• Mercury
• Acetaminophen
• Monosodium glutamate
• Thalidomide
• Valproic acid

• Glyphosate
• PBDEs (flame retardant)
• Air pollution
• Phthalates
• Ultrasound exposure
• Solvents (parental exposure)
Examples of Evidence of Environmental Liability

- mercury amalgam
  Holmes et al., 2003

- maternal immune activation
  Many sources

- acetaminophen after MMR
  Bauer et al., 2003

- autoantibodies to the folate receptor protein is related to neural tube defects and autism
  Molecular mimicry

- aluminum causes apoptosis of motor
  Shaw and Petrik (2009)

- Serum levels of Vit D₃
  - May also reflect genetic risk
  Feng et al. (2016)
71% of kids with RA had an episode of fever > 101°F. In 33% of these cases, the fever occurred *right after vaccination* (Shoffner et al., 2010).

Children with more severe autism had larger amounts of circulating anti-brain protein antibodies (Piras et al., 2014).
Conclusions: Prenatal acetaminophen exposure was associated with a greater number of autism spectrum symptoms in males and showed adverse effects on attention-related outcomes for both genders. These associations seem to be dependent on the frequency of exposure.
Autism is No More than 50% Genetic, at Least 50% Environmental (Likely more)

• Important open questions:

• Where do the >> de novo CNV in ASD come from?

• Do they predispose some families to increased genetic susceptibility to environmental toxins?
Environmental Toxin Liability Sampling Theory

- PON1
- Valproic acid
- CHD7
- ADRB2
- ERAP1
- MET
- particulate air pollution
- organophosphates
- Pregnancy-related stress
- MTHFR
- CBS
- COMT
- thimerosal
- Pre/peri-natal vitamins
Burbacher et al.

- Ethyl mercury stays in organs (including the brain) longer than methyl mercury

Demonstrates that previous notions of faster clearance of ethyl mercury cf. methyl were mistaken.

“Evidence from such studies point to a half-life of inorganic mercury in human brains of several years to several decades”


Inorganic mercury Half-life: 27 years
Screening Identifies Thimerosal as a Selective Inhibitor of Endoplasmic Reticulum Aminopeptidase 1

Athanasios Stamogiannos, Athanasios Papakyriakou, Francois-Xavier Mauvais, Peter van Endert, and Efstratios Stratikos

National Center for Scientific Research Demokritos, Agia Paraskevi GR-15310, Athens, Greece
Institut National de la Santé et de la Recherche Médicale, Unité 1151; Université Paris Descartes, Sorbonne Paris Cité; Centre National de la Recherche Scientifique, Unité 8253, 75015 Paris, France

Supporting Information

ABSTRACT: We employed virtual screening followed by in vitro evaluation to discover novel inhibitors of ER aminopeptidase 1, an important enzyme for the human adaptive immune response that has emerged as an attractive target for cancer immunotherapy and the control of autoimmunity. Screening hits included three structurally related compounds carrying the (E)-N-((1H-indol-3-yl)methylene)-1H-pyrazole-5-carboxyamide scaffold and (2-carboxylatophenyl)sulfanyl-ethylmercury as novel ERAP1 inhibitors. The latter, also known as thimerosal, a common component in vaccines, was found to inhibit ERAP1 in the submicromolar range and to present strong selectivity versus the homologous aminopeptidases ERAP2 and IRAP. Cell-based analysis indicated that thimerosal can effectively reduce ERAP1-dependent cross-presentation by dendritic cells in a dose-dependent manner.

KEYWORDS: ERAP1, ERAP2, IRAP, aminopeptidase, inhibitor, immune system, antigenic peptide, docking

Endoplasmic reticulum (ER) aminopeptidases generate antigenic peptides for loading onto Major Histocompatibility Complex (MHC) class I molecules through a two-step process involving ERAP1 and the classical ER aminopeptidase. These enzymes are involved in the generation of novel classes of antigenic peptides that can be presented to the immune system. Knowledge-based virtual screening approaches, taking advantage of key structural characteristics revealed in the recent crystal

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Invited Review Article

The retention time of inorganic mercury in the brain — A systematic review of the evidence

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ABSTRACT

Reports from human case studies indicate a half-life for inorganic mercury in the brain in the order of years—contradicting older radioisotope studies that estimated half-lives in the order of weeks to months in duration. This study systematically reviews available evidence on the retention time of inorganic mercury in humans and primates to better understand this conflicting evidence. A broad search strategy was used to capture 16,539 abstracts on the Pubmed database. Abstracts were screened to include only study types containing relevant information. 131 studies of interest were identified. Only 1 primate study made a numeric estimate for the half-life of inorganic mercury (227–540 days). Eighteen human mercury poisoning cases were followed up long term including autopsy. Brain inorganic mercury concentrations at death were consistent with a half-
<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Aluminum Content (ug)* per dose</th>
<th>Birth</th>
<th>1 mo</th>
<th>2 mos</th>
<th>4 mos</th>
<th>6 mos</th>
<th>9 mos</th>
<th>12 mos</th>
<th>15 mos</th>
<th>18 mos</th>
<th>18-23 mos</th>
<th>2-3 yrs</th>
<th>4-6 yrs</th>
<th>7-10 yrs</th>
<th>11-12 yrs</th>
<th>13-15 yrs</th>
<th>16-18 yrs</th>
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<td>Hepatitis B1 (HeplB)</td>
<td>250</td>
<td>1st</td>
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<td>Rotavirus2 (RV)</td>
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<td>Diphtheria, tetanus, &amp; acellular pertussis (DTaP, &lt;7 yrs)</td>
<td>625</td>
<td>1st</td>
<td>2nd</td>
<td>3rd</td>
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<td>4-4th dose</td>
<td>5th</td>
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<td>Haemophilus influenzae type b4, (Hib)</td>
<td>225</td>
<td>1st</td>
<td>2nd</td>
<td>3rd</td>
<td>4-3rd or 4th dose</td>
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<td>Pneumococcal conjugate6, (PCV13)</td>
<td>125</td>
<td>1st</td>
<td>2nd</td>
<td>3rd</td>
<td>4-6th dose</td>
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<td>Inactivated poliovirus5, (IPV&lt;18 yrs)</td>
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<td>1st</td>
<td>2nd</td>
<td>4-3rd dose</td>
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<td>Influenza7 (IV: LAIV)</td>
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<td>Measles, mumps, rubella (MMR)</td>
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<td>Varicella (VAR)</td>
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<td>Hepatitis A10 (HeptA)</td>
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<td>1st</td>
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<tr>
<td>Meningococcoccal11 (HiB, MenC) 6 weeks, MenACWY-D all mos, MenACWY-CRM a 2 mos)</td>
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<td>Tetanus, diphtheria, &amp; acellular pertussis15 (Tdap, 6-7 yrs)</td>
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<tr>
<td>Human papillomavirus13 (2yHPV: females only, 4yHPV, 9yHPV: males and females)</td>
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<tr>
<td>Meningococcoccal B11</td>
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<tr>
<td>Pneumococcal polysaccharoid5 (PPSV23)</td>
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<td>(3 dose series)</td>
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</tr>
</tbody>
</table>

* Total ug not adjusted to ug/kg

250 1225 975 1000 600 875
Aluminum

- HepB  
  250 µg per dose (750 µcg source)
- HepA  
  250 µg per dose (500 µcg source)
- DTaP  
  625 µg per dose (3,125 µcg source)
- HiB   
  225 µg per dose (900 µcg source)
- PCV   
  125 µg per dose (500 µcg source)

5,775 µg (typical schedule)
“The toxic effects of aluminum are best described as widespread and pernicious. Inside the cell, aluminum shuts down the transcription of protein-coding genes and miRNA genes in two ways, via direct and specific interaction with H1 linker histones and by suppressing global gene expression by down-regulating RNA polymerase II (see review in Bhattacharjee, 2013). Aluminum causes a buildup of glial fibrillary acid protein (GFAP) filaments near the cell nucleus and destruction of the actin cytoskeleton (Theiss et al., 2002). Structural effects of aluminum in rodents include the appearance of neurofibrillary tangles that resemble those from Alzheimer’s patients (Uemura et al., 1984; Somova et al., 1997).”
Environmental Toxin Liability Sampling Theory

- PON1
- ADRB2
- organophosphates
- Valproic acid
- CHD7
- Pregnancy-related stress
- thimerosal
- ERAP1
- MET
- particulate air pollution
- MTHFR
- CBS
- COMT
- Pre/perinatal vitamins
Environmental Toxin Liability Sampling Theory

- Aluminum levels in vaccines are unsafe
- We need to Risk Factors + Biomarkers Vaccine Safety Screening

**Risk Factors**
- Pregnancy-related stress
- Valproic acid
- Valproic acid
- CHD7
- THF
- CBS
- COMT
- CHD7
- MTHFR

**Biomarkers**
- organophosphates
- particulate air pollution
- thimerosal
- Pre/peri-natal vitamins

**Vaccine Safety Screening**
Aluminium Induced Endoplasmic Reticulum Stress Mediated Cell Death in SH-SY5Y Neuroblastoma Cell Line Is Independent of p53

Syed Husain Mustafa Rizvi¹, Arshiya Parveen¹, Anoop K. Verma², Iqbal Ahmad³, Md Arshad⁴, Abbas Ali Mahdi¹

¹Department of Biochemistry, King George’s Medical University, Lucknow, Uttar Pradesh, India, ²Forensic Medicine & Toxicology, King George’s Medical University, Lucknow, Uttar Pradesh, India, ³Fibre Toxicology Division, CSIR- Indian Institute of Toxicology Research, Lucknow, Uttar Pradesh, India, ⁴Department of Zoology, Lucknow University, Lucknow, Uttar Pradesh, India

Abstract
Aluminium (Al) is the third most abundant element in the earth’s crust and its compounds are used in the form of house hold utensils, medicines and in antiperspirant etc. Increasing number of evidences suggest the involvement of Al⁺³ ions in a variety of neurodegenerative disorders including Alzheimer’s disease. Here, we have attempted to investigate the role of Al in endoplasmic reticulum stress and the regulation of p53 during neuronal apoptosis using neuroblastoma cell line. We observed that Al caused oxidative stress by increasing ROS production and intracellular calcium levels together with depletion of intracellular GSH levels. We also studied modulation of key pro- and anti-apoptotic proteins and found significant alterations in the levels of Nrf2, NQO1, pAKT, p21, Bax, Bcl2, Aβ1-40 and Cyt c together with increase in endoplasmic reticulum (ER) stress related proteins like CHOP and caspase 12. However, with respect to the role of p53, we observed downregulation of its transcript as well as protein levels while analysis of its ubiquitination status revealed no significant changes. Not only did Al increase the activities of caspase 9, caspase 12 and caspase 3, but, by the use of peptide
“NO STUDY HAS EVER SHOWN”

- Analyze the data repeatedly until the positive association “goes away”
- Change the results post-peer review, post-publication, in plain site (Uno et al.)
- Use the most conservative method for multiple hypothesis testing (Bonferroni)
- Change the results post-peer review, post-publication, in plain site (Uno et al.)
- Use the most conservative method for multiple hypothesis testing (Bonferroni)
- Overfit the model using redundant, highly collinear variables
- Remove patients who are likely to have ASD features
- “Correct for” covariates related to ASD
- Reduce sample size to reduce power to detect association
- Change study design post facto to see if association can be lost
- Fail to report initial association
- Change continuous variables to discrete (cum. exposure -> “on time” vs. “late”)
<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Birth</th>
<th>1 mo</th>
<th>2 mos</th>
<th>4 mos</th>
<th>6 mos</th>
<th>9 mos</th>
<th>12 mos</th>
<th>15 mos</th>
<th>18 mos</th>
<th>19–23 mos</th>
<th>2-3 yrs</th>
<th>4-6 yrs</th>
<th>7-10 yrs</th>
<th>11-12 yrs</th>
<th>13-15 yrs</th>
<th>16-18 yrs</th>
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<tbody>
<tr>
<td>Hepatitis B' (HepB)</td>
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<tr>
<td>Rotavirus&lt;sup&gt;2&lt;/sup&gt; (RV) RV1 (2-dose series); RV5 (3-dose series)</td>
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<tr>
<td>Diphtheria, tetanus, &amp; acellular pertussis&lt;sup&gt;1&lt;/sup&gt; (dTAP; &lt;7 yrs)</td>
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<td><em>Haemophilus influenzae</em> type b&lt;sup&gt;1&lt;/sup&gt; (HiB)</td>
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<td>Pneumococcal conjugate&lt;sup&gt;6&lt;/sup&gt; (PCV13)</td>
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<tr>
<td>Inactivated poliovirus&lt;sup&gt;6&lt;/sup&gt; (IPV; &lt;18 yrs)</td>
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<td>Influenza&lt;sup&gt;7&lt;/sup&gt; (IIV; LAIV)</td>
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<td>Measles, mumps, rubella&lt;sup&gt;4&lt;/sup&gt; (MMR)</td>
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<td>Varicella&lt;sup&gt;4&lt;/sup&gt; (VAR)</td>
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<td>Hepatitis A&lt;sup&gt;9&lt;/sup&gt; (HepA)</td>
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<td>Meningococcal&lt;sup&gt;11&lt;/sup&gt; (Hib-MenCY ≥ 6 weeks; MenACWY-D ≥ 9 mos; MenACWY-CRM ≥ 2 mos)</td>
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<td>Tetanus, diphtheria, &amp; acellular pertussis&lt;sup&gt;11&lt;/sup&gt; (Tdap; ≥7 yrs)</td>
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<tr>
<td>Human papillomavirus&lt;sup&gt;11&lt;/sup&gt; (2vHPV; females only; 4vHPV; 9vHPV; males and females)</td>
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<tr>
<td>Meningococcal B&lt;sup&gt;11&lt;/sup&gt;</td>
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<td>Pneumococcal polysaccharide&lt;sup&gt;6&lt;/sup&gt; (PPSV23)</td>
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</table>

2 STUDIES SHOW ASSOCIATION

6 STUDIES SHOW ASSOCIATION

2 STUDIES SHOW ASSOCIATION

0 STUDIES EXIST

0 STUDIES EXIST

0 STUDIES EXIST

0 STUDIES EXIST

2 POSITIVE AND MANY NEGATIVE “STUDIES” EXIST RE: Thompson

1 STUDY SHOWS ASSOCIATION

1 STUDY SHOWS ASSOCIATION

0 STUDIES – GBS, PARALYSIS (NUMEROUS)

“VACCINES DO NOT CAUSE AUTISM” - CDC
Some Facts About Aluminum:

- While abundant in nature, aluminum is not usually biologically available in nature.
- >1000 studies show Aluminum is a potent neurotoxin.
- Aluminum was grandfathered in to clinical use in vaccines.
- First used in vaccines the 1920’s.
- Present in the form of Aluminum salts (Aluminum hydroxide).
- Interactions between Aluminum and other vaccine excipients are not well studied.
Dietary Aluminum

- Most (>99.9%) aluminum in the diet usually is excreted, kept from the blood via intact and properly functioning intestinal tissues.
- Bio-available forms of aluminum such as aluminum hydroxide and MF59 are not naturally part of biological exposures in humans and animals.
- Lesions in the gut will likely increase dietary aluminum exposures.

<table>
<thead>
<tr>
<th>Population</th>
<th>Year Published</th>
<th>Route of Exposure</th>
<th>NOAEL</th>
<th>LOAEL</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mice</td>
<td>1989</td>
<td>Dietary</td>
<td>62 mg Al/kg</td>
<td>155 mg Al/kg</td>
<td>Golub et al 1989</td>
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<tr>
<td>Mice</td>
<td>2001</td>
<td>Dietary</td>
<td>26 mg Al/kg</td>
<td>130 mg Al/kg</td>
<td>Golub et al, 2001</td>
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<tr>
<td>Mice</td>
<td>2005</td>
<td>Dietary</td>
<td>53 mg Al/kg</td>
<td>103 mg Al/kg</td>
<td>Colomina et al, 2005</td>
</tr>
<tr>
<td>Mice</td>
<td>2000</td>
<td>Dietary</td>
<td>-</td>
<td>100 mg Al/kg</td>
<td>Golub et al, 2000</td>
</tr>
</tbody>
</table>
Aluminum from Vaccines

• CFR/FDA Safety Levels for an adult is 850 μg per dose – no body weight

• Aluminum in parenteral sources (IV) limited to 5 μg/kg/day

• 18 Vaccines in the CDC schedule include Aluminum in various bio-available types

• Babies receive 250 micrograms on the first day of birth in the HepB shot

• 100% of Al from vaccines are absorbed (clearance in days/weeks)

• Only 0.1-0.3% of Al from diet is absorbed
“Research indicates that patients with impaired kidney function, including premature neonates, who receive parenteral levels of aluminum at greater than **4 to 5 [micro]g/kg/day** accumulate aluminum at levels associated with central nervous system and bone toxicity. Tissue loading may occur at even lower rates of administration.”
Vaccine Development and Characterization

• Sterility (21 CFR 610.12)
• General Safety (21 CFR 610.11)
  – test on final container product
  – detection of extraneous toxic contaminants
• Purity (21 CFR 610.13)
  – pyrogenicity
  – moisture content
• Identity (21 CFR 610.14)
  – on final container, e.g. SDS-PAGE, Western blot,
• Other release tests
  – in process testing critical for safety and manufacturing consistency
21 CFR 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...
21 CFR 610.15: Constituent materials.

- An **adjuvant** shall not be introduced into a product unless there is satisfactory evidence that it does not affect adversely the safety or potency of the product.

- The amount of **aluminum** in the recommended individual dose of a biological product shall not exceed:
  - (1) 0.85 milligrams if determined by assay;
  - (2) 1.14 milligrams if determined by calculation on the basis of the amount of aluminum compound added; or
  - (3) 1.25 milligrams determined by assay provided that data demonstrating that the amount of aluminum used is safe...
Question: How did CFR/FDA Come to a Vaccine MSL 850 mcg/AL per DOSE, with no reference to body weight?

• MRL - MINIMAL RISK LEVELS
• NOAEL - no-observed-adverse-effect-level
• LOAEL - lowest-observed-adverse-effect level
Aluminum toxicokinetics regarding infant diet and vaccinations

L.S. Keith*, D.E. Jones, C.-H.S.J. Chou

Agency for Toxic Substances and Disease Registry, Division of Toxicology, 1600 Clifton Road, NE, Mailstop E-29, Atlanta, GA 30333, USA

Received 4 June 2001; accepted 7 August 2001

Abstract

Some vaccines contain aluminum adjuvants to enhance the immunological response, and it has been postulated that this aluminum could contribute to adverse health effects, especially in children who receive a vaccination series starting at birth. The pharmacokinetic properties and end-point toxicities of aluminum are presented. In assessing the relevance of dietary and medical aluminum exposure to public health, we estimated infant body burdens during the first year of life for breast milk and formula diets and for a standard vaccination schedule. We then compared those body burdens with that expected for intake at a level considered safe for intermediate-duration exposure. The methodology blends intake values and uptake fractions with an aluminum retention function derived from a human injection study using radioactive 26Al. The calculated body burden of aluminum from vaccinations exceeds that from dietary sources, however, it is below the minimal risk level equivalent curve after the brief period following injection. Published by Elsevier Science Ltd.

Keywords: Aluminum; Vaccine; Diet
Keith et al.

- analyzed the pharmacokinetics of aluminum for infant dietary and vaccine exposures
- compared the resulting body burdens to those based on the minimal risk levels (MRLs) established by the Agency for Toxic Substances and Disease Registry (ATSDR)
concentration gives the daily aluminum intake through 6 months of age. During the second 6 months, introduction of semisolid food increases the aluminum intake to an average 0.7 mg per day [21]. An estimate of infant aluminum body burden during year 1 was developed using a 0.78% uptake factor and applying the Priest et al. [11] retention function to the serum aluminum levels, a condition that is now known to be preventable by using water with low aluminum content. Other more subtle neurological effects that have been induced in animal models or associated with human occupational exposure include memory loss, fatigue, depression, behavioral modifications, and learning impairment.

Fig. 1. Aluminum body burden contributions from diet and vaccines relative to MRL level intake.
Mitkus et al

• Updated the analysis of Keith et al.

• (then) current pediatric vaccination schedule, baseline aluminum levels at birth

• Adjusted the analysis using
  • an aluminum retention function that reflects changing glomerular filtration rates in infants
  • an adjustment for the kinetics of aluminum efflux at the site of injection
  • contemporaneous MRLs
  • the most recent infant body weight data for children 0–60 months of age
The determinations of the kinetics of aluminum retention by Priest [21,5] were based on experiments where human volunteers were given an intravenous injection of aluminum citrate. For vaccines, the injection is intramuscular, the aluminum is in an insoluble form (e.g., as the phosphate or hydroxide of aluminum), and muscle at the site of injection is considered to be a storage depot for aluminum. Over time the insoluble aluminum hydroxide or aluminum phosphate particles are solubilized by citrate ions in the interstitial fluids of muscle. After solubilization, the uptake and distribution kinetics of aluminum will likely be similar to the kinetics determined by the human volunteer studies. However, it is unlikely that the process of absorption from the site of intramuscular injection into the blood is instantaneous, as is assumed for intravenous exposures and as presumed by the retention functions used to generate Fig. 2 and by Keith et al. [1].

Flarend et al. [27] investigated the absorption into the blood of aluminum hydroxide and aluminum phosphate following intramuscular injection into New Zealand White rabbits. Two important observations were made in their experiments: (1) only a fraction of the injected aluminum was taken up from the site of injection into blood over the 28-day experimental period, and (2) absorption of neither adjuvant was instantaneous. Specifically, blood concentrations of aluminum hydroxide decreased to a minimum by the end of the experiment (reached a terminal phase), where as aluminum phosphate blood concentrations were relatively constant.
Disagreement Between Two Committees

Joint Expert Committee on Food Additives (FAO/WHO; 1989, 2011)

• 1989. Provisional Tolerable Weekly Intake (PTWI) established at 1 mg/kg all dietary sources and additives. Mean highest daily intake US children 0.5 mg Al/kg per day¹

• 2011. Previous PTWI of 1 mg Al/kg withdrawn. Revised PTWI to 2 mg/kg (adults)²

Agency for Toxic Substances and Disease Registry (ATSDR) CAS ID #: 7429-90-5 2008

• 2008 (CAS ID #: 7429-90-5)³

• Daily dietary intake of Al 2 mg/kg-day in adults

• Minimal Risk Level (MRL) 1 mg/kg-day (adults) same as No Observed Adverse Effect Level (NOAEL)


³Agency for Toxic Substances and Disease Registry (ATSDR) CAS ID #: 7429-90-5
ANIMAL STUDIES OF DOSE-RELATED ALUMINUM TOXICITY (DIETARY)

<table>
<thead>
<tr>
<th>Source/Dose</th>
<th>Animal (age)</th>
<th>Adverse Event(s)</th>
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<tbody>
<tr>
<td>ORAL</td>
<td></td>
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<tr>
<td>rats (adults)</td>
<td>230 mg Al/kg/day</td>
<td>erythropoiesis</td>
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<tr>
<td>rats (adults)</td>
<td>230 mg/kg/day</td>
<td>erythrocyte damage</td>
</tr>
<tr>
<td>mouse (dams)</td>
<td>230 mg/kg/day</td>
<td>increased susceptibility Infection</td>
</tr>
<tr>
<td>rats (pups)</td>
<td>54 mg/kg</td>
<td>delay in maturation</td>
</tr>
<tr>
<td>rats/mice (pups)</td>
<td>104 mg/kg/day</td>
<td>decrease in bw gain</td>
</tr>
</tbody>
</table>

Rats: Adult weight Males 300-500g, Females 250-300g Birth weight 5-6g
Mice: Adult weight Males 20-30 g, Females 18-35g Birth weight 1-2 g
How did 1 mg Al/kg/week become 1 mg/kg/day and 850 mcg per dose regardless of body weight

- 1981-CFR amended to include 1250 μg/dose
- 1996-2007 PTWI estimated at 1 mg/kg/week; 0.5 mg/kg-day US child > 2 years of age (WHO Evaluation and Certain Food Additives and Contaminants. Section 4.1 Aluminum, 1996-2007)
- 1996 Committee on Nutrition Aluminum Neurotoxicity in Infants and Children (J Pediatrics), “1” mg/kg-day (in error as to PTWI- “provisional tolerable intake”)
- 2001 850 μg "selected empirically from data because it enhances the antigenicity and effectiveness of the vaccine" (Baylor et al 2001)
- 2001-2008 ATSDR set MRL/NOAEL to 1 mg/kg/day from all sources based on Golub 26 mg/kg-day NOAEL (ATSDR references Baylor et al (2001),
- 2001 MRL/NOAEL 2 mg/kg-day in adult humans from dietary sources (Golub et al 2001; 62 mg/kg-day, Keith et al)
- 2011 MRL=1 mg/kg bw/day (ATSDR, 2008), Mitkus (2011)
- 2017: CFR is 850 μg/DOSE.
<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Aluminum Content (µg)* per dose</th>
<th>Birth</th>
<th>1 mo</th>
<th>2 mos</th>
<th>4 mos</th>
<th>6 mos</th>
<th>9 mos</th>
<th>12 mos</th>
<th>15 mos</th>
<th>18 mos</th>
<th>19-23 mos</th>
<th>2-3 yrs</th>
<th>4-6 yrs</th>
<th>7-10 yrs</th>
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<th>13-15 yrs</th>
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<tbody>
<tr>
<td>Hepatitis B1 (HepB)</td>
<td>250</td>
<td>1st dose</td>
<td>2nd dose</td>
<td>3rd dose</td>
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<td>Rotavirus2 (RV)</td>
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<td>RV1 (2-dose series); RV5 (3-dose series)</td>
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<td>Diphtheria, tetanus, &amp; acellular pertussis3 (DTaP, &lt;7 yrs)</td>
<td>625</td>
<td>1st dose</td>
<td>2nd dose</td>
<td>3rd dose</td>
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<tr>
<td>Haemophilus influenzae type b4 (Hib)</td>
<td>225</td>
<td>1st dose</td>
<td>2nd dose</td>
<td>3rd dose</td>
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<td>5th dose</td>
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<td>Pneumococcal conjugate5 (PCV13)</td>
<td>125</td>
<td>1st dose</td>
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<td>4th dose</td>
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<td>Annual vaccination (IIV only) 1 or 2 doses</td>
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<td>Meningococcal11 (Hib-MenCY ≥ 6 weeks; MenACYW-23 ≥ 2 mos; MenACWY-CRM ≥ 2 mos)</td>
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<td>Pneumococcal polysaccharide5 (PPSV23)</td>
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</table>

* Total ug not adjusted to ug/kg | 250 | 1225 | 975 | 1000 | 600 | 875 | | | | | | | | | | | |
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<th>Vaccine</th>
<th>Birth</th>
<th>1 mo</th>
<th>2 mos</th>
<th>4 mos</th>
<th>6 mos</th>
<th>9 mos</th>
<th>12 mos</th>
<th>15 mos</th>
<th>18 mos</th>
<th>19–23 mos</th>
<th>2-3 yrs</th>
<th>4-6 yrs</th>
<th>7-10 yrs</th>
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<th>13-15 yrs</th>
<th>16-18 yrs</th>
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"VACCINES DO NOT CAUSE AUTISM" - CDC
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<th>Vaccine</th>
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<th>Birth</th>
<th>1 mo</th>
<th>2 mos</th>
<th>4 mos</th>
<th>6 mos</th>
<th>9 mos</th>
<th>12 mos</th>
<th>15 mos</th>
<th>18 mos</th>
<th>18-23 mos</th>
<th>2-3 yrs</th>
<th>4-6 yrs</th>
<th>7-10 yrs</th>
<th>11-12 yrs</th>
<th>13-15 yrs</th>
<th>16-18 yrs</th>
</tr>
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<tbody>
<tr>
<td>*Total ug not adjusted to ug/kg</td>
<td></td>
<td>250</td>
<td>1225</td>
<td>975</td>
<td>1000</td>
<td>600</td>
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<tr>
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<td>Rotavirus2 (RV)</td>
<td>1st dose</td>
<td>2nd dose</td>
<td>3rd dose</td>
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<td>RV1 (2-dose series); RV5 (3-dose series)</td>
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<td>2nd dose</td>
<td>3rd dose</td>
<td>4-5th dose</td>
<td>5th dose</td>
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<td>125</td>
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<td>3rd dose</td>
<td>4-5th dose</td>
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<tr>
<td>Inactivated poliovirus5 (IPV&lt;18 yrs)</td>
<td>1st dose</td>
<td>2nd dose</td>
<td>4-3rd dose</td>
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<tr>
<td>Influenza7 (IIV, LAIV)</td>
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<td>Annual vaccination (IIV only) 1 or 2 doses</td>
<td>Annual vaccination (IIV only) 1 or 2 doses</td>
<td>Annual vaccination (IIV only) 1 or 2 doses</td>
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<td>Varicella5 (VARV)</td>
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<tr>
<td>Hepatitis A10 (Hepl A)</td>
<td>250</td>
<td>1st dose</td>
<td>2nd dose</td>
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<td>Meningococcal11 (Hi6b MenACYC, 6 weeks; MenACYW-C all mos, MenACYW-CRM&lt;2 mos)</td>
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<td>Tetanus, diphtheria, &amp; acellular pertussis (Tdap, &lt;7 yrs)</td>
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<td>Human papillomavirus13 (2HPV; females only, 2HPV, 9vHPV; males and females)</td>
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BW Corrected AL CFR/FDA Limits (Clark’s Rule)
BW-Informed FDA Dose Limits and Vaccine Exposures, Expressed as μg/kg, Birth through Adulthood
Calculated Pediatric MRL and the AL Exposures from DTaP Vaccine for Children (and Adults) using Clark's Rule to Accommodate Pediatric Body Weights (μg/kg, 2 months and Adult).
US Vaccine Aluminum Dose Accumulation and Pediatric Dose Limits (μg/kg IPAk 2017)
Males, 50th tile body weight
"So the level of aluminum in vaccines, however, is trivial. And you frankly ingest much more aluminum from either in the water that you drink, or anything made from water on this planet, and many of the foods that we eat contain quantities of aluminum far greater than you're ever going to get in vaccines."

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<thead>
<tr>
<th>Age-sex group</th>
<th>Aluminum intake (mg/day)</th>
<th>Aluminum intake (mg/kg)</th>
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<tr>
<td>6–11-Months</td>
<td>0.7</td>
<td>0.10</td>
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<tr>
<td>2-Years</td>
<td>4.6</td>
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<td>6-Years</td>
<td>6.5</td>
<td>0.30</td>
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<tr>
<td>10-Years</td>
<td>6.8</td>
<td>0.11</td>
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<tr>
<td>14–16-Years (females)</td>
<td>7.7</td>
<td>0.15</td>
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<td>14–16-Years (males)</td>
<td>11.5</td>
<td>0.18</td>
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Source: Pennington and Schoen 1995
# Pediatric Dietary Aluminum

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<th>Age</th>
<th>Aluminum intake (mg/day)</th>
<th>Aluminum intake (mg/kg-day)</th>
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<td>6 months – 1 year</td>
<td>0.7</td>
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<td>2 years</td>
<td>4.6</td>
<td>0.35</td>
</tr>
<tr>
<td>6 years</td>
<td>6.5</td>
<td>0.30</td>
</tr>
<tr>
<td>10 years</td>
<td>6.8</td>
<td>0.11</td>
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<table>
<thead>
<tr>
<th>Source</th>
<th>AI concentration</th>
<th>Daily AI exposure</th>
<th>Estimated percentage absorbed</th>
<th>AI absorbed daily (μg/kg)*</th>
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</tr>
<tr>
<td>Water</td>
<td>Average ~ 70 μg/l</td>
<td>100 μg</td>
<td>0.3 b</td>
<td>0.004</td>
</tr>
<tr>
<td>Food - total diet</td>
<td>3500-10,000 μg</td>
<td>1 μg</td>
<td>0.1 to 0.3 d</td>
<td>0.05-0.4</td>
</tr>
<tr>
<td>Air-office</td>
<td>0.15 μg/m³</td>
<td>1 μg</td>
<td>1 to 2 from lungs f</td>
<td>0.0002</td>
</tr>
<tr>
<td>Air-outside</td>
<td>0.2 - 1 μg/m³</td>
<td>4 μg</td>
<td>1 to 2 from lungs f</td>
<td>0.0003</td>
</tr>
<tr>
<td>Antiperspirants</td>
<td>5.75% i</td>
<td>50,000-75,000 μg</td>
<td>up to 0.012 j</td>
<td>up to 0.1</td>
</tr>
<tr>
<td>Vaccines, pediatric patient</td>
<td>125-330 μg/dose</td>
<td>1.4 μg</td>
<td>100 eventually l</td>
<td>0.07</td>
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<tr>
<td><strong>Elevated Exposures</strong></td>
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<tr>
<td>Antacids/phosphate Binders</td>
<td></td>
<td>up to 5,000,000 μg</td>
<td>0.1</td>
<td>80</td>
</tr>
<tr>
<td>Industrial Air</td>
<td>25-2500 μg/m³</td>
<td>250-25,000 μg</td>
<td>1 to 2 from lungs f</td>
<td>0.6-8</td>
</tr>
<tr>
<td>Allergy immunotherapy</td>
<td>150-850 μg/dose</td>
<td>7-40 μg</td>
<td>100 eventually l</td>
<td>0.1-0.6</td>
</tr>
<tr>
<td>Dialysis solution</td>
<td>If tap water 50 μg/l</td>
<td>2400 μg</td>
<td>25 n</td>
<td>9</td>
</tr>
<tr>
<td>Total Parenteral Nutrition Solutions</td>
<td>Neonatal/pediatric</td>
<td>9.23 μg/kg</td>
<td>100</td>
<td>9.23</td>
</tr>
<tr>
<td></td>
<td>Adult</td>
<td>1.5 μg/kg</td>
<td>100</td>
<td>1.5</td>
</tr>
<tr>
<td>Age-Sex group</td>
<td>Dietary Aluminum intake (mg Al/day)</td>
<td>Dietary Aluminum intake (mcg Al/kg)</td>
<td>Metabolically available (mcg Al/kg)</td>
<td>Vaccine (by schedule)</td>
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<tr>
<td>Birth</td>
<td>0.1</td>
<td>29</td>
<td>2.9</td>
<td>(HepB)</td>
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<tr>
<td>6-11 Months</td>
<td>0.7</td>
<td>100</td>
<td>10</td>
<td>(DTaP, HepB, HiB, PCV)</td>
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<tr>
<td>2-Years</td>
<td>4.6</td>
<td>350</td>
<td>35</td>
<td>(DTaP 18 month-remaining)</td>
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<tr>
<td>6-Years</td>
<td>6.5</td>
<td>300</td>
<td>30</td>
<td>(Tdap)</td>
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<tr>
<td>10-Years</td>
<td>6.8</td>
<td>110</td>
<td>11</td>
<td>(en,Tdap, HPV)-Age 11-12 yrs)</td>
</tr>
<tr>
<td>14-16-Years (females-48 kg)</td>
<td>7.7</td>
<td>150</td>
<td>15</td>
<td>(HPV-2nd dose)</td>
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<tr>
<td>14-16-Years (males-50 kg)</td>
<td>11.5</td>
<td>180</td>
<td>18</td>
<td>(HPV-2nd dose)</td>
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<td>Birth Dorea et al, 2015</td>
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<tr>
<td>6 mo-16yr Pennington and Schoen, 1995</td>
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</tbody>
</table>
**Metabolic Exposure AL From Various Sources**

- **Food**: Metabolic Exposure (ug/kg)
- **Water**: Adult
- **Men**: 0, 250
- **Women**: 0, 250

**Key Points**

- **125 μg/kg/day preterm**
- **108 μg/kg delay in maturation in rat pups**
Updated Maxims in Toxicology

• “The dose makes the poison.” – Paracelsus, 1538

• “Body weight makes the dose makes the poison.” – JLW, 2017

[Alle Dinge sind Gift und nichts ist ohne Gift, allein die Dosis macht es, dass ein Ding kein Gift ist. All things are poison and nothing is without poison, only the dosage makes a thing not poison "Die dritte Defension wegen des Schreibens der neuen Rezepte," Septem Defensiones 1538. Werke Bd. 2, Darmstadt 1965, p. 510]
US Vaccine Aluminum Dose Accumulation and Pediatric Dose Limits (μg/kg IPAK 2017) Males, 50th tile body weight

![Graph showing accumulations and MRL (μg/kg) for Males]

- *Intensity*
- *Repeatedness*
- *Duration of Exposure Matters*
senile plaque-like amyloid deposit

aluminum deposit
The science is clear: Vaccines are safe, effective, and do not cause autism

Johns Hopkins public health expert Daniel Salmon discusses vaccine safety and the potential hazards posed by fewer children being vaccinated.
“…first ever measurements of aluminium in brain tissue from 12 donors diagnosed with familial Alzheimer’s disease. The concentrations of aluminium were extremely high, for example, there were values in excess of 10 μg/g tissue dry wt. in 5 of the 12 individuals. Overall, the concentrations were higher than all previous measurements of brain aluminium except cases of known aluminium-induced encephalopathy.”

“we have previously recorded values up to ca 13.00 μg/g in AD with occupational exposure to aluminium [14] and one value of 23.00 μg/g in congophilic amyloid angiopathy (CAA) with environmental exposure to aluminium [13] the values measured herein for familial AD are more similar to those which have been associated with aluminium-induced encephalopathies”
Environmental Toxin Liability Sampling Theory

- Aluminum levels in vaccines are unsafe
- We need to Risk Factors + Biomarkers **Vaccine Safety Screening**

![Diagram showing various factors and biomarkers related to vaccine safety](image)

- PON1
- CHD7
- ADRB2
- ERAP1
- MTHFR
- CBS
- COMT
- Valproic acid
- Pregnancy-related stress
- thimerosal
- organophosphates
- particulate air pollution
- Pre/peri-natal vitamins
- Pre/peri-natal vitamins
Mean serum-level of common organic pollutants is predictive of behavioral severity in children with autism spectrum disorders

Andrew Boggess, Scott Faber, John Kern & H. M. Skip Kingston

Autism spectrum disorders (ASD), and their pathogenesis, are growing public health concerns. A study evaluated common organic pollutant serum-concentrations in children, as it related to behavioral severity determined by rating scales and the Autism Diagnostic Observation Schedule (ADOS).

Children ages 2-9, with ASD and thirty controls matched by age, sex, and socioeconomic status, were evaluated using direct blood serum sampling and ADOS. Pooling concentrations of all toxic pollutants into a single variable yielded cohort-specific neurobehavioral relationships. Pooled x concentration correlated significantly with increasing behavioral severity on the ADOS in the ASD cohort (p = 0.011, r = 0.54), but not controls (p = 0.60, r = 0.12). Logistic regression significantly correlated mean pollutant serum-concentration with the probability of diagnosis of behavioral severe autism, defined as ADOS > 14, across all participants. Odds ratio = 3.43 (95% confidence interval, 1.14–10.53).
Mean serum-level of common organic pollutants is predictive of behavioral severity in children with autism spectrum disorders

Andrew Bogges1, Scott Fohrer1, J. Koos2 & H. M. Skirring1

Autism spectrum disorders (ASD), autism phenotypes, are growing global health concerns. The study objective was to complement previous findings on the relationship between serum levels of common organic pollutants and behavioral severity in children with autism. The study aimed to investigate the concentration of key pollutants in children with ASD and controls. The results showed that the concentration correlated significantly with increasing behavioral severity in the ASD cohort (p < 0.05, r = 0.57). A multivariate regression analysis, controlling for sociodemographic factors, confirmed the significant association. Further studies are needed to elucidate the mechanisms linking these pollutants to behavioral outcomes in ASD.
Molecular mimicry

• Mothers of autistics have anti-fetal brain antibodies
• Autistics tend to have anti-brain antibodies

Many mothers report being vaccinated during pregnancy.
Specific Mechanisms

- Mitopathies
- Chronic Microglial Activation (Excitotoxicity)
- Channelopathies
- Molecular mimicry
- Encephalopathy

https://micro.magnet.fsu.edu/cells/endoplasmicreticulum/endoplasmicreticulum.html
Manuel F. Casanova, M.D.
Gottfried and Gisela Kolb Endowed Chair in Psychiatry
Vice Chair for Research
Department of Psychiatry
500 S Preston St Bldg 55A Ste 217
Louisville, Kentucky 40292-1702
Tel: 502-852-4077
Fax: 502-813-8665
E-mail: mocasao@louisville.edu

Biosketch
Dr. Manuel Casanova made his residency training in psychiatry at the Johns Hopkins Hospital. During his stay at the Johns Hopkins Hospital, his clinical experience was enhanced by appointment to the General Hospital. He spent several years as Deputy Director of the Mental Health Program and Child Abuse. His expertise in the field has led to his appointment as a Professor in the Department of Forensic Science. In this capacity, he has worked with the Johns Hopkins Brain Resource Center to identify over 5,000 cases of autism.

Dr. Casanova did his medical training at the University of Florida in 2003 as the Gottfried and Gisela Kolb Endowed Chair in Psychiatry. He later returned to his alma mater as a Medical Assistant Professor in 2006.

Research interests
Dr. Casanova has had over twenty years of experience in the study of abnormalities of cortical language. His work has shifted towards the study of abnormalities of cortical language. Using computerized tomography, he has identified differences in the morphology of the frontal lobe—the morphometric difference may play a role in the development of language and its disorders. His most recent studies have looked at the presence of abnormalities of minicolumnar organization and lateralization in the brains of patients who exhibit language disturbances, including autism, Asperger's syndrome, and dyslexia. He has summarized his work on minicolumns and provided an overview of the field in recent reviews of the literature appearing in Brain and Behavior.

Online resources
- Dyslexia and talent, presented at the Dyslexic Advantage Conference on Dyslexia and Talent, 2013 July 19
- Neurology Journals from The Lancet
- Cortical column article by Vernon B. Mountcastle at Scholarpedia
- Alopecia FAQ and coloring book
- Autism Retverse: A Literary Journey for the Autistic Mind

Figure 1. (A) The cortical section on the left is taken from a normal control patient, while the one on the right comes from an autistic patient. (B) The same image is shown overlaid with lines showing the columnar structure identified by our program. Both images contain three columns, but those in the control brain take up significantly more space than those in the other (67.8 µm v. 44.3 µm).
Early brain development in infants at high risk for autism spectrum disorder

Heather Cody Hazlett1,2, Hongbin Gu1, Brent C. Munsell1, Sun Hyung Kim1, Martin Styner1, Jason J. Wolff1, Jed T. Elson1, Meghan R. Swanson1, Hongtu Zhu1, Kelly N. Batteron1, D. Louis Collins1, John N. Constantino2, Stephen R. Dager3, Annette M. Estes2,3, Alan C. Evans1, Vladimir S. Fonov1, Guido Gerig1, Penelope Kostopoulos1, Robert C. McKinstry3,4, puli Pandey1,2, Sarah Paterson1, John R. Pratt Jr1, Robert T. Schultz2, Dennis W. Shaw1,3, Lonnie Zwaigenbaum1, Joseph Pine1,2 & the IBIS Network

Brain enlargement has been observed in children with autism spectrum disorder (ASD), but the timing of this phenomenon, and the relationship between ASD and the appearance of behavioural symptoms, are unknown. Retrospective head circumference and longitudinal brain volume studies of two-year olds followed up (see Methods for diagnostic and exclusion criteria). The three groups were comparable in mean race/ethnicity (85% white), family income, maternal age at birth (33 years old), infant birth weight (8 lb), and gestational age at birth (39 weeks). The HR-ASD group had more male children, the other two groups (83% of the HR-ASD group was male compared to...
Neocortical Laminar Layers
Early Transient -> Mature Terminal

High-resolution transcriptional profiling of rhesus monkey brain development
(Bakken et al., Nature 2016)
2007
Block&Hong, 2007
LPS

Chronic microglial activation and progressive dopaminergic neurotoxicity

PD (Parkinson's disease) is characterized by the selective and progressive loss of DA neurons (paleostriatal regions) in the substantia nigra. Inflammation and activation of microglia, the resident immune cells in the brain, have been strongly linked to neurodegenerative diseases, such as PD. Microglia can respond to immunological stimuli and neuronal death to produce a host of pro-inflammatory cytokines and ROS. In response to proper activation, microglia can also become persistently activated after a single stimulus and maintain the elevated production of both cytokines and ROS even after the initiating stimulus is gone. Current studies suggest that this chronic microglial activation may be fueled by either long-damaged neurons or autocrine and paracrine signals from local glial cells, such as oligodendrocytes. Here, we review proposed mechanisms responsible for chronic neuroinflammation and explain the interconnected relationship between chronic microglial activation, DA neuron damage, and neurodegenerative disease.

Abstract

Introduction

Microglia, the resident immune cells in the brain, are activated in response to neuronal
HOW VACCINE-INDUCED IMMUNONEUROEXCITOTOXICITY CAUSES AUTISM

1. Vaccines introduce mercury, aluminum
2. White blood cell pick up and deposit metals in brain and other organs
3. Microglial cell activation
4. Microglial change to amoeboid shape
5. Dendritic pruning and Apoptosis (NPCs)
6. Cytokine release
7. Excitotoxicity
8. Autism/ASD

Vaccines Introduce Aluminum, Mercury

WBCs

WBC’s Engulf, Deposit Metals in Organs

ASD

E

M

S

C

A

7

8
IOM 2004
“insufficient evidence exists”

IOM 2012:
Rejected 17/22 studies as flawed:

“The five remaining controlled studies (Farrington et al., 2001; Madsen et al., 2002; Mrozek-Budzyn et al., 2010; Smeeth et al., 2004; Taylor et al., 1999) contributed to the weight of epidemiologic evidence and are described below.”
“NO STUDY HAS EVER SHOWN”

- Analyze the data repeatedly until the positive association “goes away”
- Change the results post-peer review, post-publication, in plain site (Uno et al.)
- Use the most conservative method for multiple hypothesis testing (Bonferroni)
- Change the results post-peer review, post-publication, in plain site (Uno et al.)
- Use the most conservative method for multiple hypothesis testing (Bonferroni)
- Overfit the model using redundant, highly collinear variables
- Remove patients who are likely to have ASD features
- “Correct for” covariates related to ASD
- Reduce sample size to reduce power to detect association
- Change study design post facto to see if association can be lost
- Fail to report initial association
- Change continuous variables to discrete (cum. exposure -> “on time” vs. “late”)
Why Association Studies Mean **Nothing**

- “No association” → “Low power to detect”
- “No association” → “After we analyzed it 10 ways to make the association go away”
- “No association” → “After we removed all results showing no association”
- “No association” → “No Universal Effect”

Autism rates are between 0-3%.
<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Birth</th>
<th>1 mo</th>
<th>2 mos</th>
<th>4 mos</th>
<th>6 mos</th>
<th>9 mos</th>
<th>12 mos</th>
<th>15 mos</th>
<th>18 mos</th>
<th>19–23 mos</th>
<th>2-3 yrs</th>
<th>4-6 yrs</th>
<th>7-10 yrs</th>
<th>11-12 yrs</th>
<th>13-15 yrs</th>
<th>16-18 yrs</th>
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<tbody>
<tr>
<td>Hepatitis B (HepB)</td>
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<td>Rotavirus² (RV) RV1 (2-dose series); RVS (3-dose series)</td>
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<td>Diphtheria, tetanus, &amp; acellular pertussis¹ (DTaP; &lt;7 yrs)</td>
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<td>Haemophilus influenzae type b² (Hib)</td>
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<td>Pneumococcal conjugate³ (PCV13)</td>
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<td>Inactivated poliovirus⁴ (IPV; &lt;18 yrs)</td>
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<td>Influenza² (IV; LAIV)</td>
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<td>Measles, mumps, rubella⁴ (MMR)</td>
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<td>Varicella⁴ (VAR)</td>
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<td>Hepatitis A⁶ (HepA)</td>
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<td>Meningococcal⁷ (Hib-MenCY ≥ 6 weeks; MenACWY-D ≥9 mos; MenACWY-CRM ≥ 2 mos)</td>
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<td>Tetanus, diphtheria, &amp; acellular pertussis¹² (Tdap; ≥7 yrs)</td>
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<td>Human papillomavirus¹¹ (2v-HPV; females only; 4v-HPV; 9v-HPV: males and females)</td>
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<td>Meningococcal B¹⁶</td>
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<td>Pneumococcal polysaccharide⁶ (PPSV23)</td>
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"VACCINES DO NOT CAUSE AUTISM" - CDC
Environmental Exposures During Pregnancy

• Folic acid (prenatal vitamins)
• Mercury (Seafood [tuna/swordfish], Hg dental amalgams)
• Mold toxicity
• Roadside aluminum dust
• Glyphosate (RoundUp™)
• Vaccines
  • TDaP/DTaP – for whooping cough
  • Influenza vaccine w/thimerosal
  • Accidental MMR and others contraindicated during pregnancy
Potential Risk Factors/Biomarkers

- Antibrain protein antibodies
  Rossi et al., 2013; see Braunschweig et al., 2012
- Low immunoglobulin levels
  Grether et al. (2016)
- Parental age, income, %tile body weight, Vit D3, familial history, etc.

CHD7, CHD8, KATNAL2, SCN1A, SCN2A, MeCP2, AUTS2, NRXN1, MTHFS, CACNA1G, GRM5, GABA-β3 receptor subunit, MTCO1, MTCO2, SLC25A12, PIK3CA, GIRDIN, CNTN5, CNTN6, IMMMP2L, MCPH1, HOXA, microcephalin 1, GRIN2, GRIN2B, GRIN2A, GRIN2C, GRM7, CTNND2, CNTN4, NRXN1, PARK2, FOXP1, LAMC3, GluR6, GluR8, ARID1B, SETD2, BDNF, MAO-A, 5-HT2A serotonin receptor, PRKCB1, CD13, GRM3, HRAS, NRXN1, GNB2L1, MKNK2, OXTR
Vaccine Adverse Events in the NICU

Reports of increases in

• Sepsis evaluation
• Intubation
• SIDS
• Failure to Thrive
• “Sleep-related”
G x E Interactions
Bowers & Erickson (2014) Review

• Organophosphates <-> PON1 gene
• Pregnancy-related stress <-> ADRB2 gene
• Traffic-related particulate matter (pollution) <-> MET gene

• Periconceptional maternal prenatal vitamin <-> (MTHFR, CBS, COMT)

5,186 interactions of candidate genes in autism
Relevant Rulings, Regulations, and Law

• National Childhood Vaccine Injury Act (NVCIA) of 1986 42 USC 300aa-1 to 300aa-34

• Supreme Court Ruling “Unavoidably unsafe”

• 21st Century Cures Act

• Many regulations on Informed consent
Unanswered Questions from the Vaccine Injury Compensation Program: A Review of Compensated Cases of Vaccine-Induced Brain Injury

Mary Holland
NYU School of Law, hollandm@exchange.law.nyu.edu

Louis Conte
Robert Krakow
Lisa Colin

83 Instances of dx of autism in awarded cases
Family Law Trends

• “Midnight” invocation of vaccination refusal prior to custody decisions
• >300 State bills to remove non-medical exemptions
• Last-ditch vaccine concerns in custody (divorce)
  • Courts tend to side w/parent who claims they will vaccinate
• Attorney/Client relationship violated (El Paso, TX)

• Quiet regulatory shifts being explored
  • Moves to mandate vaccination for entry into preschool
  • (Obama HHS “Corrective Action”→ Region V states, esp. MI and OH)
Parental Refusal of Childhood Vaccines and Medical Neglect Laws

Efthimios Pasanidis, JD, MBioethics, and Douglas J. Opel, MD, MPH

**Objectives.** To examine the relation of vaccine refusal and medical neglect under child welfare laws.

**Methods.** We used the Westlaw legal database to search court opinions from 1905 to 2016 and identified cases in which vaccine refusal was the sole or a primary reason in a neglect proceeding. We also delineated if religious or philosophical exemptions from required school immunizations were available at the time of adjudication.

**Results.** Our search yielded 9 cases from 5 states. Most courts (7 of 9) considered vaccine refusal to constitute neglect. In the 4 cases decided in jurisdictions that permitted religious exemptions, courts either found that vaccine refusal did not constitute neglect or considered it neglect only in the absence of a sincere religious objection to vaccination.

**Conclusions.** Some states have a legal precedent for considering parental vaccine refusal as medical neglect, but this is based on a small number of cases. Each state should clarify whether, under its laws, vaccine refusal constitutes medical neglect. (Am J Public Health. 2017;107:68–71. doi:10.2105/AJPH.2016.303500)

Parental refusal of childhood vaccines is a contentious issue in pediatrics and result in harm to the child) constitute child maltreatment.

Reports solely based on failure to vaccinate, and Michigan has an explicit policy to this effect. A few states codify that vaccine refusal regardless of reason, or solely for sincere religious beliefs, does not constitute medical neglect. Furthermore, even if vaccine refusal amounts to medical neglect, it is not clear that this finding requires state intervention. Ross and Aspinwall contend that there should be a distinction between medical neglect and state intervention, arguing that vaccine refusal constitutes the former but does not warrant the latter. Chervenak et al. argue that the purpose of reporting parents who refuse childhood vaccines to CPS for neglect is not to provoke “highly intrusive measures,” such as loss of custody, but to “engage [CPS] in further efforts to persuade the parents.” Simply invoking CPS, however, may undermine parents’ views of
Thimerosal: Everything you need to know about this vaccine preservative

By Jan Christensen, CNN
(Updated 7:30 AM ET, Wed, February 15, 2007)

The science is clear: Vaccines are safe, effective, and do not cause autism

Johns Hopkins public health expert Daniel Salmon discusses vaccine safety and the potential hazards posed by fewer children being vaccinated

Childhood vaccines are safe. Seriously.

By Jen Christensen and Heidi Kimura, CNN
(Updated 2:49 PM ET, Fri, August 7, 2015)

Should I get my child vaccinated? (Q&A)

Children should get vaccinated against preventable and potentially deadly diseases. Period.

That's what a panel that reviewed more than 20,000 scientific studies and 17 papers on vaccine safety
Merck Fraud on Efficacy?
brings this action against Merck & Co., Inc. (“Merck” or “Defendant”), and alleges as follows, based on information and belief, counsel’s investigation, and a qui tam action filed by Stephen A. Krahling and Joan A. Wlochowski (the “Relators”) captioned Krahling v. Merck & Co., Inc., 2:10-cv-04374-CDJ (E.D. Pa.) (the “Qui Tam Action”):

INTRODUCTION

1. Merck is the exclusive supplier of mumps vaccine (including M-M-R®II and ProQuad®) (collectively, “Mumps Vaccine”) in the U.S.

2. This lawsuit is brought as a proposed class action against Merck for unlawfully monopolizing the U.S. market for Mumps Vaccine by engaging in a decade-long scheme to falsify and misrepresent the true efficacy of its vaccine.

3. Specifically, Merck fraudulently represented and continues to falsely represent in its labeling and elsewhere that its Mumps Vaccine has an efficacy rate of 95 percent or higher.
In reality, Merck knows and has taken affirmative steps to conceal -- by using improper testing techniques and falsifying test data -- that its Mumps Vaccine is, and has been since at least 1999, far less than 95 percent effective.

4. Merck manufactures its Mumps Vaccine using an attenuated virus. An attenuated virus is created when its pathogenicity has been reduced so that it will initiate an immune response without producing the specific disease. Pathogenicity is reduced by “passaging” the virus through a series of cell cultures or animal embryos. With each passage, the virus becomes better at replicating in the host, but loses its ability to replicate in human cells. Eventually, the attenuated virus will be unable to replicate well (or at all) in human cells, and can be used in a vaccine. When this vaccine is administered to a human, the virus in it will be unable to replicate enough to cause illness, but will still provoke an immune response that can protect against future infection.

5. However, Merck knew and understood that the continued passaging of the
2 Whistleblower Allegations:

• Tried 2 flawed methodologies to show >95%
• Both failed. Falsified efficacy (ADDED Rabbit Antibodies)
• Submitted falsified efficacy results to FDA.
• Concealed fraud
• Continue to conceal fraud after mumps outbreaks in 2006, 2009
• Sold hundreds of millions of vials of ineffective vaccine
AP Explains: Why there’s a US surge in mumps despite vaccine
AP Explanation:

• “No vaccine is perfect and it's expected that some people who get the shots will still get mumps. Also, some research suggests that 10 or more years after the second dose, immunity may fade enough to allow outbreaks to take hold. During some outbreaks, like one currently at the University of Missouri, students and others have been offered a third booster dose to increase protection and snuff out the outbreak.”

• “Congress shall make no law respecting an establishment of religion, or prohibiting the free exercise thereof; or abridging the freedom of speech, or of the press; or the right of the people peaceably to assemble, and to petition the Government for a redress of grievances.”

• In late 2016, in response to a Notice from CDC Posted in the Federal Register, Vol. 81, No. 201 of Tuesday, October 18, 2016 for a call for public comments re: Proposed Revised Vaccine Information Materials for MMR (Measles, Mumps, and Rubella and MMRV (Measles, Mumps, Rubella, and Varicella Vaccines)…
Public Comments: MMR and MMR-V VIS Experience (2016/2017)

• Proposed weakening the information on risk

• Call for Public Comments

• Anyone can access the comments
Comment by Dr. James Lyons-Weiler and Bernadette Pajer

Re: Docket Number CDC-2016-0004
Proposed Revised Vaccine Information Materials for MMR (Measles, Mumps, and Rubella) and MMRV (Measles, Mumps, Rubella, and Varicella) Vaccines
Federal Register October 18, 2016
Dec 15, 2016

We are providing this in response to the CDC’s request for public comment.

Summary of our position: The proposed Vaccine Information Statements (VISs) do not provide individuals sufficient information necessary for them to give fully informed consent, the legal agreement between an individual and a physician, first introduced by the Nuremberg Code, and outlined in the Cauterbury decision of 1972, and subsequent rulings, regulations, and laws governing informed consent requirements. (HEALTH LAW: Informed Consent: What Must a Physician Disclose to a Patient? American Medical Association Journal of Ethics, July 2012, Volume 14, Number 7: 562–565)

The steady erosion of informed consent by Congress and CDC in regards to vaccination reached a low point with the recent passage of the 21st Century Cures Act which included unprecedented expansion of informed consent waivers and extension of product liability exemptions (sections 302A, 5001A, 5092, 2001). However, informed consent and other patient rights are still protected under other rules and regulations.

The efficacy and safety of Merck’s MMR and MMRV vaccines are currently under intense scrutiny. Former Merck employees and virologists Stephen A. Krahling and Joan A. Watahcefski filed a suit against Merck in 2016, alleging fraud in vaccine testing (see complaint here). Merck delayed the suit for years, but the court has now ordered that discovery be completed by March 2017 (Former Merck Scientists Sue Merck Alleging MMR Vaccine Efficiency Fraud)

Further, CDC senior scientist Dr. William Thompson has filed for whistleblower status, presented 10,000 documents to Congressman Bill Posey, and confirmed that the Delwiche et al. (2006) study deleted positive association results between in utero vaccination and autism diagnosis for both African American Male and for Isolated Autism subgroup analyses (Statement of William W. Thompson, Ph.D., Regarding the 2004 Article Examining the Possibility of a Relationship Between MMR Vaccine and Autism). The data removed from the study would support a causal link between the timing of the administration of the MMR vaccine and autism. Jason Chaflitte of the House Oversight Committee has begun investigating (Union Chaflitte video speaking on CDC & Thompson investigation)

With the integrity, effectiveness, and safety of the MMR/MMR-V currently in question and the subject of much public controversy, revising the VISs at this time is absolutely critical in order to inform the stakeholders that the effectiveness and safety are currently unknown and under investigation. The draft presented here for consideration fail to mention this critical information.
Comment by Dr. James Lyons-Weiler and Bernadette Pajer

Re: Docket Number CDC-2016-0004
Proposed Revised Vaccine Information Materials for MMR, (Measles, Mumps, and Rubella) and MMRV (Measles, Mumps, Rubella, and Varicella) Vaccines
Federal Register October 18, 2016

Dec 15, 2016

We are providing this in response to the CDC's request for public comment.

Summary of our position: The proposed Vaccine Information Statements (VISs) do not provide to individuals sufficient information necessary for them to give fully informed consent, the legal agreement between an individual and a physician, first introduced by the Nuremberg Code and outlined in the Cantiney decision of 1972, and subsequent rulings, regulations, and laws governing informed consent requirements. (ATAA's Information: What Must a Physician Disclose to a Patient? American Medical Association Journal of Ethics, July 2012, Volume 14, Number 7: 561-566)

The steady erosion of informed consent by Congress and CDC in regards to vaccination reached a low point with the recent passage of 21st Century Cures Act which included unprecedented expansion of informed consent waivers and extension of product liability exemptions (sections 3024, 3091, 3092, 3093). However, informed consent and other patient rights are still protected under other rules and regulations.

The efficacy and safety of Merck's MMR and MMRV vaccines are currently under intense scrutiny

[Redacted]

With the integrity, effectiveness, and safety of the MMR/MMR-V currently in question and the subject of much public controversy, reviewing the VIS's at this time is absolutely critical in order to inform the stakeholders that the effectiveness and safety are currently unknown and under investigation. The facts presented here for consideration fail to mention this critical information.
The regulatory vacuum has led to rampant, perhaps willful, ignorance, as evidenced by such documents as the AAP’s "Countering Vaccine Hesitancy" guide, with unsupported statements such as:

"The opposition to the presence of aluminum as an adjuvant in some vaccines can be addressed by providing evidence for both the necessity of the aluminum for a vigorous immune response and the lack of evidence for its toxicity."

We encourage AAP, Congress, and CDC to read the literature on aluminum neurotoxicity:


Ignorance of the actual risks involved has also led to publication of an article by an academic individual in the New England Journal of Medicine contemplating the usefulness and best ways to coerce patients into accepting vaccines (Colgrove, 2016):

"Both persuasion and coercion are necessary, and neither is sufficient. Laws serve as a critical safety net as well as a powerful symbolic statement of proimmunization social norms."


Coercion of patients into medical practices and experimentation has NOT been the accepted societal norm since the practices of Dr. Mengele, the Nazi doctor who tricked children into
Lyons-Weiler & Pajer

Rebuttal to Reiss Comment

Page 1 of 11

Rebuttal to the comment by Dorit Reiss
By Dr. James Lyons-Weiler, PhD and Bernadette Pajer

Re: Docket Number CDC-2016-0094
Proposed Revised Vaccine Information Materials for MMR (Measles, Mumps, and Rubella and MMRV (Measles, Mumps, Rubella, and Varicella) Vaccines
Federal Register October 18, 2016

While we have provided our remarks on CDC’s draft VIS revisions in a separate comment (Comment Tracking Number 1k0-8tlr-fn92), we are providing this rebuttal in response to the comment of Dorit Reiss with deep concern on the incorrectness of some of her points. [Blacked out]

Ms. Reiss’s comment can be found here: https://www.regulations.gov/document?D=CDC-2016-0094-0151
Lyons-Weiler & Pajer

Rebuttal to Reiss Comment

Page 1 of 11

Rebuttal to the comment by Dorit Reiss
By Dr. James Lyons-Weiler, PhD and Bernadette Pajer

Re: Docket Number CDC-2016-0094
Proposed Revised Vaccine Information Materials for MMR (Measles, Mumps, and Rubella and MMRV (Measles, Mumps, Rubella, and Varicella) Vaccines
Federal Register October 18, 2016

While we have provided our remarks on CDC’s draft VIS revisions in a separate comment (Comment Tracking Number 1k0-8thr-fn92), we are providing this rebuttal in response to the comment of Dorit Reiss with deep concern on the incorrectness of some of her points. Ms. Reiss is a professor at a school of law and as such her comments may be taken as fact by those who do not take the time to verify them. Unfortunately, many of her claims of fact are demonstrably incorrect. Her employer is affiliated with the University of California, which for many endeavors is in partnership with Kaiser Permanente, which in turn is in partnership with Merck, the manufacturer of MMR and MMRV. Ms. Reiss has elsewhere disclosed personal conflicts of interest via family ownership of stock in at least one vaccine-manufacturing company. While these types of affiliations and partnerships are not unusual and are not proof of influence, Ms. Reiss uniformly and very actively takes positions on vaccine law and policy that favor vaccine manufacturers and restrict medical freedom of choice. (http://www.uchastings.edu/faculty/reiss/)

Ms. Reiss’s comment can be found here: https://www.regulations.gov/document?D=CDC-2016-0094-0151
Further Redaction

• “Dr. William Thompson, one of the researchers on the DeStefano et al study, mentioned above, came forward in 2014 as a whistleblower on this study, stating results that did, in fact show a causal link between the timing of the administration of the MMR and autism were removed prior to presentation of the results to the IOM.”

(This study was one of the 17/22 rejected by the IOM, but was used to deny settlements for autism in the Omnibus hearings)
Reiss claims:

"The VIS both mentions “permanent brain damage” and “long term seizures” as “severe and very rare problems following MMR vaccines.” However, recent studies do not support a link between MMR and encephalitis or brain damage, and to my knowledge, not to seizures, either. See: http://pediatrics.aappublications.org/content/early/2015/01/01/peds.2014-1822"

Rebuttal: Ms. Reiss’s citation disproves her claim:

“BACKGROUND AND OBJECTIVES: All measles-containing vaccines are associated with several types of adverse events, including seizure, fever, and immune thrombocytopenia purpura (ITP). Because the measles-mumps-rubella-varicella (MMRV) vaccine compared with the separate measles-mumps-rubella (MMR) and varicella (MMR + V) vaccine increases a toddler’s risk for febrile seizures, we investigated whether MMRV is riskier than MMR + V and whether either vaccine elevates the risk for additional safety outcomes.” (emphasis added)

The study results showed:

“Compared with MMR + V, MMRV increased risk of seizure and fever 7 to 10 days after vaccination.” (emphasis added)

This was not a vaccinated verses non-vaccinated study; it was a study that only compared outcomes for those vaccinated with MMRV versus those vaccinated with MMR + V.
The regulatory vacuum has led to rampant, perhaps willful, ignorance, as evidenced by such documents as the AAP's "Countering Vaccine Hesitancy" guide, with unsupported statements such as:

"The opposition to the presence of aluminum as an adjuvant in some vaccines can be addressed by providing evidence for both the necessity of the aluminum for a vigorous immune response and the lack of evidence for its toxicity."

We encourage AAP, Congress, and CDC to read the literature on aluminum neurotoxicity:


Ignorance of the actual risks involved has also led to publication of an article by an academic individual in the New England Journal of Medicine contemplating the usefulness and best ways to coerce patients into accepting vaccines (Colgrove, 2016):

"Both persuasion and coercion are necessary, and neither is sufficient. Laws serve as a critical safety net as well as a powerful symbolic statement of proimmunization social norms."


Coercion of patients into medical practices and experimentation has NOT been the accepted societal norm since the practices of Dr. Mengele, the Nazi doctor who tricked children into
Informed Consent

**Required** at two levels, every patient, every procedure:

(1) Acceptance of a medical procedure based on complete information on benefits & risks

(2) Participation in a clinical trial after being provided complete information on benefits & risks.
Most of the studies conducted on vaccine safety rely on post-marketing surveillance using weak “association studies” with data from passively collected data sources (such as VAERS). Patients are not informed that they, or their children are, in fact, participating in a large, shoddily-run, non-randomized retrospective clinical trial. This practice is widespread, and violates provisions of the National Research Act [Title II, Public Law 93-348], Regulations for the Protection of Human Subjects of Biomedical and Behavioral Research [45 CFR 46] and revisions of various regulations, rules, and laws ([21 CFR 50, [21 CFR 56], [45 CFR 46 Subpart D], [10 CFR 745]. Pregnant women and fetuses are afforded special protections by [45 CFR 46 Subpart B], and children are afforded additional protections by [45 CFR 46 Subpart D]. Yet the rights of pregnant women and fetuses are violated with each and every vaccine administered to them because not only is there a paucity of pre-licensing clinical trials, no vaccine is actually licensed for use to protect fetuses, and pregnant women are not told any of this as they are pressured to get vaccinated. (FDA: Vaccines For Use in Pregnancy)

Of note, in the Common Federal Policy for the Protection of Human Subjects ("Common Rule") [10 CFR 745] Sec 745.103(b)(3), none of these rights were revoked by any subsequent legislation, including [21 CFR 50.24], which allows the relaxation of requirements for informed consent during emergencies. In fact the Common Rule re-asserted safeguards both for informed consent, and for special protections against coercion:

§46.116 General requirements for informed consent.

Except as provided elsewhere in this policy, no investigator may involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally sufficient, properly witnessed, informed consent of the subject. [10 CFR 745.103(b)(3)]
Failure to Secure Informed Human Subject Research Consent

National Research Act [Title II, Public Law 93-348]
Regulations for the Protection of Human Subjects of Biomedical and Behavioral Research [45 CFR 46] et sub
Revisions of various regulations, rules, and laws ([21 CFR 50, [21 CFR 56], [45 CFR 46 Subpart D], [10 CFR 745].

**Pregnant women and fetuses are afforded special protections** [45 CFR 46 Subpart B]
Children are afforded additional protections [45 CFR 46 Subpart D].

The human rights of pregnant women and fetuses are violated with each and every vaccine administered to them because not only is there a paucity of pre-licensing clinical trials, no vaccine is actually licensed for use to protect fetuses, and pregnant women are not told any of this as they are pressured to get vaccinated.

Common Federal Policy for the Protection of Human Subjects ("Common Rule")

[10 CFR 745] Sec 745.103(b)(3), none of these rights were revoked by any subsequent legislation, including [21 CFR 50.24], which allows the relaxation of requirements for informed consent during emergencies. In fact the Common Rule re-asserted safeguards both for informed consent, and for special protections against coercion:

§46.116 General requirements for informed consent.
Except as provided elsewhere in this policy, no investigator may involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence.
The information that is given to the subject or the representative shall be in language understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

“When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.”
Scale of Injuries

• >$US 3Billion Paid out via Special Masters Court for vaccine injuries

• Supreme Court ruled vaccines “unavoidably unsafe”

• Vaccine Court has limited recognition of vaccine injuries, allowing encephalopathy, specifically excluding “autism”
Excerpt from “Cures vs. Profits”:

Why would the CDC publish such a page in 2014, a full ten years after the study?

In 2014, one of the authors of the CDC study, Dr. William Thompson, Ph.D., was recorded by one Dr. Hooker. Dr. Hooker had allegedly spent 10 years since the CDC study petitioning for access to the entire data behind the study.

In the interview, Dr. William Thompson is heard making the following statements:

“Oh my God, I cannot believe we did what we did. But we did. It's all there.”

"The higher-ups wanted to do certain things and I went along with it."

“It was the lowest point in my career that I went along with that paper. And I went along with this, and didn't report significant findings”

“I have great shame now when I meet families with kids with autism because I’ve - I’ve been part of the problem.”
CDC Whistleblower Dr. William Thompson

• Hired Whistleblower lawyer re-asserting that YES, they removed results
• Was suspended prior to the IOM report for informing then-director Julie Gerberding

• My independent analyses of reveal many repeated instances of
  • Analysis-to-result
  • Changes to study design
  • Wrongful exclusion
  • Model overfit
  • Obvious misinterpretation
Typical Moderate or Serious Adverse Event Experience

“It is common practice for office staff to reassure parents over the phone that a vaccine reaction is normal, expected, and not any cause for concern. They generally recommend Tylenol for the pain and fever, but won't advise an in-person medical evaluation. This may be proper procedure for mild reactions like fussiness, moderate fever, and mild swelling and redness at the injection site. But all moderate to severe reactions, like hives, lethargy, seizures, fever of 105 degrees, or inconsolable crying lasting 3 hours or more (encephalitis), warrant prompt in-person medical attention.”
Encroachments

- Product mislabeling
- Possible fraud (Merck)
- Failure to consider all of the science (CDC)
- Denial of Informed Consent (2 levels)
  - Changing conversation from risk to efficacy
  - 21st Century Cures Act
- Overt calls for **coercion**
- Denial of rights to public services
- Denial of access to medical care
- Job Loss
- Overt calls for Denial of 1st Amendment Rights
- Censorship of American Citizens
Implications of the “Recipe”

- A large component of consumer demand for flu vaccination is contingent upon things we can’t control (e.g., timing, severity, extent, duration of the disease and resulting illness).

- Fostering demand, particularly among people who don’t routinely receive an annual influenza vaccination, requires creating concern, anxiety, and worry. For example:
  - A perception or sense that many people are falling ill;
  - A perception or sense that many people are experiencing bad illness;
  - A perception or sense of vulnerability to contracting and experiencing bad illness.

SAFER • HEALTHIER • PEOPLE™
“The decision to dismiss a family who continues to refuse immunization is not one that should be made lightly, nor should it be made without considering and respecting the reasons for the parents’ point of view,” the report states. “Nevertheless, the individual pediatrician may consider dismissal of families who refuse vaccination as an acceptable option.”
Rules and Regulations on Informed Consent


• Ignorance of the actual risks involved has also led to publication of an article by an academic individual in the New England Journal of Medicine contemplating the usefulness and best ways to coerce patients into accepting vaccines (Colgrove, 2016):

  • “Both persuasion and coercion are necessary, and neither is sufficient. Laws serve as a critical safety net as well as a powerful symbolic statement of proimmunization social norms.”

Legally Censoring Speech on Vaccines and Autism: A Response

Friday 11 December 2015 at 8:52 AM ET

JURIST Guest Columnist Mary S. Holland from the New York University School of Law discusses the legality of censoring speech on vaccines and autism...
Manipulation of the Perception of Risk without Actually Minimizing Risk
Review and Challenges...

- Autism is no more than 50% genetic, and at least 50% environmental.
- Vaccines contribute to total load, and contribute to mitopathies, channelopathies, chronic microglial activation, encephalopathy, and many NDs, including autism.
- **Research is needed on causes of increased CNVs.**
- **Either/or thinking is not helpful. Think Synergy + Interactions.**
- Vaccines **must** be made more safe: **Ethical Vaccinomics.**

- Cost of vaccines in terms of NDs and lifelong suffering and death are not sufficiently determined.
- **Coercion, and attempts to use the law to silence the minority viewpoint are the tools of tyrants, and have no place in our society.**
Challenges

• Need to re-cast research on neurodevelopment disorders completely
  • -it’s not ‘in their heads’
  • behavioral intervention alone will only frustrate
  • genetic information can guide (Genes MATTER)
  • Diet and supplements MATTER
  • Environmental exposures MATTER
  • Vaccines MATTER
  • Detoxifying Kids MATTERS

• Recognize that Vaccine risk denialism
  • Reduces vaccine uptake
  • Hurts children (has been preventing prevention)
  • Has prevented research on interventions
  • Polarizes society
  • Pits pediatricians against parents
  • Protects major income streams – for now
Disease: Cystitis * Deafness * DEATH * Dementia * Demyelization * Development Delay
* Diabetes * Diarrhea * Dizziness * Throbbing in Ear * Earache * Eczema * Eczema Vaccinatium * Encephalitis * Encephalomyelitis * Encephalopathy * Epilepsy * Erythema
* Multiform Fatigue * Fever * Fibromyalgia * Flu * Guillain barre syndrome (GBS) * Gulf War Syndrome * Hallucinations * Headache * Heart attack * Hemolytic anemia * Herpes Zoster * Hib Disease * High Blood Pressure * High-Pitched Screaming * Hives
* Hyperactivity * Hypotension * Hypotonic/ Hypo responsive Immune system problems
* Indurations * Inflammatory Bowl Disease * Influenza accidental/inadevent * Insomnia*
* Moneuropathy * Multiple Sclerosis * Mumps * Muscle Aches * Myopericarditis * M
* Neurological Damage * Neuropathy * Nodules * Optic Neuritis * Orchitis *
* Media(inner ear infection) * Pain at Injection Site (unusual or prolonged)
* Pervasive Development Disorder (P.D.D) * Polio * Polyneuropathy * Prolonged *
* Psychotic Behavior * Radiculoneuritis * Rash * Redness at the Injection Site * Reg *
* Respiratory Distress * Respiratory Infection * Retinal Hemorrhage * Retinitis *
* Rosella * Rubella * Sensory Processing Disorder (SPD) * Schizophrenia * Screaming *
* Seizure * Seizure Disorder * Sepsis * Shaken Baby Syndrome (SBS) * Sudden Infant Death Syndrome (SIDS) * Shingles * Shock * Shortness of Breath * Skin Disorders * Sleepiness
* Small pox * Sore arms * Sore throat * Stiff neck * Stroke * Sub acute Sclerosing Pain * SV-
* 40 related Cancer * Sweating * Swelling at the Injection Site * Swollen Lymph Nodes
* Tenderness, localized * Thrombocytopenia * Transverse myelitis * Urticaria * Vaccinia
* Violent Behavior * Vomiting * Weakness

$3.4B
Vaccine Risk Awareness 2017

MEDICAL EXEMPTIONS.... WAIVERS... RIGHTS TO INFORMED CONSENT...

"Anti-Vax" "Refusniks"

Marketing

CDC

RX
A Media Guide to Vaccine Risk Awareness

• Anti-vax: “I want to ban all vaccines. Vaccines can never be made safer.”

• VRA: “Vaccine risk is real, and should be minimized.”

If you believe those who are injured are "Anti-Vaccine", do you also believe those injured by faulty brakes are "Anti-Brake"?
- Dr. Toni Bark, MD
Professional Responsibility and Early Childhood Vaccination
Frank A. Chervenak, MD, Laurence B. McCullough, PhD, and Robert L. Brent, MD, PhD, DSc (Hon)

The recent outbreaks of measles and other childhood infectious diseases in the US and other countries have garnered considerable public attention and prompted controversy about early childhood vaccination. A newcomer to this controversy would be for thinking that there is a scientific and ethical basis for controversy about the professional responsibilities of physicians regarding early childhood vaccination. For example, there are reports of physicians stating publicly that they have not authorized vaccination of their own children. At least 1 physician who holds federal elected office and is an announced Republican Party candidate for the nomination to become president of the US, Senator Rand Paul of Kentucky, has stated that parents’ refusals of vaccination should be respected by physicians and the government. Andrew Wakefield, a former physician who has been eliminated from the General Register in the United Kingdom, fabricated data supporting a connection of the measles vaccine to autism, in a paper that was formally withdrawn.

The safety and effectiveness of early childhood vaccination are well established. In response to the recent measles outbreaks, the American Academy of Pediatrics has recently released a statement urging parents to have their children vaccinated. This article, using the professional responsibility model of pediatric ethics, we address the ethics of early childhood vaccination, including counseling parents, the physician’s public role, and implications for policy makers.

Parental Refusal of Childhood Vaccines and Medical Neglect Laws
Ethinoula Panidis, JD, MPhil, and Douglas J. Opel, MD, MPH

Objective. To examine the relation between vaccine refusal and medical neglect under child welfare laws.

Methods. We used the Westlaw legal database to search court opinions from 1995 to 2016 and identified cases in which vaccine refusal was the sole or a primary reason in a neglect proceeding. We also delineated if religious or philosophical exemptions from required school immunizations were available at the time of adjudication.

Results. Our search yielded 9 cases from 5 states. Most courts (7 of 9) considered vaccine refusal to constitute neglect. In the 4 cases decided in jurisdictions that permitted religious exemptions, courts either found that vaccine refusal did not constitute neglect or considered it neglect only in the absence of a sincere religious objection to vaccination.

Conclusions. Some states have a legal precedent for considering parental vaccine refusal as medical neglect, but this is based on a small number of cases. Each state should clarify whether, under its laws, vaccine refusal constitutes medical neglect. (Am J Public Health. 2017;107:68-71. doi:10.2105/AJPH.2016.303500)

Parental refusal of childhood vaccines is a contentious issue in pediatrics and result in harm to the child constitute child maltreatment.
Contempt for Safety, or Blinded by Profits?

• Pharma: >$30Billion/year from vaccines – no liability for faulty products

• Media: DTC Marketing #1 source of revenue

• Medical establishment
Genetically Susceptible Subgroup(s)

- Individual risk
- Identifiable risk

Sharyl Attkisson is an investigative correspondent for CBS News.

Perhaps the most puzzling thing about autism and ADD is that more than a decade into this public health crisis, our best, smartest government scientists and public health officials still say they have no idea what’s causing it. Scary stuff, when parents having a child today realize there’s at least an estimated 1 in 150 chance their child will have an autism disorder (1 in 90 if it’s a boy).

While the government has been utterly unable to stop it, or even tell us what is causing it, they say they do know one thing: it’s not vaccines. But today, in an exclusive interview with CBS News, Dr. Bernadine Healy becomes the most well-known medical voice yet to counter the government on that claim.
Sharyl Attkisson (2008) on Healy:

• The more she dug, she says, the more she came to believe the government and medical establishment were intentionally avoiding the question because they were afraid of the answer.

• Why? Healy says some in the government make the mistake of treating vaccines as an all-or-nothing proposition. The argument goes something like this: everybody gets vaccinated at the same time with the same vaccines or nobody will get vaccinated and long-gone deadly diseases will re-emerge. (When I asked about cases of brain damage resulting in autism that have been quietly compensated by the government in vaccine court over the years, one government official recently told me that "it's still better overall to get vaccinated than not to get vaccinated.")

• Healy says the argument need not be framed in those terms (vaccinate or don't vaccinate). Instead, she says, we should vaccinate, but work to do it in the safest manner possible based on what we know and what we can find out.
The Future of Artificial Immunization

• Screen for **unsafe** epitopes
• Use **more** antigen
• Use far less, or NO aluminum or mercury
• Deliver to the proper tissue
  • to activate dendritic cells
• RCT’s, not correlation studies
• Compare Schedules
• **Actively** track, report, study injuries
Genetically Susceptible Subgroup

• Individual risk
• Identifiable risk

NEURODEVELOPMENT RESEARCH REFORM

2017
Neurodevelopment Research 2017+

Program 1. Neurodevelopmental Treatment, Therapy and Prognosis (NTTP)
Program 2. Neurodevelopmental Biomarkers of Patient-Specific Risk (NSRB)
Program 3. Neurodevelopmental Differential and Integrative Diagnosis (NDIDB)
Program 4. Neurodevelopmental Predictive Medicine Analysis (NPMA)
Program 5. Medico-Education of Neurodivergent Americans (MENA)
Program 6. Medical Education Vaccine Training Reform (MEVTR)
Program 7. Neurodevelopmental Philosophy and Bioethics (NPAB)
## TABLE 4. EXAMPLES OF POSSIBLE FUTURE TREATMENTS OF AUTISM BY PHENOTYPE

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aggression</td>
<td>Aripiprazole</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Fecal matter transplants, vancomycin</td>
</tr>
<tr>
<td>Language delay/loss</td>
<td>Adenosine receptor agonists</td>
</tr>
<tr>
<td>Microglial activation</td>
<td>Amantadine, luteolin, cannabinoids, many others</td>
</tr>
<tr>
<td>Renal peptiduria</td>
<td>Vitamin E, selenium</td>
</tr>
<tr>
<td>Repetitive Motor</td>
<td>Fluoxetine, risperidone, adenosine receptor agonists</td>
</tr>
<tr>
<td>Seizures</td>
<td>Carbamazepine, ketogenic diet</td>
</tr>
<tr>
<td>Social</td>
<td>Oxytocin, tetrahydrobiopterin (cofactor BH4)</td>
</tr>
</tbody>
</table>

### Gene-Directed Treatment Examples

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitochondrial dysfunction</td>
<td>Carnitine, various drugs</td>
</tr>
<tr>
<td>SCN1A (serotonin)</td>
<td>Clonazepam (microdoses)</td>
</tr>
</tbody>
</table>
Legal Issue: Equal Protection??

75-97%
No or truly minimal risk

3-25%
IDENTIFIABLE (Biomarkers)

I'm Not Misbehaving
I Have Autism...
Please Be Understanding

WE CAN DO BETTER!
Do you think it's better to live in stupefying security... or to take risks and live life on the edge?

I think it's better to accept danger and live to the fullest!

I take it by your silence that you agree...
Citations

• >1,000 at envgencauses.com
Figure 3. (A) Old vs. New surveys of incidence/prevalence of various autoimmune diseases. (B) The list of various diseases in specific countries and the years’ ranges

<table>
<thead>
<tr>
<th>Disease</th>
<th>Countries</th>
<th>Survey</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA</td>
<td>Canada</td>
<td>1995-2010</td>
</tr>
<tr>
<td>AT</td>
<td>Brazil, Denmark</td>
<td>1992-2012</td>
</tr>
<tr>
<td>Chron’s</td>
<td>Sweden, USA</td>
<td>1991-2007</td>
</tr>
<tr>
<td>IBD</td>
<td>Canada</td>
<td>1994-2005</td>
</tr>
<tr>
<td>IDDMM</td>
<td>Canada, Israel, Serbia, Europe</td>
<td>1982-2010</td>
</tr>
<tr>
<td>Celiac</td>
<td>Canada, Denmark, Finland, Israel, Netherlands, USA, Sweden, UK, Czech Republic, Scotland, Spain, Estonia, New Zealand</td>
<td>1950-2011</td>
</tr>
<tr>
<td>MG</td>
<td>Denmark, Norway, Italy, Japan</td>
<td>1950-2006</td>
</tr>
</tbody>
</table>


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Figure 2. (A) The net %/year increases of diseases’ categories. (B) The table below is detailing the different diseases and countries surveyed.

### Table

<table>
<thead>
<tr>
<th>Disease Kind</th>
<th>Statistical Significance (p; old vs. new)</th>
<th>Mean Net Increase %/Year</th>
<th>Countries</th>
<th>Diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurological</td>
<td>&lt;0.0001</td>
<td>3.7 ± 2.5</td>
<td>Finland, Denmark, Norway, Italy, Spain</td>
<td>MS, Myasthenia Gravis</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>&lt;0.0001</td>
<td>6.2 ± 11.5</td>
<td>Denmark, Canada, Sweden, USA, Finland, Israel, Netherlands, UK, Czech, Scotland, Spain, Estonia, New Zealand</td>
<td>Autoimmune Hepatitis, IBD, Chron’s, Celiac Disease</td>
</tr>
<tr>
<td>Endocrinological</td>
<td>0.02</td>
<td>6.3 ± 4.2</td>
<td>Brazil, Canada, Israel, Serbia, Europe</td>
<td>Autoimmune thyroiditis, IDDM</td>
</tr>
<tr>
<td>Rheumatic</td>
<td>0.02</td>
<td>7.14 ± 1.5</td>
<td>Canada, UK</td>
<td>SARD, RA, SLE</td>
</tr>
</tbody>
</table>


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Figure 4. The net increase %/year of 3 autoimmune diseases in the surveyed countries


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Annual systemic lupus erythematosus prevalence by gender.

Frances Rees et al. Ann Rheum Dis
doi:10.1136/annrheumdis-2014-206334
The Allergy-Epidemic
Cezmi A Akdis (Swiss Institute of Allergy and Asthma Research)

Prevalence

Allergy Asthma and One Health „The size of the problem“
Prevalence of Chronic Disease in the U.S.

ESRD: \( \uparrow \) Incidence and Prevalence

Greatest Increase from Diabetic ESRD

Diabetes is the most common cause in Caucasians, Hispanics, Asians, and overall. Among African-Americans, hypertension is the most common cause of ESRD.

Autism Prevalence On The Rise*
There has been a 600% increase in prevalence over the last two decades.

AUTISM SPEAKS™
It's time to listen.
www.AutismSpeaks.org

*Recent research has indicated that changes in diagnostic practices may account for at least 25% of the increase in prevalence over time, however much of the increase is still unaccounted for and may be influenced by environmental factors.