DOWN SYNDROME

A Susceptible Subgroup for Vaccine Injury

Laurette Janak AutismOne May 2013

Personalized vaccines: the emerging field of vaccinomics *Expert Opin Biol Ther 2008 Nov; 8(11): 1659-1667*

"…a new 'tension' is developing in the field of vaccinology between the traditional public health population-level paradigm and the newly evolving individual-level paradigm that recognizes genetically encoded unique individual variations in response to biologic agents."

NIH-PA Author Manuscript

Author Manuscript

Vaccine. Author manuscript; available in PMC 2009 November 18.

Published in final edited form as:
Vaccine. 2008 November 18; 26(49): 6183–6188. doi:10.1016/j.vaccine.2008.06.057.

Vaccine Immunogenetics: Bedside to Bench to Population

NIH-PA Author Manuscript

NIH Public Access
Author Manuscript
Pediatr Infect Dis J. Author manuscript; available in PMC 2010 May 1.

Published in final edited form as:
Pediatr Infect Dis J. 2009 May ; 28(5): 431–432. doi:10.1097/INF.0b013e3181a6a511.

Adversomics: The Emerging Field of Vaccine Adverse Event Immunogenetics

NIH-PA Author Manuscript

NIH Public Access
Author Manuscript
Pharmacogenomics. Author manuscript; available in PMC 2010 March 1.

Published in final edited form as:
Pharmacogenomics. 2009 May ; 10(5): 837–852. doi:10.2217/PGS.09.25.

Application of pharmacogenomics to vaccines

Gregory A Poland[1,2,3,†], Inna G Ovsyannikova[1,2], and Robert M Jacobson[1,3,4]
[1]Mayo Vaccine Research Group, MN, USA

One-size-fits-all?

Routine vaccine schedule

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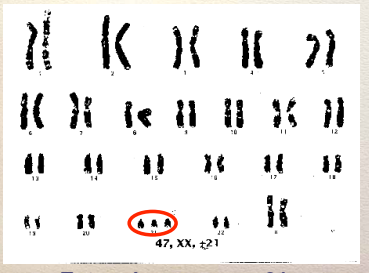
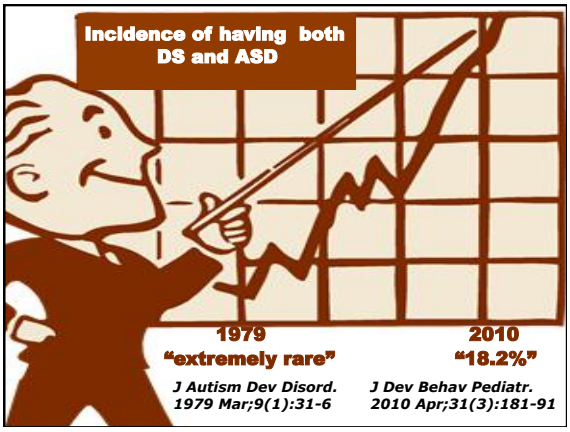
Genetics of Down syndrome



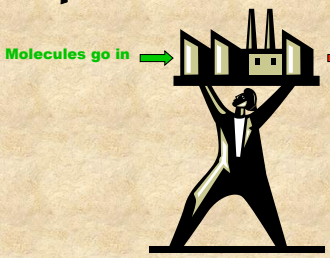
Extra chromosome 21

Incidence of having both DS and ASD



1979	2010
"extremely rare"	"18.2%"
J Autism Dev Disord. 1979 Mar;9(1):31-6	*J Dev Behav Pediatr. 2010 Apr;31(3):181-91*

Analogy for biochemistry



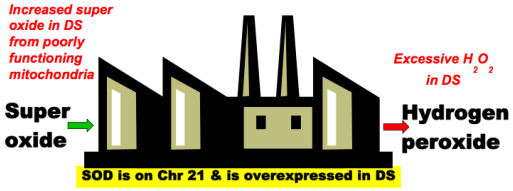
Manufacture
Recycle
Detoxify / Dispose
Up regulation
Down regulation
Over expression

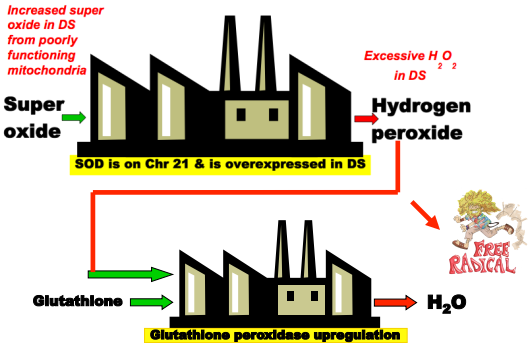
Factories = enzymes in your body

Factories are built and run by your genes (DNA)

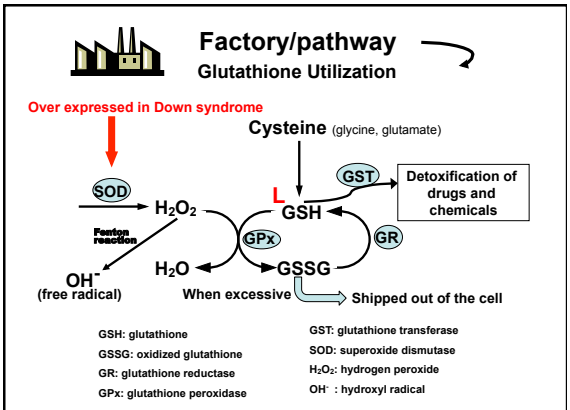
Genetically normal child

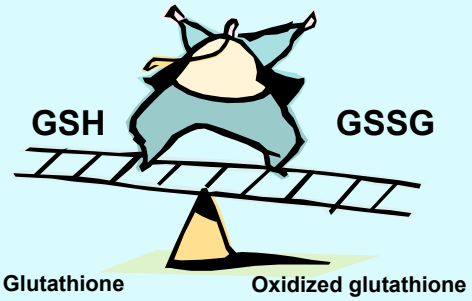
Down syndrome overexpression



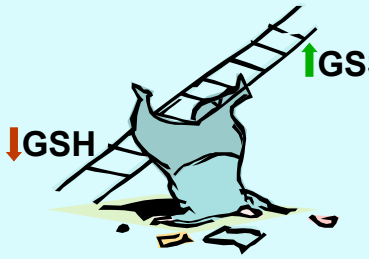


Results in lower levels of glutathione (GSH) in DS





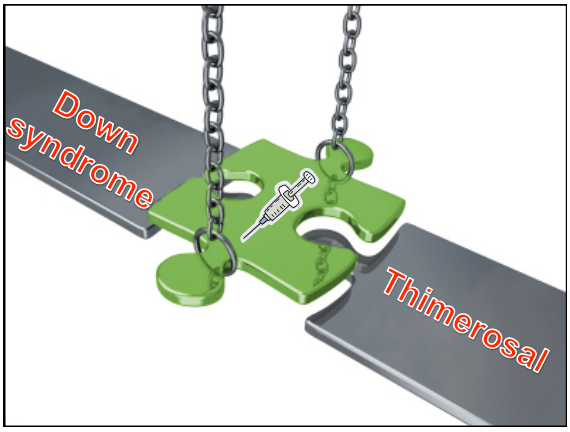
Glutathione Oxidized glutathione



Oxidative stress

Notes on Glutathione

- ✓ Is an antioxidant made in your body
- ✓ Environmental chemicals, heavy metals, dietary deficiencies and medications can deplete glutathione
- ✓ Glutathione has antiviral properties
- ✓ Protects DNA and mitochondria
- ✓ Plays a role in protection against autoimmunity
- ✓ Utilization can be altered by genetic differences



IOM 2004

With respect to the hypothesis that there may be a subgroup of children who are genetically more sensitive to the toxic effects of thimerosal (a mercury preservative found in vaccines), the IOM had this to say:

"This hypothesis cannot be excluded by epidemiological data from large population groups that do not show an association between a vaccine and an adverse outcome. Depending upon the frequency of the genetic defect, a rare event caused by genetic susceptibility could be missed even in large study samples."

Neurotox Res. 2009 Sep

Are Neuropathological Conditions Relevant to Ethylmercury Exposure?

Aschner M, Ceccatelli S.

"The conclusion is that there are no reliable data indicating that administration of vaccines containing thimerosal is a primary cause of autism. **However, one cannot rule out the possibility that the individual gene profile and/or gene-environment interactions may play a role in modulating the response to acquired risk by modifying the individual susceptibility."**

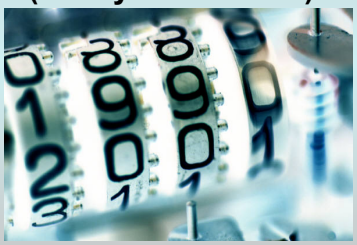
If we could scientifically present evidence that there is **one** subgroup of the population that's more sensitive to mercury then we would have to assume there may be others as well.

Where would one begin to look for such a population?

How does mercury effect human biochemistry to cause toxicity?

Mercury reduces glutathione (GSH) levels which can result in free radicals causing oxidative stress and damage to the body.

Should they have known?
Could they have known?
Would they have known (if they had looked)?



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The role that glutathione (GSH) plays in mercury toxicity and oxidative stress was known long before the 2004 IOM declaration.

Shenker BJ et al. 1993
Queiroz ML et al. 1998
Makani S et al. 2002

In MANY studies using multiple cell types and adding a variety of metals, BSO has been used to deplete GSH by inhibiting its synthesis.

I have NEVER seen any of these experiments wherein BSO has:

Before After

Studies show decreased levels of GSH in DS

- *J Pediatr. 2003 May;142(5):583-5.*
- *Am J Hum Genet. 2001 Jul;69(1):88-95.*

Mercury and other metals deplete GSH in a dose- dependent manner

- *Immunopharmacol Immunotoxicol. 1993 Mar-Jun;15(2-3):273-90.*

2004 IOM declaration

Before After

An animal model of DS which showed decreased GSH in hippocampal neurons stated:

–**"Additional lowering of GSH levels led to enhanced cell death…..Based on these results we suggest that a GSH level which is decreased under a specific threshold by increased consumption, reduced synthesis or lack in precursor contributes to cell loss and neurodegeneration in Down syndrome."**

–Brain Res 1997 Aug 15;765(2):313-8

2004 IOM declaration

Before After

Studies show that levels of oxidative stress are increased in Down syndrome

Heavy metals (including mercury) increase oxidative stress and cause damage

2004 IOM declaration

Before After

Animal models and human studies have found cholinergic dysfunction in DS

- *Eur J Neurosci. 2000 Sep;12(9):3259-64.*
- *Brain Res. 1994 Sep 26;658(1-2):27-32.*
- *Neurosci Lett. 1997 Feb 7;222(3):183-6.*

Exposure to mercury can induce cholinergic dysfunction

- *J toxicol Sci 1979 Nov;4(4):351-62*
- *Res Commun Chem Pathol Pharm 1980 Nov;30(2):381-4*
- *Brain Res Dev Brain Res 1995 Mar 16;85(1):96-109*

2004 IOM declaration

Before After

Other abnormalities that are noted in DS and may be impacted by mercury exposure include:

- **Calcium dysregulation**
- **Alterations in glutamate metabolism**
- **Autoimmune disorders**
- **Leukemia**

2004 IOM declaration

Before After

The co morbid occurrence of autism and DS is at least 7%.
Kent L. et al. 1999

2010 study found DS-ASD co-morbidity to be 18.2%
J Dev Behav Pediatr. 2010 Apr;31(3):181-91.

2004 IOM declaration

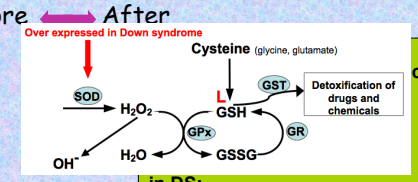
Before ⟷ After

Despite all that was known about both DS and the mechanisms by which mercury induces toxicity…

I have been unable to find any study that has investigated the toxic effects of thimerosal in individuals with DS.

2004 IOM declaration

Before ⟷ After



ct

in DS:

–The toxicity of thimerosal was, "greatly augmented when the cells suffered oxidative stress induced by (H_2O_2)."

– *Toxicol In Vitro 2004 Oct;18(5):563-9.*

2004 IOM declaration

Genetic differences in glutathione-S-transferase (GST) have been shown to contribute to the inter-individual variance in detoxification of mercury.

Environ Res. 2009 Aug;109(6):786-96
Sci Total Environ. 2007 Oct 15;385(1-3):37-47

"GST activity was significantly decreased to 40.9% in the DS group as compared to controls."

"…individuals with lower overall GST activity… are at greater risk from xenobiotic contamination as compared to those with higher overall GST activity observed in normal individuals."

Res Dev Disabil. 2011 Sep-Oct;32(5):1470-82

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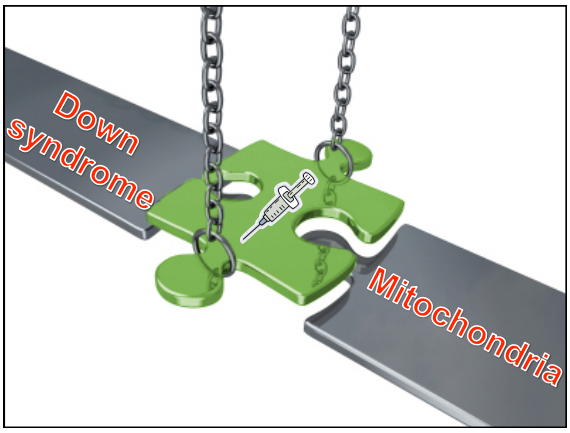
Let's be perfectly clear...

Thimerosal toxicity has NOT been investigated in identifiable subgroups with increased sensitivity!

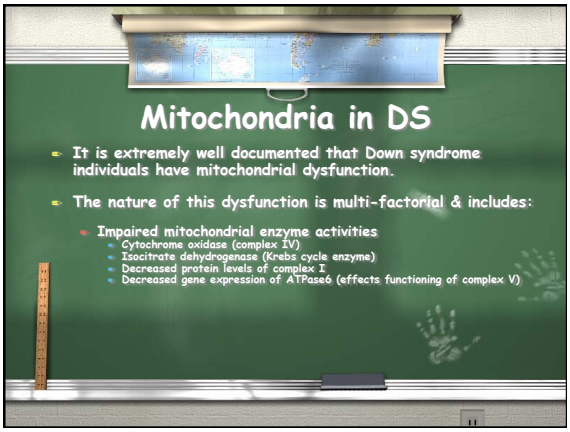
During a May 2008 CBS interview with former head of the National Institutes of Health Dr. Bernadine Healy, had the following to say:

Full video can be viewed at: *http://www.cbsnews.com/video/watch/?id=4088138n*

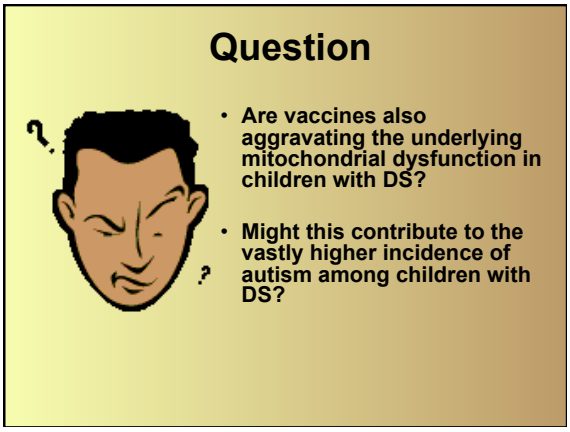

Down syndrome
Mitochondria


November 9, 2007
NEWS
U.S. Government conceded a vaccine-autism case in the Court of Federal Claims
Vaccinations aggravated an underlying mitochondrial disorder resulting in features of autism.

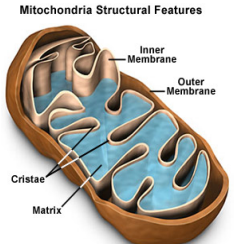

Media Puppets
Mitochondrial disorders are rare!


Mitochondria in DS
It is extremely well documented that Down syndrome individuals have mitochondrial dysfunction.
The nature of this dysfunction is multi-factorial & includes:
Impaired mitochondrial enzyme activities
Cytochrome oxidase (complex IV)
Isocitrate dehydrogenase (Krebs cycle enzyme)
Decreased protein levels of complex I
Decreased gene expression of ATPase6 (effects functioning of complex V)


Mitochondria in DS
Accumulation of toxic free radicals begins in-utero.
Clin Biochem. 2007 Feb;40(3-4):177-80
Studies on fetal DS brain and in fetal DS amniocytes demonstrate mitochondrial dysfunction occurs prior to birth.
J Neural Transm Suppl. 2001;(61):109-16.
Mol Cells. 2003 Apr 30;15(2):181-5.


Question
Are vaccines also aggravating the underlying mitochondrial dysfunction in children with DS?
Might this contribute to the vastly higher incidence of autism among children with DS?

Mitochondria in DS/ASD



Cristae - the site of the electron transport chain

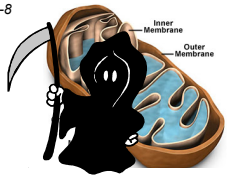
Matrix- the site of the citric acid cycle

- DS mitochondria have a lower mitochondrial membrane potential which, is "underlying the presence of an increasing susceptibility of these organelles to damaging agents".
  - *FEBS Lett. 2007 Feb 6;581(3):521-5.*

CAN THIMEROSAL BE ONE OF THESE "DAMAGING AGENTS"?

Mitochondria and Thimerosal

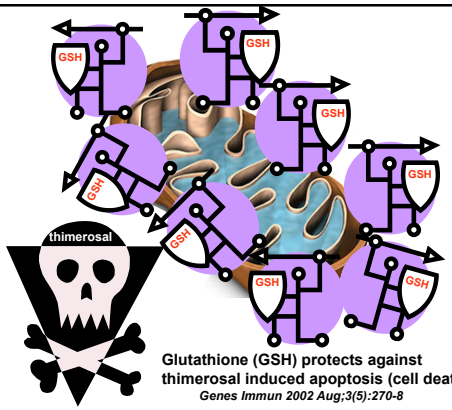
- **Thimerosal induces programmed cell death via the mitochondrial pathway by inducing oxidative stress and depletion of glutathione (GSH).**
  - *Genes Immun 2002 Aug;3(5):270-8*



Mitochondria and Thimerosal

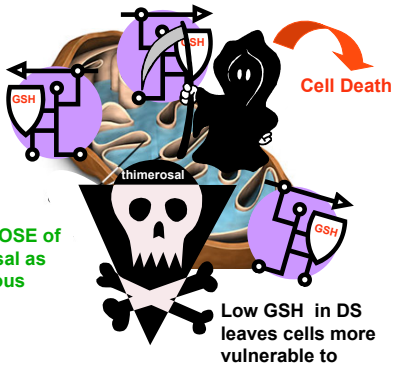
Does dose make the poison

?



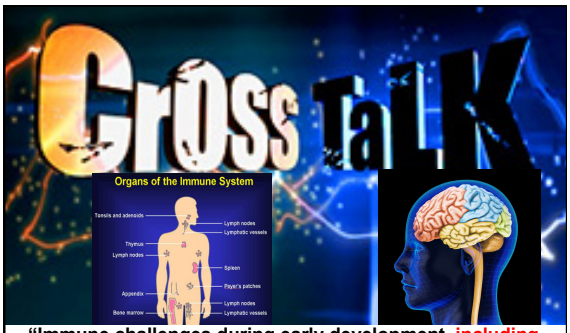
Glutathione (GSH) protects against thimerosal induced apoptosis (cell death)

Genes Immun 2002 Aug;3(5):270-8



SAME DOSE of thimerosal as in previous slide!

Low GSH in DS leaves cells more vulnerable to toxins

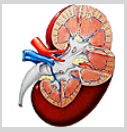


"Immune challenges during early development, including those vaccine-induced, can lead to permanent detrimental alterations of the brain and immune function"

Lupus. 2012 Feb;21(2):223-30

Facts about aluminum

- In typical healthy people, the gastrointestinal tract excludes greater than 95% of dietary Al.



- Even with normal renal excretion, tissue accumulation of Al occurs.

Facts about Aluminum

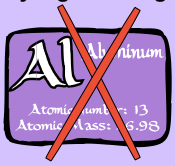
Al Aluminum
Atomic Number: 13
Atomic Mass: 26.98

- The mean aluminum absorption in DS exceeds that of controls by a factor of 6.
  - *Moore PB et al., 1997*

Facts about Aluminum

- "Our findings suggest that it may be prudent to minimize the uptake of Al from the diet of patients who are at high risk of developing Alzheimer-type pathology, in particular DS patients, subjects with a strong family history of AD, and patients who are showing early signs of cognitive decline."
  - *Moore PB et al.,*

1997



Journal of Alzheimer's Disease 23 (2011) 567–598
DOI 10.3233/JAD-2010-101494
IOS Press

567

Date: 2011

Review

Aluminum and Alzheimer's Disease: After a Century of Controversy, Is there a Plausible Link?

Lucija Tomljenovic*

"...incremental acquistion of small amounts of Al over a lifetime favors its selective accumulation in brain tissues."

Abstract. The brain ... of metabolic errors. Alzheimer's disease (AD) is the ... and is characterized by regional specificity of neural aberrations associated with higher cognitive functions. Aluminum (Al) is the most abundant neurotoxic metal on earth, widely bioavailable to humans and repeatedly shown to accumulate in AD-susceptible neuronal foci. In spite of

Journal of Alzheimer's Disease 23 (2011) 567–598
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IOS Press

Date: 2011

Review

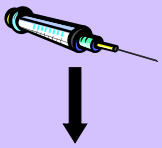
Aluminum and Alzheimer's Disease: After a Century of Controversy, Is there a Plausible Link?

Lucija Tomljenovic*
Neural Dynamics R
Universit

"The hypothesis that Al significantly contributes to AD is built upon very solid experimental evidence and should not be dismmised. Immediate steps should be taken to lessen human exposure to Al, which may be the single most aggravating and avoidable factor related to AD."

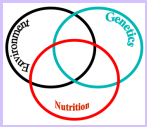
Abstract. The [illegible] metabolic errors. Alzheimer's disease (AD) [illegible] is characterized by regional specificity of neural aberrations associated with higher cognitive functions. Aluminum (Al) is the most abundant neurotoxic metal on earth, widely bioavailable to humans and repeatedly shown to accumulate in AD-susceptible neuronal foci. In spite of

Facts about Aluminum

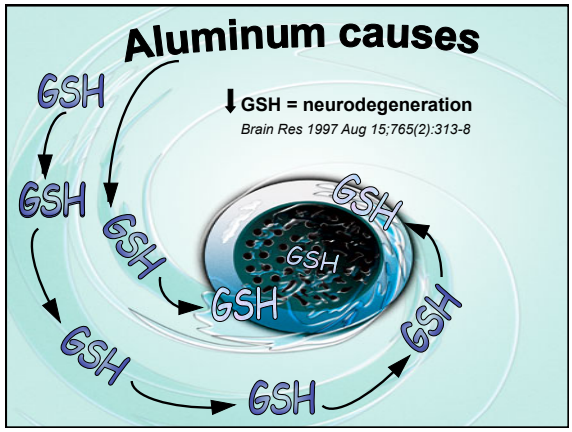


Are DS and AD patients warned about the amount of aluminum used in vaccines?

Where are the safety studies on injected aluminum in these populations?



Aluminum causes



Comparing DS and Autism

- **Autoimmune disorders**
  - **In DS - increased occurrence of autoimmune disorders with target organs including pancreas, thyroid, joints, adrenal gland, gastric mucosa and brain.**
  - **In autism there is a familial presence of autoimmune diseases including pancreas, thyroid, joints, brain and gastric mucosa.**

Decreased glutathione

Glutathione: a key player in autoimmunity.

Autoimmun Rev. 2009 Jul;8(8):697-701

Oxidative stress in Egyptian children with autism: relation to autoimmunity.

J Neuroimmunol. 2010 Feb 26;219(1-2):114-8.

Mechanisms of aluminum adjuvant toxicity and autoimmunity in pediatric populations.

Lupus. 2012 Feb;21(2):223-30.

Journal of Autoimmunity 36 (2011) 4–8
Contents lists available at ScienceDirect
Journal of Autoimmunity
journal homepage: www.elsevier.com/locate/jautimm

Review

'ASIA' – Autoimmune/inflammatory syndrome induced by adjuvants

Yehuda Shoenfeld [a,b,*], Nancy Agmon-Levin [a]

"…although the independent role of each vaccine ingredients as well as host risk factors are yet to be defined, the accumulated data suggest the possibility of accelerated autoimmunity/inflammation following vaccination."

Contents lists available at SciVerse ScienceDirect

Journal of Inorganic Biochemistry

journal homepage: www.elsevier.com/locate/jinorgbio

Do aluminum vaccine adjuvants contribute to the rising prevalence of autism?

Lucija Tomljenovic [a,*], Christopher A. Shaw [a,b]

"….children from countries with the highest ASD prevalence appear to have the highest exposure to Al from vaccines;"

"… the increase in exposure to Al adjuvants significantly correlates with the increase in ASD prevalence in the United States observed over the last two decades"

"… a significant correlation exists between the amounts of Al administered to preschool children and the current prevalence of ASD in seven Western countries, particularly at 3–4 months of age"

BIG Question

- Should such a damaging agent be given to a DS population, all of whom are at high risk for neurodegeneration, Alzheimer's and autoimmunity ?

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Vaccines and Your Child: Separating Fact from Fiction

by Paul A. Offit (page 78) copy write 2011

Offit quotes a saying by a 17th century chemist who said,

"Dose makes the poison".

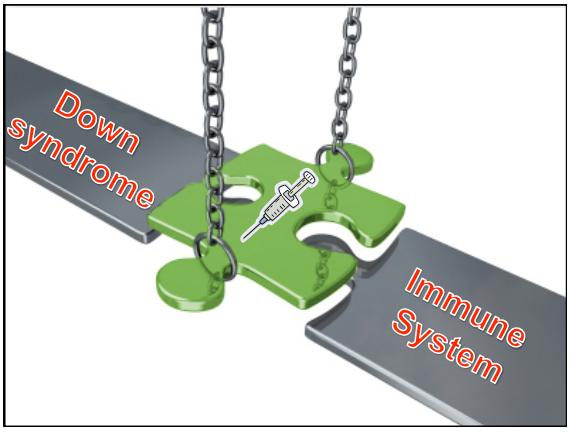
Offit then goes on to say," In other words, although large quantities of a particular substance might be harmful, small quantities aren't. Indeed, everyone living on the planet has very small quantities in their bodies of a variety of heavy metals including arsenic, cadmium, thallium, beryllium, and lead. All of these substances can be harmful in large quantities. But the small quantities we all encounter from exposure to these metals don't pose a risk."

How long will it take for all the water to leak out of this bucket?

"For a person exposed to a single chemical at a low concentration, GSH consumption is trivial. However, if the exposure is to a large number of chemicals for a long time, GSH use is relevant and depletion can happen because of GSH conjugation."

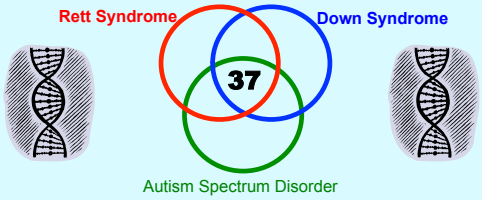
Environ Health Perspect. 2009 Dec;117(12):1799-802

The biochemistry found in children represents the combination of their genetics, environmental exposures and nutritional status.



Genome-wide expression studies in Autism spectrum disorder, Rett syndrome, and Down syndrome

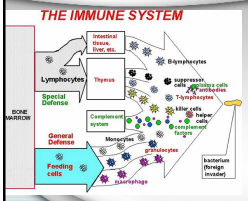
Neurobiol Dis. 2010 Dec 2.



"The 37 genes shared by RTT, ASD and DS are all surprisingly involved in immune-related functions."

"Our results surprisingly converge upon immune and not neurodevelopment genes"

The immune system is altered in DS



Clin Exp Immunol. 2011 Apr;164(1):9-16

J Pediatr. 2010 May;156(5):804-9

Pediatr Res. 2010 May;67(5):563-9

Pediatr Int. 2009 Aug;51(4):474-7

Clin Exp Immunol. 2009 May;156(2):189-93

J Paediatr Child Health. 2008 Apr;44(4):182-6

Immun Ageing. 2010 Jan 25;7:2

Neuro Endocrinol Lett. 2006 Dec;27(6):773-8

Immunodeficiency, Inflammation and Autoimmunity

Comparing DS and Autism

- Altered immune system
  - DS
    - Immune suppression
    - Decreased NK cell activity
    - Disruptions in CD4, CD8, and CD26
    - Decreased IL-2
    - T and B cell derangement
  - Autism
    - Decreased NK cell activity
    - Abnormal CD4/CD8 ratios
    - Decreased IL-2

Comparing DS and Autism

- Response to MethylB12
  - DS - in vitro study shows a positive metabolic response to MeB12
  - Autism - shows positive metabolic response to MeB12
- MeB12 has been shown to:
  - Be useful in RA
  - Increase NK cell activity
  - Positively alter the CD4/CD8 ratio
  - Increase methionine synthase activity

Immune overload

73

CDC -Genomics - Vaccine Safety 3/23/11 11:02 AM

Centers for Disease Control and Prevention
Your Online Source for Credible Health Information

Vaccine Safety

Vaccine Safety and Human Genetic Variations

Serious health problems following vaccination are rare, even though millions of people are vaccinated every year in the United States. Why do only a small number of people develop these health problems called vaccine-associated adverse events (VAEs)? Do they have genetically determined differences in their immune responses to vaccination, compared to those who do not experience adverse events?

Few studies have l ead responsibility for monitoring th ning research to inform safe vaccin relationship between human genetics a

"While substantial research has been done on the genetic basis of medication safety, relatively little research has been done on the genetic basis of vaccine safety."

Identifying genetic

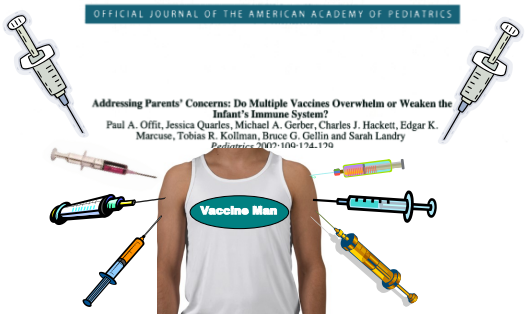
- Screening for
- Improved gui
- Development of safer vaccines.

ISO's Genomics Initiative

CDC's Immunization Safety Office (ISO) is developing a genomics initiative to–

PEDIATRICS
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Addressing Parents' Concerns: Do Multiple Vaccines Overwhelm or Weaken the Infant's Immune System?
Paul A. Offit, Jessica Quarles, Michael A. Gerber, Charles J. Hackett, Edgar K. Marcuse, Tobias R. Kollman, Bruce G. Gellin and Sarah Landry
Pediatrics 2002;109:124-129



"...each infant would have the theoretical Capacity to respond to about 10 000 vaccines at any one time..."

Bacterial infections, immune overload, and MMR vaccine (Arch Dis Child.2003; 88: 222-223)

Inclusion criteria:

hospitalization for:
- meningococcal infection
- septicaemia
- bacterial meningitis
- pyogenic arthritis
- acute osteomyelitis
- lobar (pneumococcal) pneumonia

Exclusion criteria:

Predisposed to bacterial infection
- Immunosuppression
- Malignancy
- Cystic fibroisis
- Congenital heart defect

Full text available at: http://adc.bmj.com/cgi/reprint/88/3/222

PEDIATRICS
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

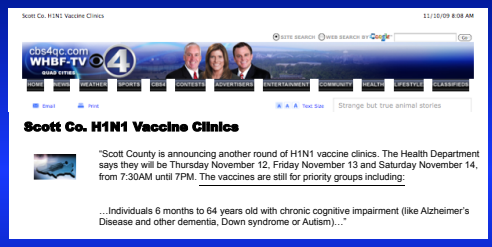
Diphtheria, pertussis, poliomyelitis, tetanus, and Haemophilus influenzae type b vaccinations and risk of eczema and recurrent wheeze in the first year of life: the KOALA Birth Cohort Study.

Pediatrics. 2007 Feb;119(2):e367-73.

"**Exclusion criteria** were prematurity (gestational age <37 weeks) and congenital abnormalities related to immunity (such as **Down syndrome**)."

Specifically excluded from studies but....

specifically targeted for vaccines!



Scott Co. H1N1 Vaccine Clinics

"Scott County is announcing another round of H1N1 vaccine clinics. The Health Department says they will be Thursday November 12, Friday November 13 and Saturday November 14, from 7:30AM until 7PM. The vaccines are still for priority groups including:

…Individuals 6 months to 64 years old with chronic cognitive impairment (like Alzheimer's Disease and other dementia, Down syndrome or Autism)…"

BUT WAIT…..THERE' MORE….

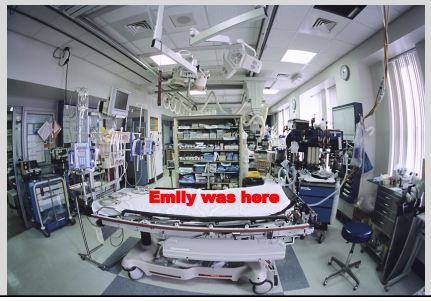
Influenza A/H1N1 vaccination response is inadequate in down syndrome children when the latest cut-off values are used.

Pediatr Infect Dis J. 2012 Dec;31(12):1284-5..

"…only 27% reached the level of >= 1:110 which was recently described to predict the conventional 50% clinical protection rate in children."

At 3 months of age my daughter Emily got a DPT, OPV, HIB, and Hep B

Within days of vaccination…



Emily has a systemic infant strep B infection

I asked the Doctor:

"Could this have anything to do with the vaccine she had a few days ago?"

American Journal of Therapeutics 11, 344–353 (2004)

Urinary Tract Diseases Revealed after DTP Vaccination in Infants and Young Children

Cytokine Irregularities and Down-regulation of Cytochrome P-450 Enzymes Induced by the Vaccine May Uncover Latent Diseases in Genetically Predisposed Subjects

Joseph Prandota*

"…the vaccine may uncover latent disease, especially in genetically predisposed subjects."

The genetic susceptibilities they are talking about are genetic variants of TNF-alpha and IL-6.

DTP vaccination increases the proinflammatory cytokine IL-6. Some studies show IL-6 to already be elevated in children who have Down syndrome.

The authors point out that as far back as 1967 it was hypothesized that immunizations could convert a latent infection into a clinically apparent disease.

Immune overload

This DTP vaccination study is actually an example of system overload.

Aaby P. et al. BMJ. 2010 Nov 30;341:c6495.

With regard to the DPT and MMR vaccines this study said:

"Previous studies have suggested that a short interval between these vaccines is associated with increased mortality, and administration of measles vaccine and DPT vaccine at the same time has been linked to negative health outcomes."

86

THE JOURNAL OF INFECTIOUS DISEASES

VOL. 131, NO. 6 * JUNE 1975

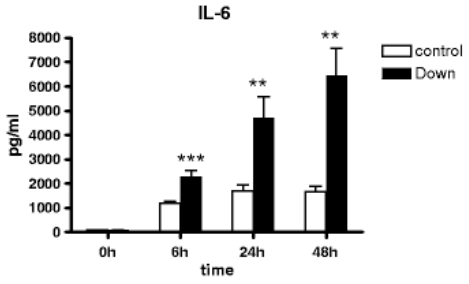
From the National Institutes of Health

Report of a Workshop: Disease Accentuation after Immunization with Inactivated Microbial Vaccines

"Disease was accentuated when the subject was exposed again, experimentally or under natural circumstances, weeks or even years after completion of the immunization regimen. Pro-longed, intensive surveillance of immunized subjects apparently is a requirement of any carefully designed field trial for vaccine. One can only wonder whether or not recipients of certain currently licensed vaccines (i.e., influenza) that provide variable and transient immunity are being followed adequately."

Increased Pro-Inflammatory Cytokine Production in Down Syndrome Children Upon Stimulation with Live Influenza A Virus

J Clin Immunol. 2011 Dec 15



"For subjects experiencing AEs, vaccination appears to trigger an acute inflammatory response that is excessive."

J Infect Dis 2008 July 1; 198(1): 16-22

ELSEVIER journal homepage: www.elsevier.com/locate/bbadis

Brain IL-6 elevation causes neuronal circuitry imbalances and mediates autism-like behaviors

Hongen Wei [a,c], Kathryn K. Chadman [c], Daniel P. McCloskey [d], Ashfaq M. Sheikh [a], Mazhar Malik [a], W. Ted Brown [b], Xiaohong Li [a,*]

"Mice with an elevated IL-6 in brain developed autism-like behaviors, including impaired cognition ability, deficits in learning, abnormal anxiety-like trait and habituation, as well as a decreased social interaction initiated at later stages. These findings suggest that an IL-6 elevation in the brain could modulate certain pathological alterations and contribute to the development of autism."

Vaccination during Mild Illness

- **In 1996, JAMA reported it is safe to give MMR to children who presented with mild illnesses such as upper respiratory infection, otitis media and diarrhea.**
  - *(King GE et al., 1996)*
  - Position supported by the American Academy of Pediatrics (AAP)
  - GSH has antiviral properties and the MMR contains live viruses

Glutathione and Mild Infections

Common childhood illness such as ear infections (otitis media) and tonsillitis:

- ↓ serum antioxidant vitamins
- ↓ levels of glutathione (GSH)
- ↑ malondialdehyde - a marker of oxidative stress

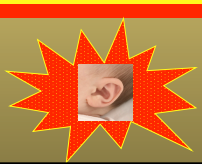
Cemek et al. 2005

Ann Epidemiol 2001 Jan;11(1):13-21.

Adverse events associated with hepatitis B vaccine in U.S. children less than six years of age, 1993 and 1994.

Fisher Ma, Eklund SA, James SA, Lin X

Hepatitis B vaccine was found to be associated with prevalent arthritis, incident acute ear infections, and incident pharyngitis/nasopharyngitis.



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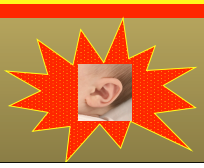
Children With Persistent AOM Have Poor Immune Responses to Pneumococcal and HiB Vaccines.

***Medscape.* Dec 02, 2009**

"We found that among children with recurring infections, particularly ear and nose infections, a lot of them failed to respond appropriately to their pediatric vaccinations," said Dr. Vaughn."



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Glutathione and Measles

- **Viral infections such as measles can decrease GSH and other antioxidants.**
  - *Cemek et al. 2007*
- ***CAN THE MEASLES VACCINE DO THE SAME?***

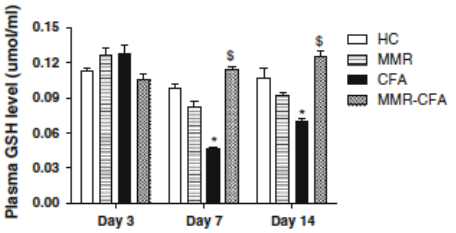
96

Measles Vaccine and Glutathione

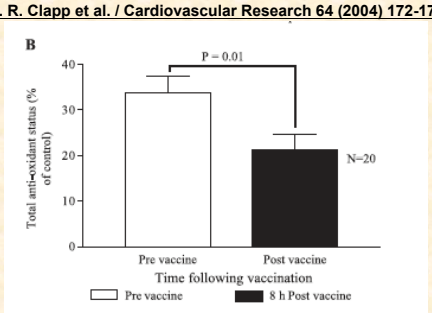
and found the following animal study:

Protective potential of MMR vaccine against complete Freund's adjuvant-induced inflammation in rats.

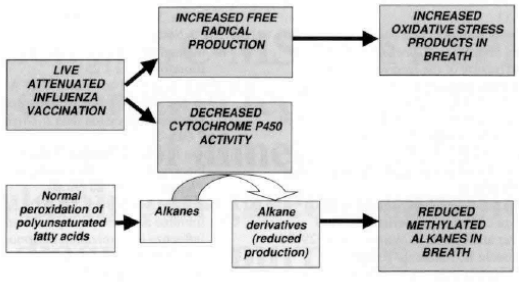
Inflammopharmacology. 2011 Dec;19(6):343-8.



B. R. Clapp et al. / Cardiovascular Research 64 (2004) 172-178



"TAOS decreased significantly 8 h following vaccination (33.7 +/- 3.7% at baseline to 21.3 +/- 3.4% at 8 h; P=0.01; Fig 3B) indicating an increase in oxidant stress at this time."



J Breath Res. 2010 Jun;4(2):026001

Effect of influenza vaccination on oxidative stress products in breath.

"LAIV vaccination in healthy humans elicited a prompt and sustained increase in breath biomarkers of oxidative stress….The breath biomarker response was observed throughout the 14 days of the study…"

ELSEVIER
doi:10.1016/S0891-5849(03)00023-6

Original Contribution

INHIBITION OF INFLUENZA INFECTION BY GLUTATHIONE

JIYANG CAI,* YAN CHEN,* SHAGUNA SETHI,† SATORU FURUKAWA,‡ RICHARD W. COMPANS,† and DEAN P. JONES*
*Department of Biochemistry, †Department of Microbiology and Immunology, Emory University School of Medicine, Atlanta, GA, USA; and ‡Nutri-Quest, Inc., Chesterfield, MO, USA

(Received 27 August 2002; Revised 23 December 2002; Accepted 9 January 2003)

"Our results suggest that GSH provides an alternative strategy to limiting influenza infection."

"…GSH may be particularly useful for prevention of influenza infection in some at-risk populations."

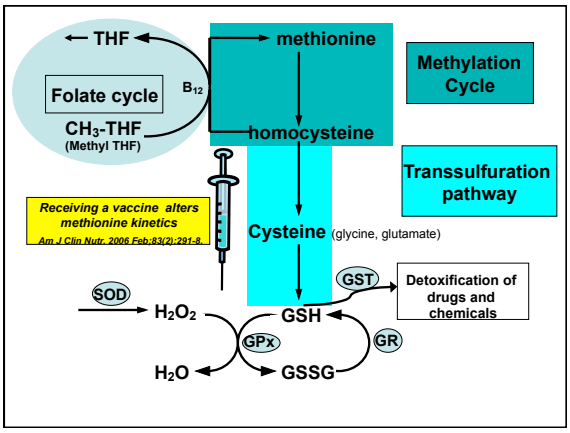
"These results indicate that supplemental GSH has an anti-influenza activity and suggests that oxidative stress in vivo may enhance susceptibility to infection."

OPEN ACCESS Freely available online
PLOS MEDICINE

Association between the 2008–09 Seasonal Influenza Vaccine and Pandemic H1N1 Illness during Spring–Summer 2009: Four Observational Studies from Canada

Danuta M. Skowronski[1]*, Gaston De Serres[2], Natasha S. Crowcroft[3,4], Naveed Z. Janjua[1], Nicole Boulianne[2], Travis S. Hottes[1], Laura C. Rosella[3,4], James A. Dickinson[5], Rodica Gilca[2], Pam Sethi[3], Najwa Ouhoummane[2], Donald J. Willison[3], Isabelle Rouleau[2], Martin Petric[1], Kevin Fonseca[6], Steven J. Drews[5], Anuradha Rebbapragada[3], Hugues Charest[2], Marie-Ève Hamelin[7], Guy Boivin[7], Jennifer L. Gardy[1], Yan Li[8], Trijntje L. Kwindt[1], David M. Patrick[1], Robert C. Brunham[1], for the Canadian SAVOIR Team[†]

"In this paper we report the expected finding that 2008-2009 TIV was associated with a significant (56%) reduction in the risk of medically attended illness due to seasonal influenza. However, we also report the unexpected finding that TIV receipt was subsequently associated with a statistically significant (1.4 to 2.5 fold) increased risk of medically attended illness due to the novel pH1N1 virus."



Points of Interest

Am J Clin Nutr. 2006 Feb;83(2):291-8.

No matter the age or the nutritional status of the subject, vaccination significantly increased the movement toward cysteine synthesis thereby making this glutathione precursor more readily available.

Even the mild inflammatory stress of vaccination causes an increased utilization of cysteine. This led to a trend for a decrease in blood glutathione in the elderly subjects.

RBC glutathione (mmol/L) in the elderly

Before vaccination	After vaccination
2.03 +/-0.10	1.83 +/-0.14

Full text at: http://www.ajcn.org/cgi/reprint/83/2/291

Major Point of Interest

Am J Clin Nutr. 2006 Feb;83(2):291-8.

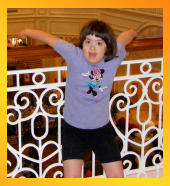
The consequences of giving a vaccine which is a source of inflammation to a group of patients who already have underlying inflammation, "warrants further study."

Other persons with underlying inflammation

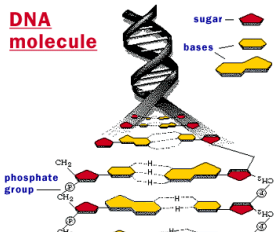
Obesity

Elderly

Down syndrome



DNA molecule



Low glutathione levels can make people more sensitive to DNA damage from a variety of mutagenic environmental exposures.

Illuminating Cancer in DS

- Cancer in DS
  - Children with DS have a 15-20 fold increased occurrence of leukemia.

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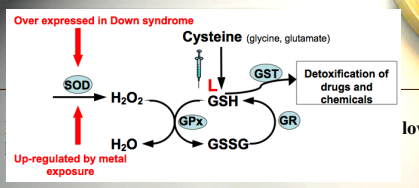

- low
- The mutagenic property of mercury has been shown to be causally related to its ability to induce H_2O_2.
  - *Environ Mol Mutagen 1998;31(4):352-61*
- Therefore: children with low glutathione may be at higher risk for cancer from exposure to heavy metals and other environmental toxins.

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Illuminating Metal DNA Damage in DS

"The mechanism of carcinogenesis in Down syndrome could be explained by our findings: SODs enhance metal-mediated DNA damage induced by H_2O_2. We conclude that SODs may increase the frequency of mutations due to oxidative DNA damage in cells, increasing carcinogenic potential."

» *FEBS Lett. 2001 Apr 27;495(3):187-90.*

112

Illuminating Mercury and Leukemia in a non-down syndrome population

- Biological mechanisms are consistent with epidemiology studies showing an increased mortality from leukemia with exposure to mercury.
  - Age standardized cancer mortality ratios in areas heavily exposed to methyl mercury.
    - *N.Int Arch Occup Environ Health. 2007 Aug;80(8):679-88.*
  - Cancer mortality in Minamata disease patients exposed to methylmercury through fish diet.
    - *J Epidemiol. 1996 Sep;6(3):134-8.*

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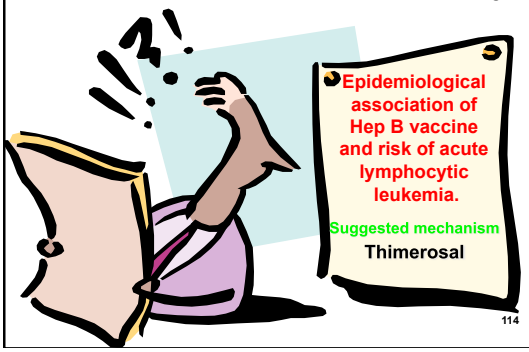
Poster Presentation April 9, 2002

American Association for Cancer Research Annual Meeting



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Thimerosal

Hep B vaccine ? Leukemia

- 167 matched case-control pairs from the Northern California Childhood Leukemia study diagnosed 1995-1999
- OR = 2.6 for 3 or more doses of Hep B vaccines
- OR = 5.0 for 3 or more doses of Hep B vaccine during infancy
- Thimerosal free Hep B vaccines became available in Fall 1999
  - *MMWR July 21, 2000 / 49(28); 642,651*

115

Safety of immunization and adverse events following vaccination against hepatitis B.

J Hepatol. 2003;39 Suppl 1:S83-8.

- "…the safety of hepatitis B vaccine has repeatedly been under attack."
- By claims of being associated with: RA, diabetes, MS, "and more recently lymphoblastic leukemia."

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1999 thimerosal free Hep B introduced in U.S.

2002 OR = 5.0 for 3 or more in infancy
OR = 2.6 for 3 or more
Case cohort (1995-1999)

2005 OR = 1.8 (born on or before 1995)
OR = 1.08(born after 1995)
Case cohort (1995-2002)

2007 No association
Case cohort (2003-2004)

Following the thread of science

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It is NOT just about the thimerosal !!!

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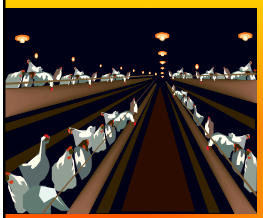
In goes the MMR and then begins the

Crying
Fever
Diarrhea
Rash
Insomnia
Worsening of rash
Ear infections
Bruxism (teeth grinding)
Continued diarrhea
Head banging, hand flapping and ASD
Bloody diarrhea
Thrombocytopenia (platelets 7,000)

Emily was not an 18 month old baby.
She was over 3 years of age.

95 days post MMR, Emily was diagnosed with leukemia.

The MMR doesn't contain thimerosal BUT….



- Materials used as the growth medium for the manufacture of vaccines can contain retroviruses
- "Influenza and MMR vaccines are usually prepared in embryonated eggs or in cultures of chick embryo fibroblasts (CEF)."

Emerg Infect Dis. 2001 Jan-Feb;7(1):153-4

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The MMR contains retroviruses

- U.S. made MMR vaccines have been found to contain avian leucosis virus (ALV) as well as endogenous avian virus (EAV).
  - J Virol 1999 Jul;73(7): 5843-51

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MMR retrovirus transmission to humans

- ABSRACT:
  - "The present data do not support transmission of either ALV or EAV to recipients of the U.S-made vaccine and provide reassurance for current immunization policies."
- BUT the actual study says something more.

J Virol 1999 Jul;73(7):5843-51

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Looking closely at the study we find:

- "The relatively small number of MMR recipients studied here and the single tissue (PBMC) analyzed from these subjects limit the strength of our conclusions regarding transmissibility."
  - (N = 33)

J of Virology July 1999 p. 5843-5851

123

- A study in a larger sample size (206 MMR recipients) was performed and we are still being told the retroviruses are not being transmitted via vaccine.
  - *Emerg Infect Dis. 2001 Jan-Feb;7(1):66-72*
- *Cancer Detect Prev. 1995;19(6):472-86.*
  - Found antibodies to ALV in human sera of workers in poultry slaughter plants as well as in non-exposed people.
  - Viruses of the ALV group
    - can infect and cause cancer in mammals including primates and can transform human cells in culture medium'

124

- ***Cancer Detect Prev. 1995;19(6):472-86.***
  - The authors recommend that future studies on ALV investigate its detection in tumor cells from exposed subjects with cancer.
- **Multiple studies have found increased leukemia among people exposed to chickens.**
  - *Can J Public Health. 1994 May-Jun;85(3):208-11.*
  - *Am J Epidemiol. 1998 Apr 15;147(8):727-38.*
  - *Cancer Causes Control. 2009 Oct 22.*
- **Despite my requests to have my child tested for ALV, nobody has agreed to test her.**

125

Measles Viral Damage in DS

- **When investigating Down syndrome and leukemia, it was found that there was an increase in DNA damage of lymphocytes from children with Down's syndrome compared to control children before and after measles infection.**
- **"Patients with Down's syndrome show more chromosomal breaks after virus infection than do normal control subjects."**
  - *Pediat Res 7: 582-587 (1973) Higurashi*

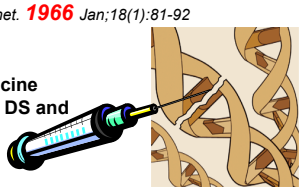
What We Knew Then…

Chromosomal breaks have been documented in patients receiving attenuated measles vaccines.

- **"Breakage here was of the same type as seen with the clinical disease."**
  - *Am J Hum Genet.* ***1966*** *Jan;18(1):81-92*

Reconfirmed vaccine breakage in both DS and typical children.

Ilyinskikh NN 1981



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Natl Cancer Inst Monogr 1968 Dec;29:453-5.

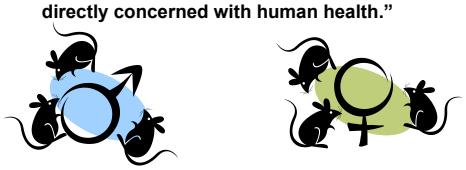
Monitoring vaccines for human oncogenicity

Miller Rw.

"The procedure involves matching lists of vaccinees against a national registry of cancer deaths among U.S. children, beginning in 1960."

Vaccines and Chromosomal Damage

Studies on the effect of vaccines on the DNA of the inoculated organisms is, "very meager, although it is directly concerned with human health."



"…the chromosomes of male mice are comparatively more susceptible to aberration on exposure to measles vaccine than that of the female mice."

Int J hum Genet, 3(1): 51-58 2003

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More Study Needed

- **"Further study is essential to unveil the exact mechanism of the clastogenic action of different vaccines on the hereditary materials of the inoculated organisms."** *Int J Genet, 3(1): 51-58 (2003)*
- **DO UPCOMING VACCINES UNDERGO TESTING ON THE CLASTOGENIC PROPERTIES OF THE VACCINE PRIOR TO PUBLIC RELEASE?**

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LOOK

- sanofi pasteur **Influenza A (H1N1) 2009 Monovalent Vaccine**
  - HIGHLIGHTS OF PRESCRIBING INFORMATION
    - www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM182404.pdf
- Multi-dose vials contain 25 mcg of mercury per 0.5mL dose.
  - Children 36 months - 9 years get 2 doses one month apart.
- "Neither Fluzone vaccine nor Influenza A (H1N1) 2009 Monovalent Vaccine have been evaluated for carcinogenic or mutagenic potential, or for impairment of fertility."

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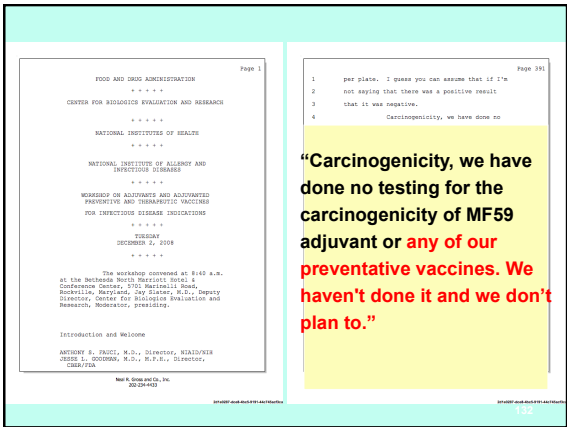

Page 1

FOOD AND DRUG ADMINISTRATION

CENTER FOR BIOLOGICS EVALUATION AND RESEARCH

NATIONAL INSTITUTES OF HEALTH

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

WORKSHOP ON ADJUVANTS AND ADJUVANTED PREVENTIVE AND THERAPEUTIC VACCINES FOR INFECTIOUS DISEASE INDICATIONS

TUESDAY
DECEMBER 2, 2008

The workshop convened at 8:40 a.m. at the Bethesda North Marriott Hotel & Conference Center, 5701 Marinelli Road, Rockville, Maryland, Jay Slater, M.D., Deputy Director, Center for Biologics Evaluation and Research, Moderator, presiding.

Introduction and Welcome

ANTHONY S. FAUCI, M.D., Director, NIAID/NIH
JESSE L. GOODMAN, M.D., M.P.H., Director, CBER/FDA

Neal R. Gross and Co., Inc.
202-234-4433

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per plate. I guess you can assume that if I'm not saying that there was a positive result that it was negative.

Carcinogenicity, we have done no

"Carcinogenicity, we have done no testing for the carcinogenicity of MF59 adjuvant or any of our preventative vaccines. We haven't done it and we don't plan to."

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IOM 2004

Epidemiology vs Biological Studies

IOM is correct; you cannot determine subgroups of sensitive persons from large epi studies.

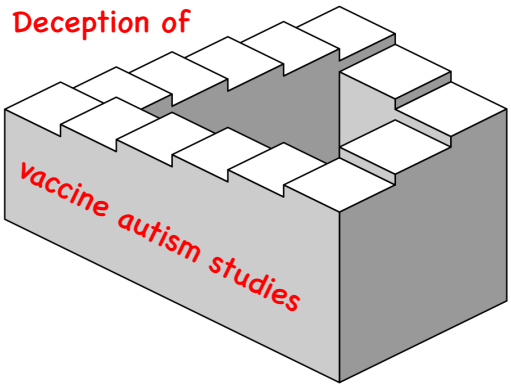
The biology of DS is consistent with what the medical literature indicates for increased damage from exposure to mercury, aluminum, viruses & foreign DNA.

One group of genetically sensitive individuals means it is likely that there are others.

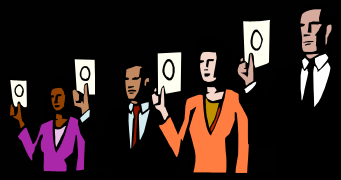
Decreased response to these vaccines in DS

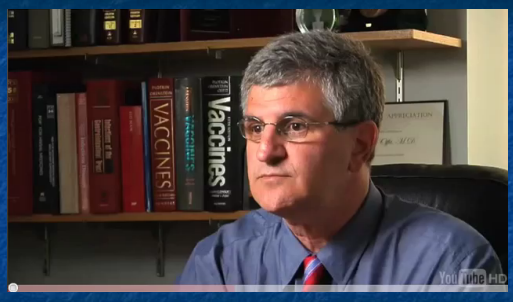
- Pneumococcal polysaccharide vaccine
- Tetanus vaccine
- Pertussis (acellular)
- Hep B
- Influenza
- Polio (oral)

Clin Exp Immunol. 2009 May;156(2):189-93.



How confident do I feel that sufficient mechanistic studies have been done on mandatory vaccines?





Thank You

Ed and Teri Arranga

AutismOne

&

Andi Durkin