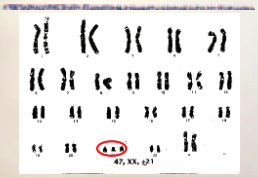
Dispelling medical and media myths about autism from the perspective of children with Down syndrome

Laurette Janak
Autism One
May 29, 2011

Genetics of Down syndrome



Extra chromosome 21

Analogy for biochemistry

Molecules go in → New molecules come out

Positive effect
Negative effect
No effect at all

Factories are built and run by your DNA

Factories = enzymes in your body

Genetically normal child

Super oxide → Hydrogen peroxide

Super oxide dismutase (SOD)

Down syndrome overexpression

Increased super oxide in DS from poorly functioning mitochondria

Excessive H_2O_2 in DS

Super oxide → Hydrogen peroxide

SOD is on Chr 21 & is overexpressed in DS

Child: care, health and development

Editorial

The continuing challenge of diagnosing autism spectrum disorder in children with Down syndrome

"[The Consultant said] he didn't think anything would be gained by having [my child] assessed'.

"Everyone I approached thought he either couldn't, definitely didn't or shouldn't have autism."

DS and ASD?

Subjectivity verses Objectivity

It's just down syndrome.

It's down syndrome and autism.

Neuroanatomic correlates of autism and stereotypy in children with Down Syndrome

(Neuroreport. 2008 Apr 16;19(6):653-6)

- Included MRIs of 15 children with DS, 15 children with DS-ASD and 22 controls.
- DSM-IV criteria was used for ASD diagnosis.
- Aberrant Behavior Checklist (ABC)
  - Irritability
  - Lethargy
  - Stereotypy (repetitive movements)
  - Hyperactivity
  - Inappropriate speech

Mean ABC scores

	All DS	DS only	DS-ASD
Irritability	7.1	2.3	11.9
Lethargy	9.3	2.5	16.1
Stereotypy	6.9	0.7	13.1
Hyperactivity	11.7	4.7	18.7
Inappropriate speech	1.5	0.1	2.9
Total score	36.4	10.2	62.7

MRI findings

- Brain volumes were significantly decreased in DS versus controls.
- A distinguishing feature of significantly more white matter in the brainstem and cerebellum of DS-ASD children compared to DS alone.
  - This pattern resembles that seen in children with autism alone.
  - Increased white matter correlated with the ABC stereotypy subscale score.

DS and ASD?

Subjectivity verses Objectivity

~~It's just down syndrome.~~

It's down syndrome and autism.

Incidence of having both DS and ASD

1979
"extremely rare"
J Autism Dev Disord
1979 Mar;9(1):31-6

2010
"18.2%"
J Dev Behav Pediatr.
2010 Apr;31(3):181-91

Dr. David Gorski

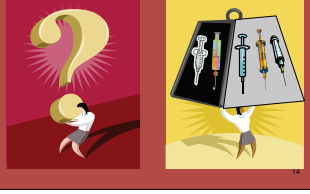
Serves as a professor of surgery at Wayne State University School of Medicine

Professionalism ?

Pediatr Infect Dis J. 2009 May;28(5):431-432

"...the field of advocacy is growing due to scientific interest in understanding the basis for vaccine reactions, "push" from the growing field of individualized medicine, and consumer demand for safer vaccines."

Immune overload



PEDIATRICS

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Addressing Parents' Concerns: Do Multiple Vaccines Overwhelm or Weaken the Infant's Immune System?

Neil A. Offit, Jessica Quarles, Michael A. Gerber, Charles J. Hackett, Edgar R. Marcuse, Tobias R. Kollman, Bruce G. Gellin and Sarah Landry

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

THE ORANGE COUNTY REGISTER

Correction for April 18

2011-04-18 15:49:24

An OC Register article dated Aug. 4, 2008 entitled "Dr. Paul Offit Responds" contained several disparaging statements that Dr. Offit of Children's Hospital of Philadelphia made about CBS News investigative Correspondent Sharyl Attkisson and her report. Upon further review, it appears that a number of Dr. Offit's statements, as quoted in the OC Register article, were unsubstantiated and/or false. Attkisson had previously reported on the vaccine industry ties of Dr. Offit and others in a CBS Evening News report "How Independent Are Vaccine Defenders?" July 25, 2008.

Unsubstantiated statements include: Offit's claim that Attkisson "lied"

For full story go to:

http://www.ocregister.com/articles/correction-296910-dated-entitled.html

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.

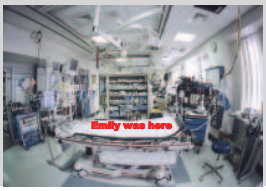
"Exclusion criteria were prematurity (gestational age <37 weeks) and congenital abnormalities related to immunity (such as Down syndrome)."

Specifically excluded from studies but….

specifically targeted for vaccines!

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

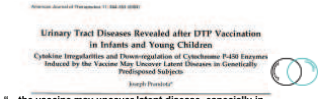
Within days of vaccination…



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?"



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 Posniak*

"…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.

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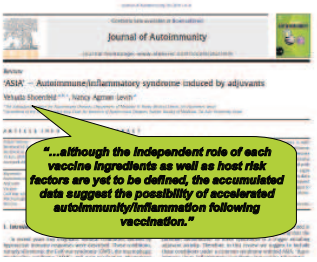
The Immune system is altered in DS

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

"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

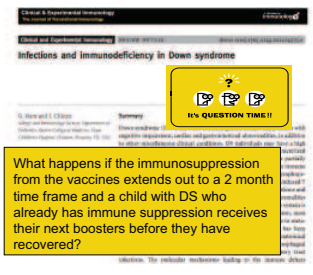


Cytokine profile after rubella vaccine inoculation: evidence of the immunosuppressive effect of vaccination *Pukhalsky AL et al 2003*

Blood samples were collected before vaccination, and then again at 1 week and 1 month later.

"…a profound decrease of T-cell proliferation value on day 30 following vaccination was observed."

"In conclusion, live attenuated rubella vaccine inoculation may cause sustained immunosuppression including defective lymphocyte response to mitogen and impaired cytokine production. The signs of immunosuppression may persist for at least 1 month after vaccination."



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."

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THE JOURNAL OF INFECTIOUS DISEASES

VOL. 131, NO. 6 * JUNE 1975

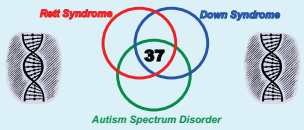
From the National Institutes of Health

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."

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"

CDC Centers for Disease Control and Prevention

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 ... used responsibility for monitoring the ... long research to inform safe vaccine ... relationship between human genetics a...

Identifying genetic ...

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

"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."

ISO's Genomics Initiative

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

Personalized vaccines: the emerging field of vaccinomics

Expert Opin Biol Ther 2008 Nov; 8(11): 1689-1697

"...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."

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.

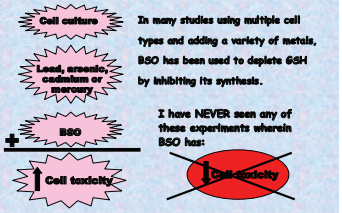
Where would one begin to look for such a population?

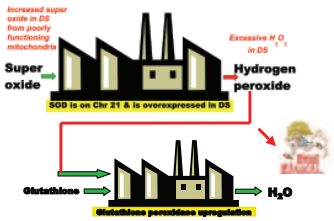
How does mercury effect human biochemistry to cause toxicity?

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

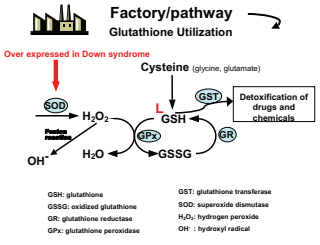
The role that glutathione (GSH) plays in mercury toxicity and oxidative stress was known long before the 2004 IOM declaration.

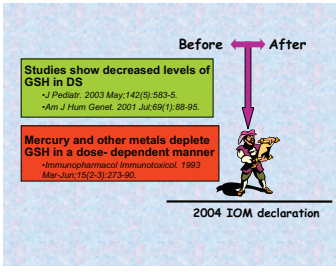
Shenker BJ et al. 1993
Queiroz ML et al. 1998
Makani S et al. 2002

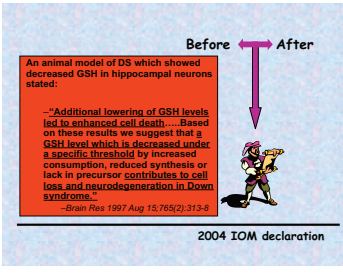


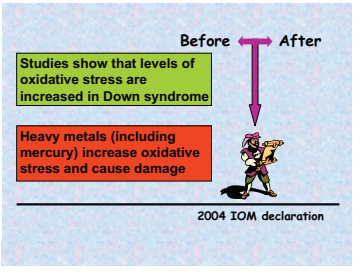


Results in lower levels of glutathione (GSH) in DS









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

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

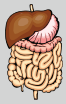
Let's be perfectly clear...

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

Facts about aluminum

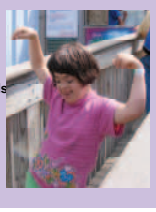


- In typical healthy people, the gastrointestinal tract excludes greater than 95% of dietary Al.

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

Facts about Aluminum

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



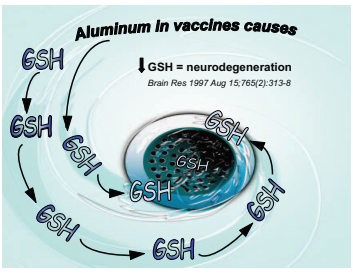
Facts about Aluminum

- "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*

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?



A BIG Question

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

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Media Puppets

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)

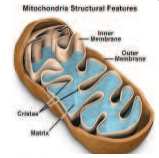
Mitochondria in DS

- 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?
- Could this explain 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.*

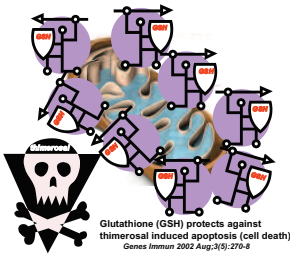
CAN THIMEROSAL BE ONE OF THESE "DAMAGING AGENTS"?

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*

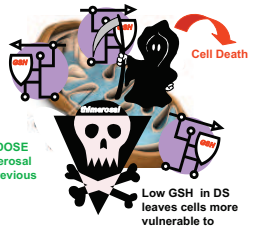
Mitochondria and Thimerosal

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

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

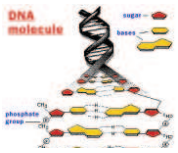
Genetic differences in glutathione-S-transferase (GST) have been shown to contribute to the inter-individual variance in detoxification of mercury.

Environ Res. 2009 Aug;109(6):786-96

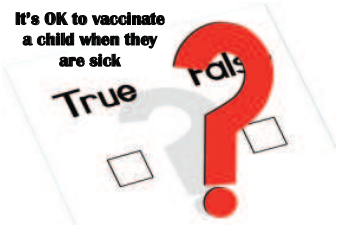
Sci Total Environ. 2007 Oct 15;385(1-3):37-47

Human intervention studies have demonstrated, "that regular intake of broccoli for a relatively short period of time could significantly affect glutathione-S-transferase (GST) activity and cell protection against DNA damage."

Int J Vitam Nutr Res. 2008 Dec;78(6):261-8.



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



Glutathione and Mild Infections

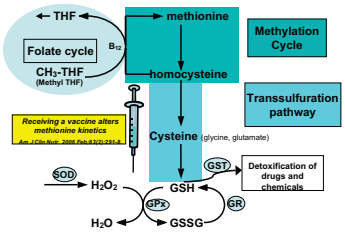
Common childhood illness such as ear infections (otitis media) and tonsillitis:

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

Cernek et al. 2005

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



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

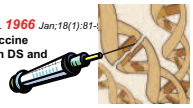
What We Knew back then…

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

– *Am J Hum Genet.* ***1966*** *Jan;18(1):81-*

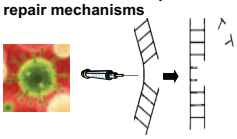
Reconfirmed vaccine breakage in both DS and typical children.

Ilyinskikh NN 1981



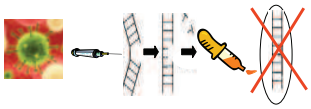
Think on this

- **Measles vaccine can damage DNA**
  - **DS individuals have poor DNA repair mechanisms**



Think on this

- **Instructed to give acetaminophen (Tylenol) to help with pain and/or fever post vaccination**
  - **Both Tylenol and vaccination can decrease GSH**
  - **Tylenol cause transitory decreases in DNA repair ability**
  - **Low GSH is a risk factor for leukemia (and autoimmunity)**
  - **DS children have a 15-20 fold increased risk of leukemia**



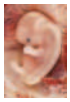
Vaccines and Chromosomal Damage

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."

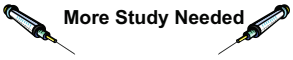
Int J hum Genet, 3(1): 51-58 2003

Of Mice and Men

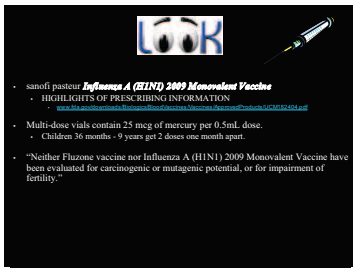


- **Clastogenicity of "rubella vaccine in mouse bone marrow, recorded here, is in agreement with the earlier reports on the induction of chromosomal breaks in human embryonic cell cultures."**
  - *Int J hum Genet, 3(1): 51-58 2003*

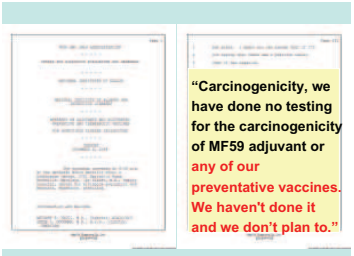
More Study Needed



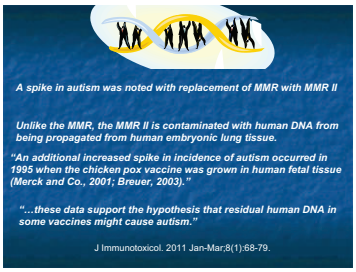
- **"Further study is essential to unveil the exact mechanism of the clastogenic action of different vaccines on the hereditary materials of the inoculated organisms."** *Int J Genet, 3(1): 51-58 (2003)*
- **DO UPCOMING VACCINES UNDERGO TESTING ON THE CLASTOGENIC PROPERTIES OF THE VACCINE PRIOR TO PUBLIC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



- sanofi pasteur ***Influenza A (H1N1) 2009 Monovalent Vaccine***
  - HIGHLIGHTS OF PRESCRIBING INFORMATION
    - www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM182454.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."



"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."



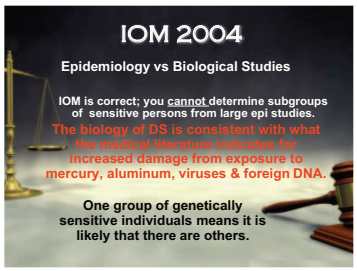
A spike in autism was noted with replacement of MMR with MMR II

Unlike the MMR, the MMR II is contaminated with human DNA from being propagated from human embryonic lung tissue.

"An additional increased spike in incidence of autism occurred in 1995 when the chicken pox vaccine was grown in human fetal tissue (Merck and Co., 2001; Breuer, 2003)."

"…these data support the hypothesis that residual human DNA in some vaccines might cause autism."

J Immunotoxicol. 2011 Jan-Mar;8(1):68-79.



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

Paul Offit