

Vaccine Adverse Events – Separating Myth from Reality

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Case: TK

- 3 month old male in Pediatric Infectious Diseases clinic
 - Discuss recent hospitalization
- Born healthy at term
 - Hepatitis B vaccine in the hospital
- Breastfed with occasional supplementation
- Healthy with no illnesses.
- Presented to 2 month well child check growing and developing well
 - due for the usual childhood vaccines.

Case

- Mother requested he only get one shot
- She requested only DTaP
 - (He actually received the DTaP-IPV-HiB combination (Pentacel®))

Case

- Received vaccine uneventfully
- 3 hours after the vaccine, nursed for about 10 minutes followed by formula
- After feeding, was burped and laid on the changing table

Case

- On changing table, turned completely white and unresponsive.
 - Eyes “rolled into the back of his head”
 - did not have any abnormal movements
- Very limp and still
- Did not turn blue
- MOC picked him up, still limp
- Lied him back down and he stooled

Case

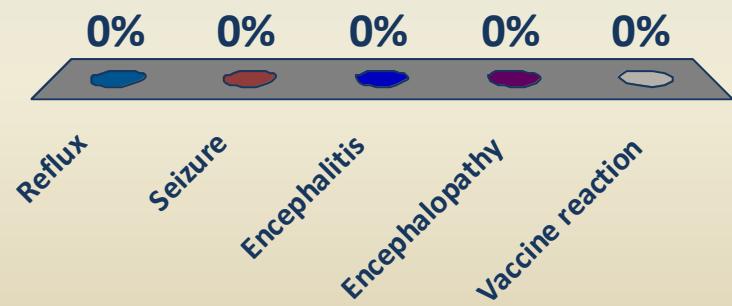
- Next several minutes
 - in and out of consciousness
 - occasionally looking around but not responding to anything
- Called 911, taken to ED
- At ED
 - Seemed only responsive to pain
 - IV was placed
 - became more responsive, and shortly thereafter seemed to be back to normal

Case

- Episode lasted a total of 45 minutes
- Admitted to the hospital
 - blood, urine, and spinal fluid obtained.
- All tests including CBC, LFTs, spinal fluid, and UA were normal
- Bacterial cultures negative
- HSV pcr negative
- Negative CT head
- Rapid RSV and influenza tests negative.
- Uncomplicated hospital stay
 - discharged at 48 hours.

What did this child have?

- A. Reflux
- B. Seizure
- C. Encephalitis
- D. Encephalopathy
- ★ E. Vaccine reaction



Hypotonic-Hyporesponsive Episode

- Triad of signs
 - sudden onset of reduced muscle tone
 - hypo-responsiveness
 - change in skin color (pallor or cyanosis)
- Also termed “collapse” or “shock-like state”
- First described in 1961
- Has been reported after Diphtheria, tetanus, Hib, and Hep B vaccines
 - most common and conclusively linked to pertussis containing vaccines, usually after the first dose.
- Pathophysiology is unclear

Hypotonic hyporesponsive episode

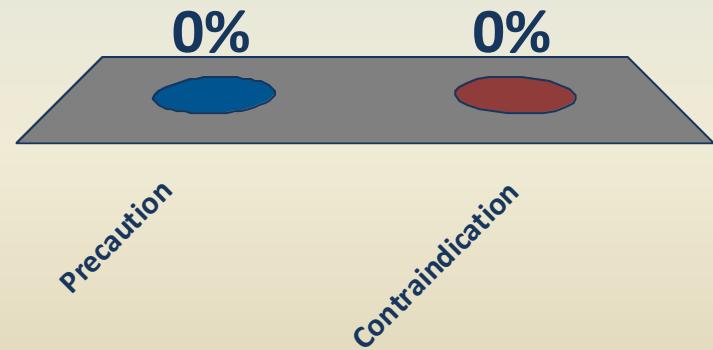
- Red Book: 1/1750 doses
- Less likely with DTaP than old DTP

Hypotonic hyporesponsive episode

- Median time to onset of symptoms 3-4 hours
 - range of immediate to 48 hours
- Median duration of the triad of signs 6-30 minutes
 - rarely has been reported as long as 10 days
- Fever in up to 1/3
- No lab or radiologic findings are contributory

Is this a precaution or contraindication for future vaccination?

- A. Precaution
- B. Contraindication



Should you immunize this child?

- Contraindication or precaution?
- From The Red Book, 2012:
- **“PRECAUTIONS FOR DTaP IMMUNIZATION...** Although these events once were regarded as contraindications, they now are considered precautions, because they have not been proven to cause permanent sequelae:
 - A seizure
 - Persistent, severe, inconsolable screaming or crying
 - **Collapse or shock-like state (HHE) within 48 hours of immunization**
 - Temperature of 40.5°C (104.8°F)

Prognosis

- Long term prognosis very good
- Episodes with future doses have happened, but very rare

Objectives

- To understand the importance of un- and under-immunized children
- To provide a basic framework for understanding vaccine safety studies
- To equip providers with the knowledge necessary to counsel parents about vaccine adverse events
- To provide a useful reference for providers for families with specific questions about vaccines

Outline

- Introduction
- Vaccine Safety Monitoring
- What Vaccines Don't Cause
- What Vaccines Do Cause
- What Vaccines Might Cause

Vaccine Disease Prevention

| Disease | # Cases/yr prior to Vaccine ¹ | Year universal rec. | # Cases 2011 | # Cases 2012 | # Cases 2013 | # Cases 2014 so far... |
|---|--|-------------------------|-----------------|-----------------|-----------------|------------------------|
| Invasive ⁶ <i>H. influenzae</i> , type b | ~20,000 | 1985 | 14 | 11 | 31 | 15 |
| Invasive ⁶ <i>S. pneumoniae</i> | ~89,400 | 2000 | 771 | 562 | 740 | 602 |
| Hepatitis B (acute) | 21,102 | 1991 | 1,737 | 1,578 | 1,799 | 1,622 |
| Varicella | ~4,000,000 | 1995 | 8,818 | 7,469 | 6,766 | 5,279 |
| Varicella deaths | 115 | | NA ⁸ | NA ⁸ | NA ⁸ | NA ⁸ |
| Hepatitis A (acute) | 26,796 | 1999 ⁷ /2006 | 820 | 819 | 1,078 | 68 |

⁶Children <6 years of age. ⁷Recommended for highest risk communities in 1996, for communities and states with increased risk (1999) and then for universal use (2006).

⁸Data not available.

Vaccine Disease Prevention

| Disease | # Cases prior to Vaccine ¹ | Year universal rec. | # Cases 2011 ² | # Cases 2012 ³ | # Cases 2013 | # Cases 2014 so far... |
|-------------------------|---------------------------------------|---------------------|---------------------------|---------------------------|--------------|------------------------|
| Smallpox | 48,164 | Early 1900s | 0 | 0 | 0 | 0 |
| Diphtheria | 175,885 | Mid 1940s | 0 | 1 | 0 | 1 |
| Pertussis ⁴ | 147,271 | Mid 1940s | 9,883 | 23,636 | 15,823 | 16,760 |
| Tetanus | 1,314 | Mid 1940s | 36 | 22 | 26 | 16 |
| Paralytic Poliomyelitis | 16,316 | 1955 | 0 | 0 | 1 | 0 |
| Measles | 503,282 | 1963 | 222 | 44 | 187 | 582 |
| Mumps | 152,209 | 1967 | 194 | 116 | 415 | 965 |
| Rubella | 47,745 | 1969 | 4 | 6 | 9 | 6 |
| Congenital | 823 | | 0 | 2 | 1 | 0 |

¹CDC. 1999. MMWR 48:243. ²MMWR. ³MMWR.

⁴Cases of pertussis were at a historic low of 1010 in 1976. ⁵Imported, vaccine-associated.

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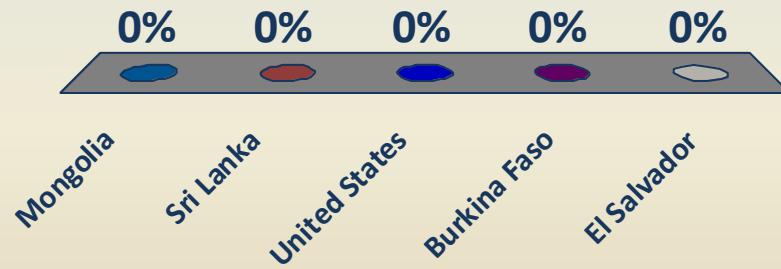
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Which of the following countries has the lowest rate of measles vaccination?

- A. Mongolia
- B. Sri Lanka
- C. United States
- D. Libya
- E. El Salvador



US, Mexico, and Canada Vaccine UTD

Coverage per WHO, 2012

| | USA | Canada | Mexico |
|---------|-----|--------|--------|
| Polio | 94 | 99 | 98 |
| DTP | 96 | 95 | 99 |
| Measles | 92 | 98 | 99 |
| Hib | 94 | 95 | 99 |
| PCV | 94 | 97 | 99 |

http://www.who.int/immunization/monitoring_surveillance/data/en/

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Why are Un- and Under-Immunized Children so Important?

- They are at risk of disease
- The immunized may also be at risk
 - no vaccine is 100% effective

For example, Measles:

- The proportion of the population that needs to be immune to keep virus from transmitting person to person is 95% (but 5% remain susceptible after vaccination)
- If 2 are unimmunized, 5 more are also susceptible (5% of the 98): the immune level is about 93%
- In the US, MMR coverage is 92%, immune level, therefore, is ~87%

Community (Herd) Immunity Thresholds

- Measles: >94%
- Poliomyelitis: 50-93% (following IPV, unknown)
- Diphtheria: 85%
- Mumps: 86%
- Pertussis: 94%
- Rubella: 83-85%
- Smallpox: 80-85%

After Fine P. in Orenstein & Plotkin 4th Edition, 2004.

Why are immunization coverage levels low in some communities?

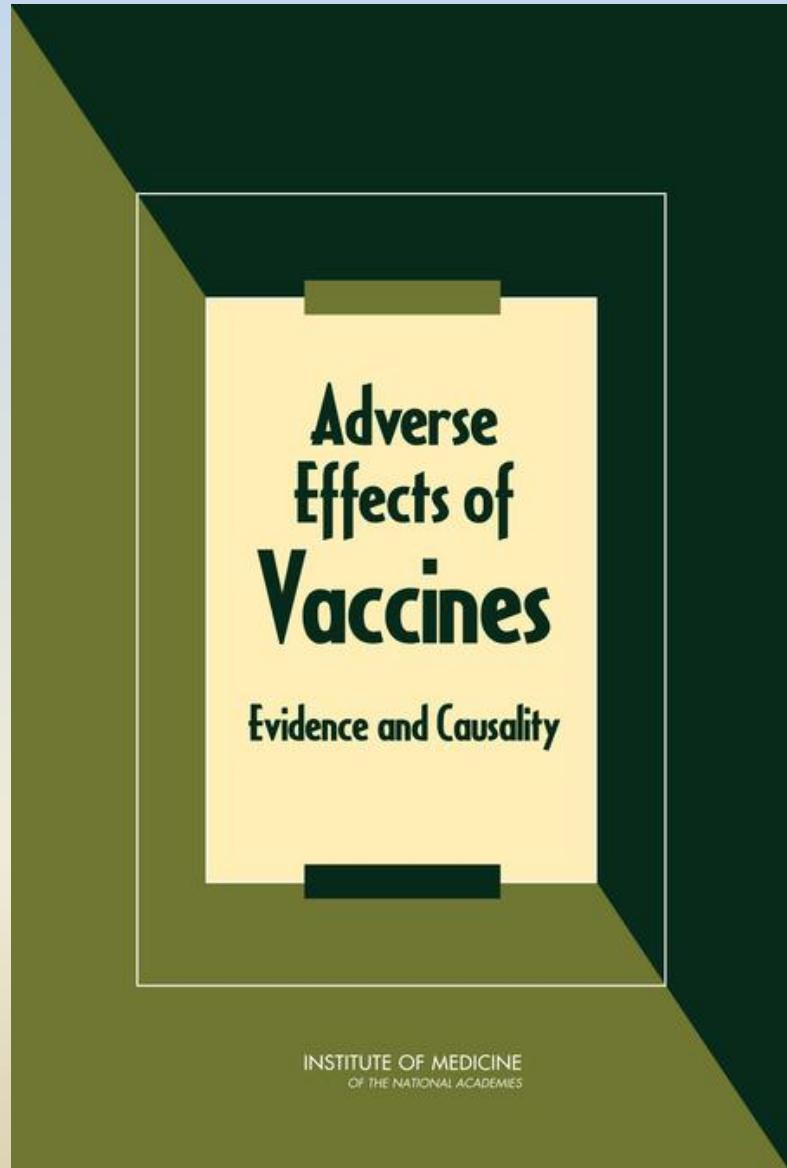
Multiple Reasons

- Poverty
- Disparities in access
- Fear of being identified by the government
- **Risk-benefit misperceptions**

Missing Information

- Many don't understand that their children are at risk from vaccine preventable diseases
 - Loss of diseases' visibility.
 - Loss of a sense of urgency.
 - Lack of fear

- IOM: “The data are insufficient to support or reject the hypothesis”
- Most of the vaccine safety questions they examine they state there is “insufficient evidence” which gives fuel to anti-vaccine proponents



The Challenge

- Most vaccination literature written to address common concerns
 - don't address the specific concerns of many parents
- Much of the anti-vaccination literature is written at a very high level with “leaps of logic” that those not accustomed to examining medical literature will not recognize

The Challenge

- Parental concerns
 - Children are vulnerable
 - Choice is very important
 - They want to better understand and weigh the risks and benefits of vaccinations

Our Job

- To fully inform parents, we must:
 - Listen to and understand what their concerns are
 - Show empathy for their beliefs, even if their risk perceptions are inaccurate
 - Correct them without patronizing or ridiculing them

Our job (cont)

- Explain the known science in lay terms
- Speculate responsibly -- express your expectations, acknowledging you could be wrong
- Use risk comparisons to help put risks in perspective (i.e. driving to appointment)
- Balance the use of anecdotes and data (statistics)
- Separate science from pseudoscience

Our job (cont)

- Explain the known science in lay terms
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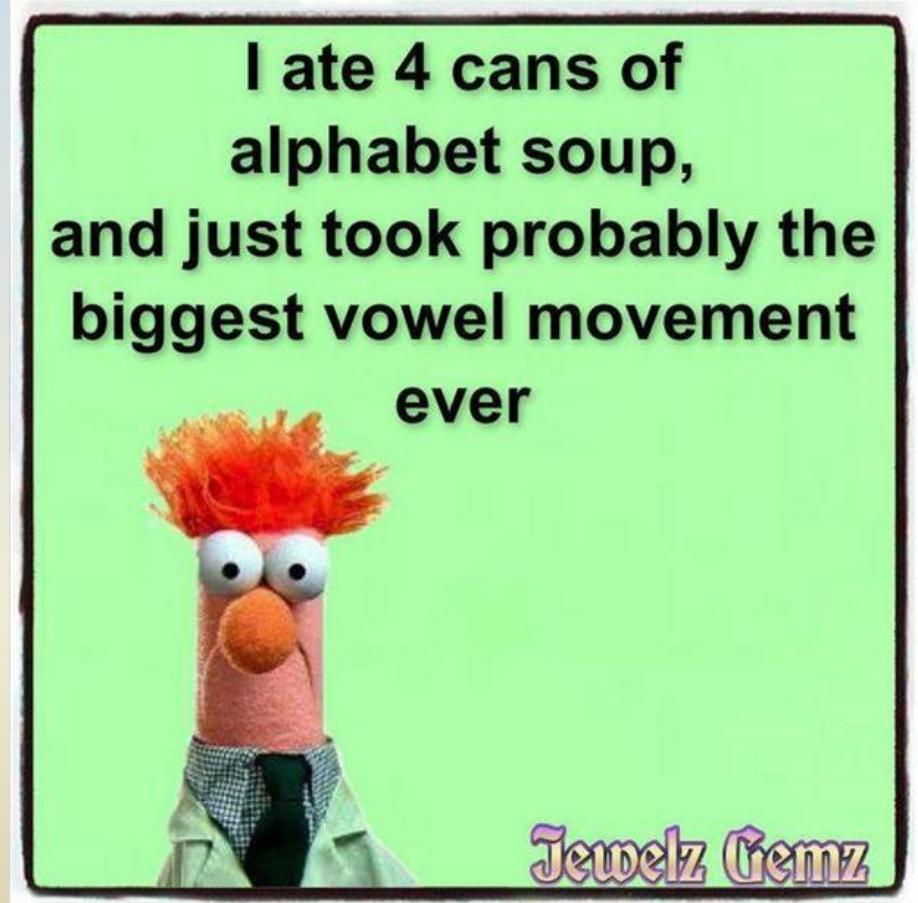
- Show empathy for those suffering from the “alleged adverse event” -- for instance, recognize the burden of parents of autistic children
- Avoid distant, abstract, unfeeling language about deaths, injuries, and illnesses -- they are all tragedies

Our job (cont)

- Given the level of concern of many parents today, be as fully informed as possible about all aspects of immunization
 - Not enough to trust the “experts” anymore
 - Know the risks of the diseases we’re trying to prevent
 - ***Know the risks of the vaccines we are giving***

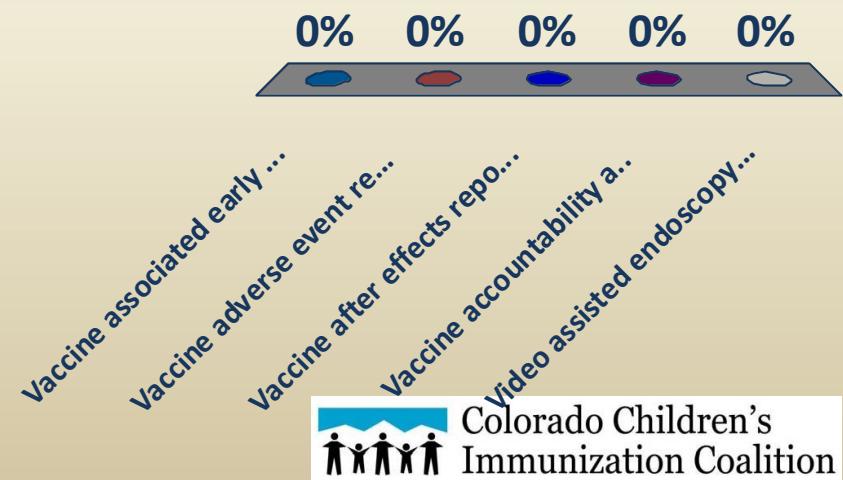
Alphabet Soup

- VICP
- VAERS
- VSD



What does VICP stand for?

- A. Vaccine Injured Children's Parents
- ★ B. Vaccine Injury Compensation Program
- C. Vaccine-related Illness Coordination Program
- D. Viral Induced Chorea and Paresis
- E. Vaccines, Immunizations, Children, and Parents



Vaccine Injury Compensation Program

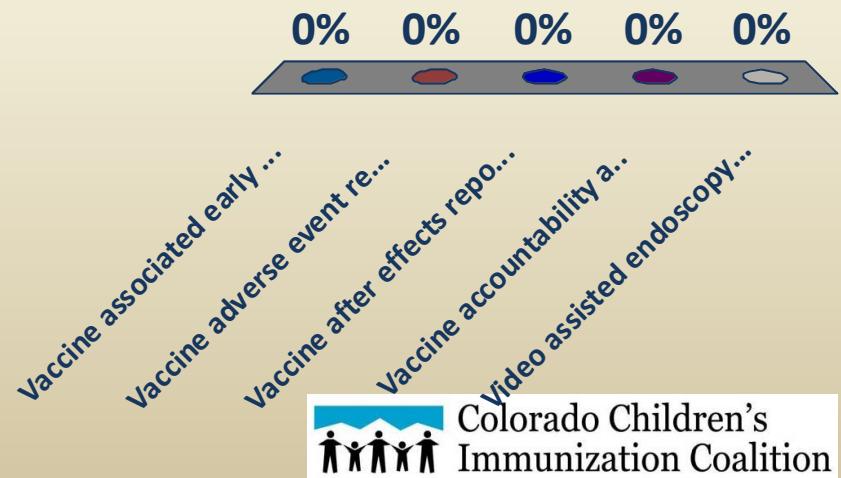
- No fault system established in 1998 as an alternative to civil litigation
- Small tax (\$0.75) on all childhood vaccines funds the program
- People seeking compensation for alleged injuries from covered vaccines must first file claims with the VICP before civil litigation against manufacturers or vaccine providers
- Program has decreased # of lawsuits against providers and manufacturers and has assisted establishing a stable vaccine supply and marketplace

Vaccine Injury Compensation Program

- People who file claims may qualify for compensation in 3 ways
 - Show that a known vaccine adverse event (as defined in a ‘Vaccine Injury Table’) occurred in a specified time interval after a vaccine
 - Prove that the vaccine caused the injury
 - Prove that the vaccine worsened a pre-existing condition
- Examples of things in the Vaccine Injury Table include anaphylaxis after several vaccines and intussusception after rotavirus vaccine
- <http://www.hrsa.gov/vaccinecompensation/index.html>

What does VAERS stand for?

- A. Vaccine associated early response system
- ★ B. Vaccine adverse event reporting system
- C. Vaccine after effects reportable syndromes
- D. Vaccine accountability and expendability regulation system
- E. Video assisted endoscopy for residents and students



Vaccine Adverse Event Reporting System (VAERS)

- Co-administered by CDC and FDA
- Why?
 - Rare adverse events are very difficult to detect pre-licensure
- Objectives
 - Detect new, unusual, or rare vaccine adverse events (VAEs);
 - Monitor increases in known adverse events;
 - Identify potential patient risk factors for particular types of adverse events;
 - Identify vaccine lots with increased numbers or types of reported adverse events; and
 - Assess the safety of newly licensed vaccines.

VAERS

- Passive reporting system – providers are encouraged to report *any* event taking place after a vaccine, even if they don't think it is related
- Hypothesis *generating*, not testing
- Publicly available
- 30,000 reports annually, 13% serious
 - 37% vaccine manufacturers
 - 36% providers
 - 10% state immunization programs
 - 7% parents/guardians or patients
 - 10% other

VAERS

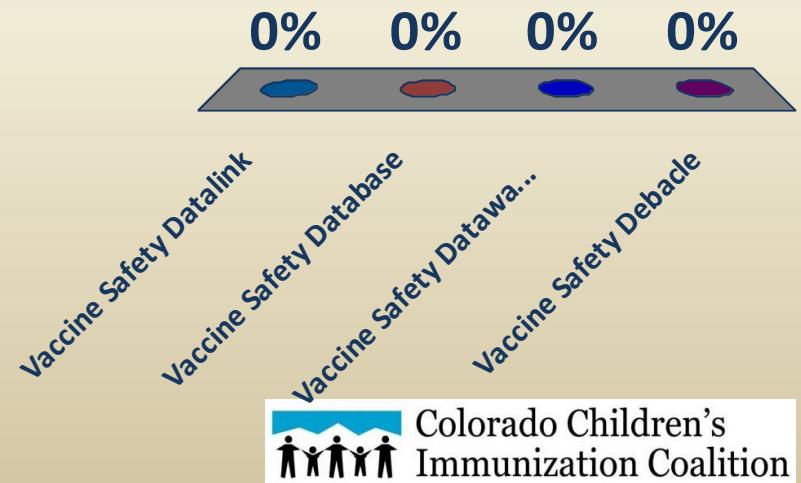
- Strengths
 - National scope
 - Ability to detect rare events fairly quickly
 - Serious reports are followed up
- Limitations
 - Variability in reporting standards
 - Reporter bias (lawyers!)
 - Under reporting
 - *Inability to assess causality*

VAERS

- No denominator data
- *Crucial* to understand that data in VAERS cannot support a determination of whether or not a vaccine cause an adverse event

What does VSD stand for?

-  A. Vaccine Safety Datalink
- B. Vaccine Safety Database
- C. Vaccine Safety Datawarehouse
- D. Vaccine Safety Debacle



Colorado Children's
Immunization Coalition

Vaccine Safety Datalink (VSD)

- Established in 1990
- 9 large HMOs (including Kaiser Permanente Colorado) involved in data sharing agreement, managed in collaboration with CDC
- Population: 18 million persons spanning 18 years

VSD Strategic Priorities

- Evaluate the safety of newly licensed vaccines
- Evaluate the safety of new vaccine recommendations for existing vaccines
- Evaluate clinical disorders after immunizations
- Assess vaccine safety in special populations at high risk
- Develop and evaluate methodologies for vaccine-safety assessment

VSD Novel Techniques and Study Designs

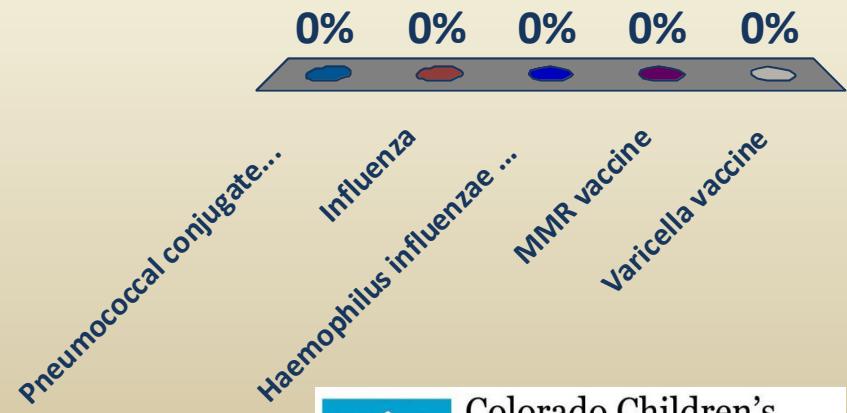
- Rapid Cycle Analysis
 - Near real time surveillance
 - Compare suspected adverse events with expected number of events
- Self Controlled Case Series and similar methodologies
 - Because there are few unvaccinated persons, each person acts as own control

Case to Illustrate Methodology

- 13 month old infant presents to the office with a one day history of easy bruising and epistaxis
- Exam shows well appearing infant with diffuse petechiae and purpura
- CBC with normal WBC, hgb and hct but platelets of 4K
- Had received 12 month vaccines 2 weeks prior

Of the following vaccines, which most likely triggered this child's ITP?

- A. Pneumococcal conjugate vaccine
- B. Influenza
- C. Haemophilus influenzae type b vaccine
- D. MMR vaccine
- E. Varicella vaccine



Illustrative Study

- How do we know ITP is associated with MMR vaccine in the infant series?

1.8 million children 0-17 years enrolled in 5 health plans 2000-2009

696 possible cases identified using an ICD-9 code for thrombocytopenia and one platelet count <50000 within 6 weeks of diagnosis OR two platelet counts <50000

248 cases excluded based on presence of pre-existing conditions known to cause ITP using ICD-9 codes

448 possible cases for chart review

251 cases excluded for:

- other hematologic or oncologic diagnosis (94)
- acute illness (46)
- ITP with unknown onset date (40)
- exclusionary medications (28)
- Lab error (14)
- ITP found on routine screening (12)
- incomplete records (10)
- recurrent ITP (7)

197 confirmed cases of ITP

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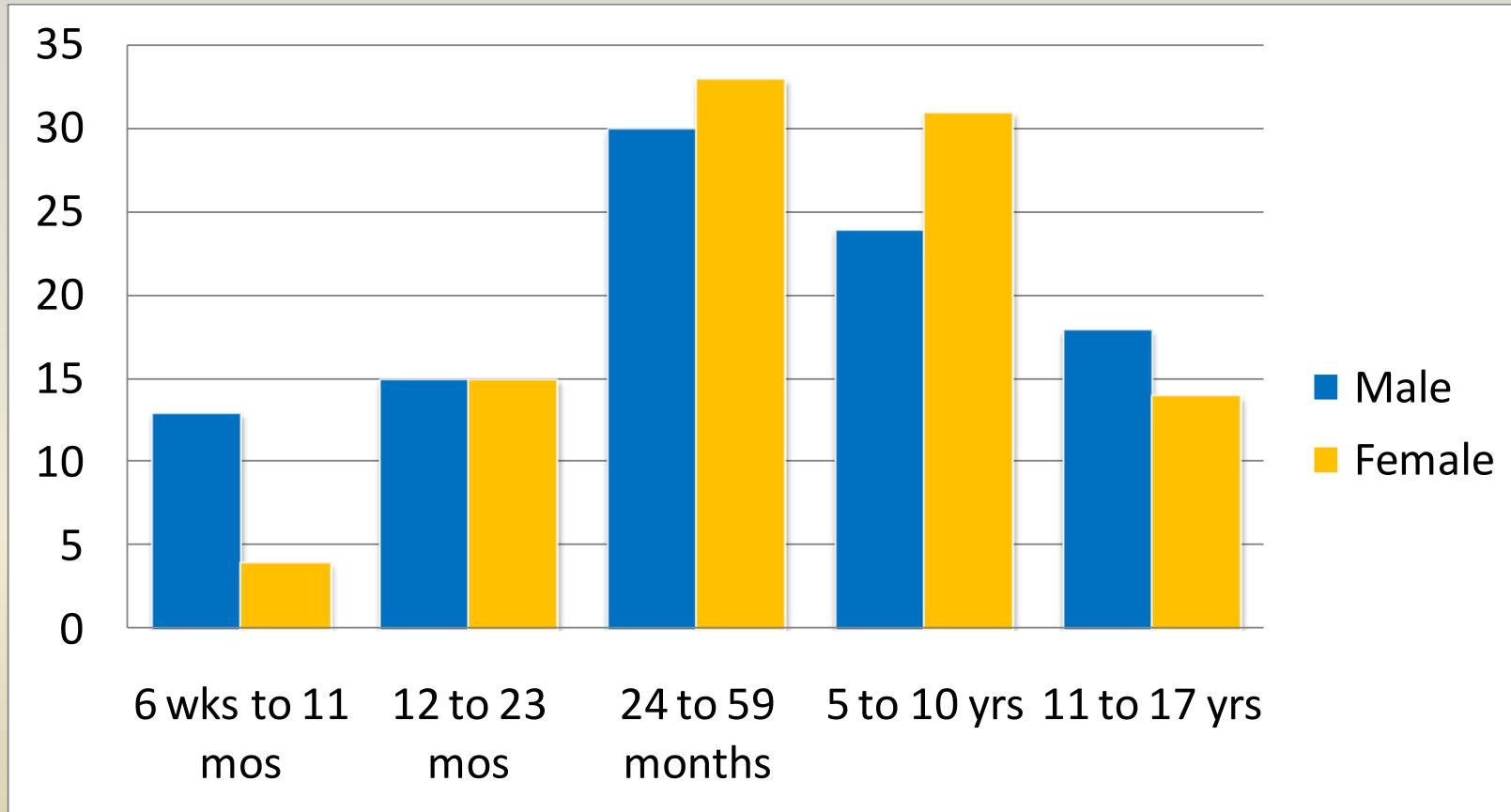
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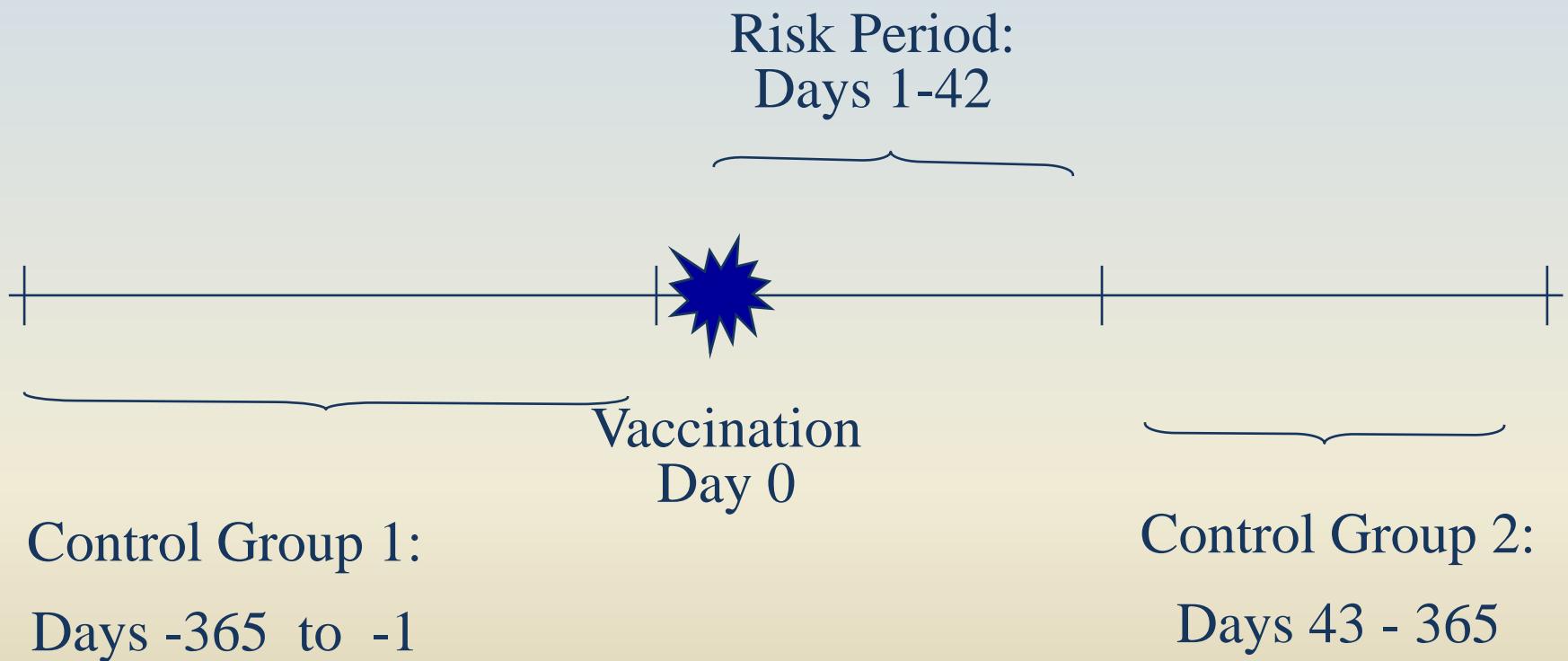
Study Population



Incident Rate Ratio

- All cases are exposed to the vaccine of interest
 - # of cases in 1-42 day exposure window/
exposed person-time of all cases
 - # of cases outside 1-42 day exposure
window/unexposed person-time of all cases

Risk and Control Periods:



Risk and Control Periods:

“Exposed Case”



Risk Period:
Days 1-42



Vaccination
Day 0

Control Group 1:

Days -365 to -1

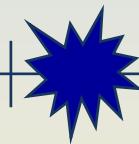
Control Group 2:

Days 43 - 365

Risk and Control Periods:

“Exposed Case”

Risk Period:
Days 1-42



Vaccination
Day 0

Control Group 1:

Days -365 to -1



Control Group 2:

Days 43 - 365

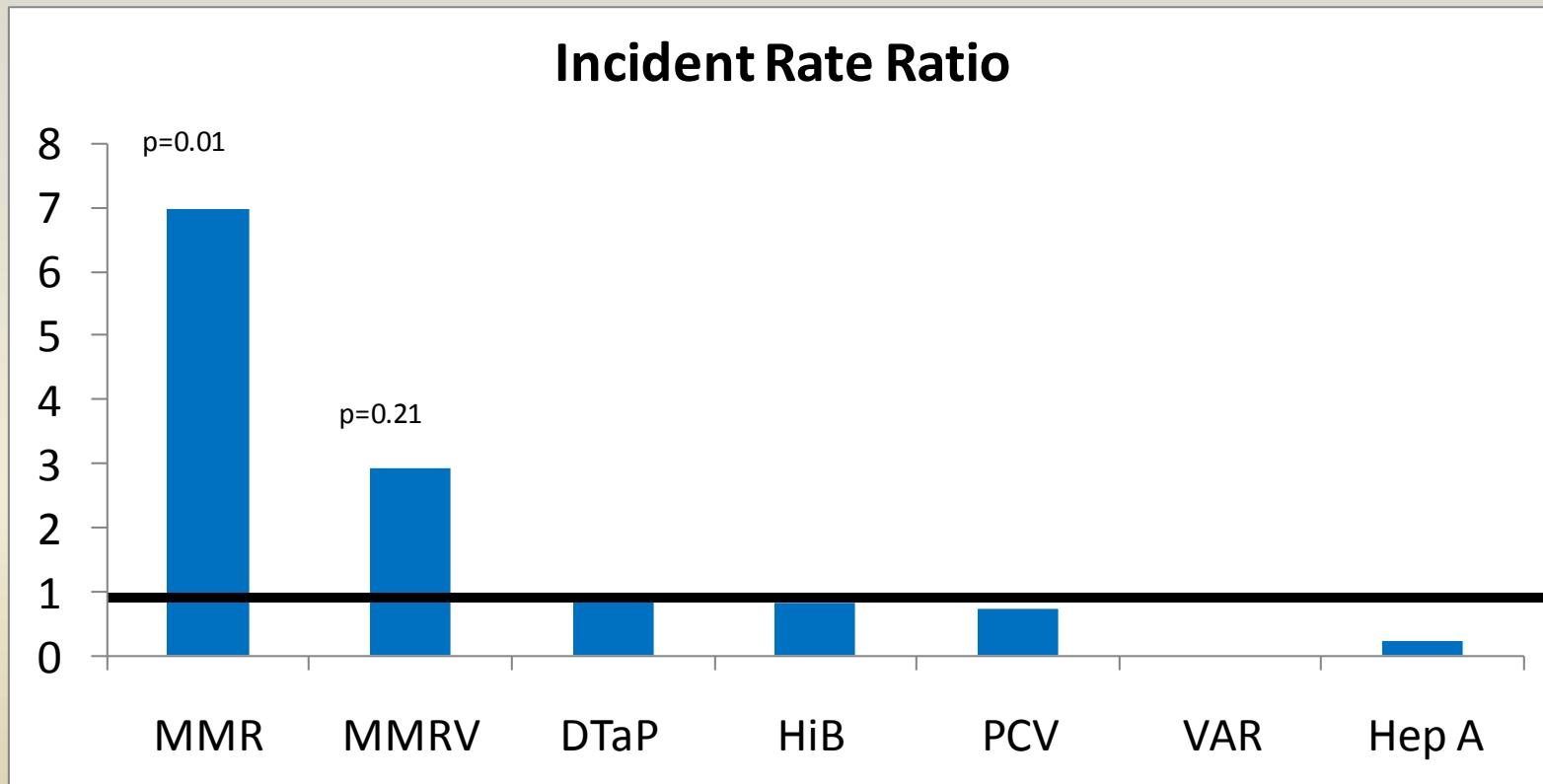


“Unexposed Case”

Results – Infant Series of Vaccines

- No increased risk of ITP for any vaccine in the infant series (6 wks to 11 months)

The Risk of ITP After Vaccines, 12-19 months of Age



What Vaccines *Don't* Cause

Asthma

- Hypotheses on how vaccines might cause asthma
 - Might stimulate a harmful immune response
 - Might suppress a beneficial immune response
- IOM, 2013:
 - “In summary, research examining the association between the cumulative number of vaccines received and the timing of vaccination and asthma, atopy, and allergy has been limited; the findings from the research that has been conducted are reassuring, however. No data have demonstrated harm (an increased risk of atopy) from immunizations. Indeed, the opposite may be the case.”

Asthma

- Several studies have shown that it is extremely unlikely that vaccines play any role in the development of asthma
- A meta-analysis from 2007 of all the studies that looked at DTP vaccine showed no association
 - Is childhood vaccination associated with asthma? A meta-analysis of observational studies. Balicer RD, Grotto I, Mimouni M, Mimouni D. Pediatrics. 2007 Nov;120(5):e1269-77.

Asthma

- Conclusion: the available scientific evidence shows that it is very unlikely that multiple vaccines contribute to asthma
- Caveat: there is some data that LAIV (the live intranasal influenza vaccine) may trigger episodes of wheezing in children 6-23 months of age
 - Safety and efficacy of live attenuated influenza vaccine in children 2-7 years of age. Belshe RB, Ambrose CS, Yi T. Vaccine. 2008 Sep 12;26 Suppl 4:D10-6.
 - Emerging data on the safety and efficacy of influenza vaccines in children. Vesikari T. Pediatr Infect Dis J. 2008 Nov;27(11 Suppl):S159-61.

Type I Diabetes Mellitus

- The hypothesis: diabetes is thought to result from an environmental trigger in genetically susceptible individuals. Could a vaccine be that trigger?
- The evidence:
- IOM, 2002: “The epidemiologic and clinical evidence favors rejection of a causal relationship between multiple immunizations and an increased risk of Type 1 DM.”

Type I DM: The Evidence (cont)

- Many other studies confirming this. Most notably:
 - A Vaccine Safety Datalink (VSD) case-control study showing no link between any childhood vaccines and DM
 - Childhood vaccinations, vaccination timing, and risk of type 1 diabetes mellitus. DeStefano F, Mullooly JP, Okoro CA, and the Vaccine Safety Datalink Team. Pediatrics. 2001 Dec;108(6):E112.
 - A study out of Denmark of 740000 children also demonstrating no link
 - Childhood vaccination and type 1 diabetes. Hviid A, Stellfeld M, Wohlfahrt J, Melbye M. N Engl J Med. 2004 Apr 1;350(14):1398-404.

Multiple Sclerosis

- In 1996, after a mass immunization campaign in France, there were reports that hepatitis B vaccine was causing MS
- The IOM in 2002 found that the evidence favored rejection of a causal link
- Numerous studies since then confirming that there is likely no link
 - Vaccinations and risk of central nervous system demyelinating diseases in adults. DeStefano F, Verstraeten T, Jackson LA, et al and the Vaccine Safety Datalink Research Group, National Immunization Program, Centers for Disease Control and Prevention. Arch Neurol. 2003 Apr;60(4):504-9.

Chronic Arthritis

- The hypothesis: joint pain and arthritis can occur during rubella infection, and chronic joint pain can occur as well.
- Joint pain occurs in 8 of 1000 children after rubella vaccination, and arthritis occurs in 11% of women after vaccination.
- The evidence: Numerous studies showing no increased rate of chronic arthritis after rubella vaccine. Notably:
 - Risk of chronic arthopathy among women after rubella vaccination. Vaccine Safety Datalink Team. Ray P, Black S, Shinefield H, et al. JAMA. 1997 Aug 20;278(7):551-6.
 - Randomized double-blind placebo-controlled study on adverse effects of rubella immunisation in seronegative women. Tingle AJ, Mitchell LA, Grace M, et al. Lancet. 1997 May 3;349(9061):1277-81.

Inflammatory Bowel Disease

- Report from Great Britain in 1995 that measles vaccines might cause IBD
- Many studies that have subsequently shown no link, notably, one large Cochrane review:
 - Vaccines for measles, mumps, and rubella in children. Demicheli V, Jefferson T, Rivetti A, Price D. Cochrane Database Syst Rev. 2005 Oct 19;(4):CD004407.

SIDS

- SIDS by its very nature occurs around the time of childhood vaccinations, and therefore a subset will occur immediately or shortly after vaccinations, raising concern for a possible causal link
- Very difficult studies to do, but the evidence appears that vaccines are actually mildly protective for SIDS
 - Sudden infant death syndrome: no increased risk after immunisation. Vennemann MM, Butterfass-Bahloul T, Jorch G, et al; GeSID Group. Vaccine. 2007 Jan 4;25(2):336-40.

AIDS

- In 1999, Edward Hooper, a British journalist, published *The River: A Journal to the Source of HIV and AIDS*, speculating that HIV originated with early trials of an oral poliovirus vaccine.
- Baseless, and the hypothesis has been firmly rejected many times.
 - Origin of AIDS: contaminated polio vaccine theory refuted. Worobey M, Santiago ML, Keele BF, et al. *Nature*. 2004 Apr 22;428(6985):820.

Encephalitis

- Hypothesis: 1 in 1000 children with measles will develop encephalitis, so it is plausible that a live vaccine strain could as well
- The evidence:
- One study of 300000 children found no cases of encephalitis in the 30 day window after MMR vaccination
 - Risk of hospitalization because of aseptic meningitis after measles-mumps-rubella vaccination in one- to two-year-old children: an analysis of the Vaccine Safety Datalink (VSD) Project. Black S, Shinefield H, Ray P, et al. *Pediatr Infect Dis J*. 1997 May;16(5):500-3
- No excess encephalitis in a study of 561000 children who had received MMR
 - Neurologic disorders after measles-mumps-rubella vaccination. Makela A, Nuorti JP, Peltola H. *Pediatrics*. 2002 Nov;110(5):957-63.



Mad Cow Disease (vCJD)

- Cattle products have been used to manufacture some vaccines, so there is a theoretical risk of transmission of a prion disease (although no nervous tissue is used)
- FDA statisticians have calculated that the chance of transmission of the agent of BSE is remote, 1 in 2 billion to 1 in 200 billion doses
- There have been no cases of vCJD related to vaccines
 - Creutzfeldt-Jakob disease in the United States: 1979-1998. Gibbons RV, Holman RC, Belay ED, Schonberger LB. JAMA. 2000 Nov 8;284(18):2322-3

Birth Defects

- The hypothesis: several of the agents for which vaccines are available can cause birth defects (rubella, varicella), therefore it is plausible that the live vaccine may also cause birth defects
- The evidence: the risk of a fetus being harmed by a vaccine is only theoretical -- there is no evidence that such vaccinations have ever caused harm
- The recommendations:
 - all susceptible pregnant women should receive immunizations for tetanus and influenza.
 - All live vaccines are contraindicated in pregnancy except in special circumstances based on theoretical risks.

Stroke

- The hypothesis: Chicken pox has been associated rarely with ischemic stroke, so it is plausible that the live vaccine could also have such an association.
- The evidence: A retrospective cohort study using the Vaccine Safety Datalink of more than 3 million children showed no increased risk of stroke after varicella vaccination
 - Varicella vaccination and ischemic stroke in children: is there an association? Donahue JG, Kieke BA, Yih WK, et al; Vaccine Safety DataLink Team. Pediatrics. 2009 Feb;123(2):e228-34

And No...

...Not Autism Either

- Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children. Wakefield AJ, Murch SH, Anthony A, et al. Lancet. 1998 Feb 28;351(9103):637-41.
 - Retraction of an Interpretation. Murch SH, Anthony A, Casson DH, Malik M, Berelowitz M, Dhillon AP, Thomson MA, Valentine A, Davies SE, Walker-Smith JA. Lancet. 2004 Mar 6;363(9411):750
 - “We wish to make it clear that in this paper no causal link was established between MMR vaccine and autism, as the data were insufficient. However, the possibility of such a link was raised and consequent events have had major implications for public health. In view of this, we consider now is the appropriate time that we should together formally retract the interpretation placed upon these findings in the paper, according to precedent.”

Early report

Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children

A J Wakefield, S H Murch, A Anthony, J Linnell, D M Casson, M Malik, M Berelowitz, A P Dhillon, M A Thomson, P Harvey, A Valentine, S E Davies, J A Walker-Smith

Summary

Background We investigated a consecutive series of children with chronic enterocolitis and regressive developmental disorder.

Introduction

We saw several children who, after a period of apparent normality, lost acquired skills, including communication. They all had gastrointestinal symptoms, including abdominal pain, diarrhoea, and bloating and, in some

Wakefield, A.J., et al. Lancet 351: 637-641, 1998.

- ‘Following the judgment of the UK General Medical Council's Fitness to Practise Panel on Jan 28, 2010, it has become clear that several elements of the 1998 paper by Wakefield et al are incorrect, contrary to the findings of an earlier investigation. In particular, the claims in the original paper that children were “consecutively referred” and that investigations were “approved” by the local ethics committee have been proven to be false. **Therefore we fully retract this paper from the published record.**’

Autism, continued

- IOM, 2004: All studies consistently show no association between MMR and autism.
- No evidence of persisting measles virus in peripheral blood mononuclear cells from children with autism spectrum disorder. D'Souza Y, Fombonne E, Ward BJ. Pediatrics. 2006 Oct;118(4):1664-75.
- Absence of detectable measles virus genome sequence in blood of autistic children who have had their MMR vaccination during the routine childhood immunization schedule of UK. Afzal MA, Ozoemena LC, O'Hare A, et al. J Med Virol. 2006 May;78(5):623-30.
- Has the measles-mumps-rubella vaccine been fully exonerated? Katz SL. Pediatrics. 2006 Oct;118(4):1744-5.
- Measles vaccination and antibody response in autism spectrum disorders. Baird G, Pickles A, Simonoff E, et al. Arch Dis Child. 2008 Oct;93(10):832-7.

Autism, continued

- No evidence for MMR-ASD link. Baird G, Brown D, Simonoff E, et al. *Practitioner*. 2008 Mar;252(1704):6.
- MMR vaccination and pervasive developmental disorders: a case-control study. Smeeth L, Cook C, Fombonne E, et al. *Lancet*. 2004 Sep 11-17;364(9438):963-9.
- MMR vaccine and autism: an update of the scientific evidence. DeStefano F, Thompson WW. *Expert Rev Vaccines*. 2004 Feb;3(1):19-22.
- Age at first measles-mumps-rubella vaccination in children with autism and school-matched control subjects: a population-based study in metropolitan atlanta. DeStefano F, Bhasin TK, Thompson WW, et al. *Pediatrics*. 2004 Feb;113(2):259-66.

MMR-Autism: Scientific Studies

- Taylor, B, et al. Lancet 1999;351:2026-29
- Dales L, et al. JAMA 2001;285:1183-85
- Kaye JA, et al. Brit Med J 2001;322:460-
- Madsen KM, et al. N Engl J Med 2002;347:1477-82
- Peltola H, et al. Lancet 1998;351:1327-8.
- Makela A, et al. Pediatrics 2002;110:957-63
- DeStefano R, et al. Pediatrics 2004;113:259-66
- Farrington CP, et al. Vaccine 2001;19:3632-5
- Fombonne E, et al. Pediatrics 2001;108:e58
- Taylor, B, et al. British Med J 2002;324:393-6



**Statement from the American Academy of Pediatrics
regarding the Decisions of the U.S. Court of Federal Claims
in the Omnibus Autism Proceeding
(Posted February 12, 2009)**

The American Academy of Pediatrics (AAP) acknowledges that autism is a serious condition that has profound effects on a child and the child's family. Further research is needed to better understand the cause of autism spectrum disorders and the most effective treatments.

The U.S. Court of Federal Claims on Feb. 12, 2009, found the scientific evidence is "overwhelmingly contrary" to the theory that measles, mumps and rubella (MMR) vaccine and the vaccine preservative thimerosal is linked to autism. This decision is in keeping with the numerous medical studies that have been performed worldwide. The AAP hopes the determination by the Special Masters will reassure parents that vaccines do not cause autism.

[View full reports of the Special Masters](#)

Autism fears stifle measles fight

Somalis in Minneapolis, caught up in a measles outbreak, are afraid despite widespread studies on vaccine safety.

By Steve Karnowski *The Associated Press*

MINNEAPOLIS» Health officials struggling to contain a measles outbreak that's hit hard in Minneapolis' large Somali community are running into resistance from parents who fear the vaccine could give their children autism.

Fourteen confirmed measles cases have been reported in Minnesota since February. Half have been in Somali children, six of whom were not vaccinated and one who was not old enough for shots. State officials have linked all but one of the cases to an unvaccinated Somali infant who returned from a trip to Kenya in February. The state had reported zero or one case of measles a year for most of the past decade.

Amid the outbreak, a now-discredited British researcher who claimed there was a link between vaccines and autism has been meeting with local Somalis. Some worry Andrew Wakefield is stoking vaccination fears, but organizers say the meetings were merely a chance for par-

the truth. He's basically encouraging people to get vaccinated but do your homework and know the risks," said Wayne Rohde, a co-founder of the Vaccine Safety Council of Minnesota, which says parents should have other options for immunizing their children.

Measles has been all but eradicated in the U.S. but accounts for about 200,000 annual deaths worldwide, according to the Centers for Disease Control and Prevention. None of those infected in Minnesota have died, though eight have required hospitalization.

The infections come as autism concerns have surged over an apparent rise in cases in Minnesota's Somali community, the largest in the U.S. Officials, though, haven't determined whether that's really happening. The Minnesota Department of Public Health found in 2009 that young Somali children in Minneapolis public schools were over-represented in autism programs but cautioned that alone didn't prove a higher rate of autism. The CDC and National Institutes of Health are working with the advocacy group Autism Speaks on a more systematic study.

Health officials are working with Somali community leaders to urge more parents to get their children vaccinated, though few people have tak-





The Thimerosal Issue

- In 1999, the FDA determined in a review that it was theoretically possible for an infant to receive, in one day depending on the combination of vaccines given, a dose of *ethylmercury* that would exceed the FDA safe intake level of 0.1 micrograms/kg/day of *methylmercury*.
- Although there was no evidence that thimerosal caused harm, and these are two very different chemicals, the AAP and the U.S. Public Health Service issued a joint statement saying that it would be prudent to take all mercury out of vaccines.

Thimerosal continued

- Many pseudo-scientific hypotheses came after this, the most common being that children with autism metabolize mercury differently and therefore are more prone to its effects.
- The evidence: there is no scientific evidence to support this hypothesis, and many studies refuting it.
- Court panel of special masters: "...the evidence advanced by the petitioners has fallen far short" of showing a link between thimerosal and autism.

Thimerosal continued

- Continuing increases in autism reported to California's developmental services system: mercury in retrograde. Schechter R, Grether JK. Arch Gen Psychiatry. 2008 Jan;65(1):19-24.
- Thimerosal and the occurrence of autism: negative ecological evidence from Danish population-based data. Madsen KM, Lauritsen MB, Pedersen CB, et al. Pediatrics. 2003 Sep;112(3 Pt 1):604-6.
- Association between thimerosal-containing vaccine and autism. Hviid A, Stellfeld M, Wohlfahrt J, Melbye M. JAMA. 2003 Oct 1;290(13):1763-6.

Thimerosal, continued

- Early thimerosal exposure and neuropsychological outcomes at 7 to 10 years. Thompson WW, Price C, Goodson B, et al and the Vaccine Safety Datalink Team. *N Engl J Med.* 2007 Sep 27;357(13):1281-92.
- Safety of thimerosal-containing vaccines: a two-phased study of computerized health maintenance organization databases. Verstraeten T, Davis RL, DeStefano F, et al and the Vaccine Safety Datalink Team. *Pediatrics.* 2003 Nov;112(5):1039-48.
- Thimerosal exposure in infants and developmental disorders: a retrospective cohort study in the United kingdom does not support a causal association. Andrews N, Miller E, Grant A, Stowe J, Osborne V, Taylor B. *Pediatrics.* 2004 Sep;114(3):584-91.





Aluminum Adjuvants

- Al+ used as vaccine adjuvant 70+ years;
 - Remarkable safety record
- 3 compounds; hydroxide, phosphate, alum
 - All have differing physical properties
- Actions: repository of antigen in tissue; facilitate antigen presentation, activate immunostimulatory cytokines
- Facilitate type II response with production of IgGs, not CMI or CTLs

Al+ Adjuvants - 2

- Adverse reactions: sterile abscesses, granulomatous inflammation, contact hypersensitivity
- Vaccines that include Al+ adjuvant:
 - DTP, DTaP, some HIB, Hepatitis A & B, HPV, anthrax, rabies
- No aluminum: IPV, influenza
- Immune enhancement most marked in primary immunization; little benefit in boosters

So what about aluminum?

- Found in numerous foods and beverages, baby formulas, honey
 - Typical adults ingest 7-9 milligrams of aluminum per day
- Aluminum contained in vaccines is similar to that found in a liter of infant formula
 - Infants receive about 4.4 milligrams of aluminum in the 1st six mths of life from vaccines
 - Breastfed infants ingest about 7 milligrams
 - Formula-fed infants ingest about 38 milligrams
 - Soy fed infants ingest about 117 milligrams

Quantities of Aluminum in Vaccines

| | |
|---|--|
| Pneumococcal vaccine | 0.125 mg/dose |
| Diphtheria-tetanus-acellular pertussis (DTaP) vaccine | < 0.17 to < 0.625 mg/dose |
| Haemophilus influenzae type b (Hib) vaccine | 0.225 mg/dose |
| Hib/ Hep B vaccine | 0.225 mg/dose |
| Hepatitis A vaccine (Hep A) | 0.225 to 0.25 mg/dose (pediatrics) 0.45 to 0.5 mg/dose (adults) |
| Hepatitis B vaccine (Hep B) | 0.25 to 0.5 mg/dose |
| Hep A/ Hep B vaccine | 0.45 mg/dose |
| DTaP/inactivated polio/ Hep B vaccine | < 0.85 mg/dose |

Quantities of Aluminum in Other Things

| | |
|-----------------------|----------------------------------|
| Breast milk | 0.04 milligrams per liter (mg/L) |
| Ponds, lakes, streams | 0.1 mg/L |
| Infant formula | 0.225 mg/L |
| Soy-based formula | 0.46 to 0.93 mg/L |
| Buffered aspirin | 10 to 20 mg/tablet |
| Antacid | 104-208 mg/tablet |

Do Multiple Vaccines Overwhelm or Weaken the Infant's Immune System?

- One hundred years ago children received one vaccine- smallpox
- Forty years ago children received 5 vaccines- diphtheria, pertussis, tetanus, polio, smallpox
- Today- children receive 11 vaccines routinely and as many as 20 shots by 2 yrs of age
- Parents are concerned about the number of shots kids get

Do Multiple Vaccines Overwhelm or Weaken the Infant's Immune System?

- Infant has theoretical capacity to respond to about 10,000 vaccines at any one time!
 - $(10^7 \text{ B cells per mL by } 10^3 \text{ epitopes per vaccine})$
- Most vaccines contain fewer than 100 antigens, therefore if 11 vaccines given at one time then 0.1% of the immune system would be “used up”

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Children are Exposed to Fewer Antigens Than in the Past

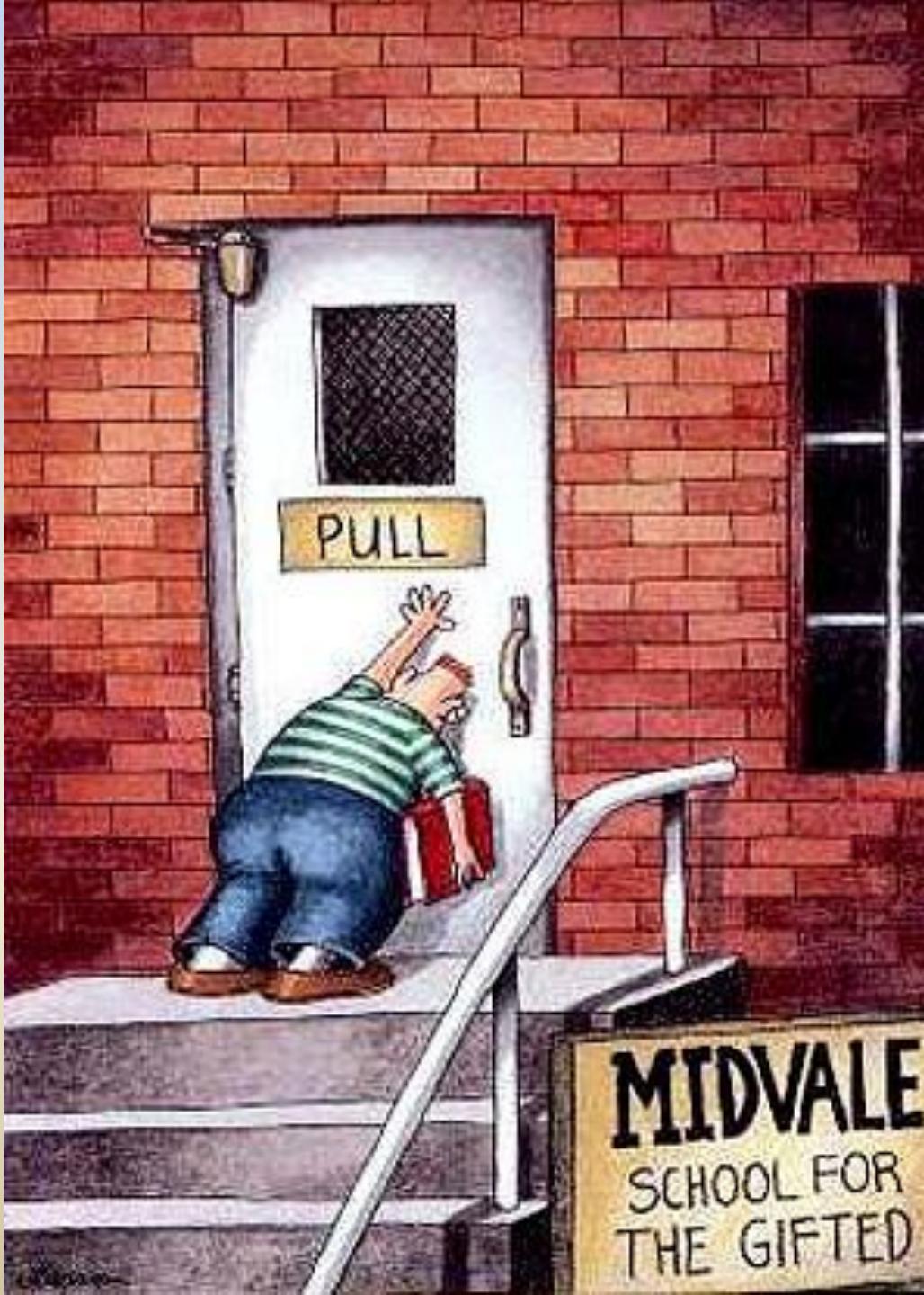
TABLE 2. Number of Immunogenic Proteins and Polysaccharides Contained in Vaccines Over the Past 100 Years

| 1900 | | 1960 | | 1980 | | 2000 | |
|-------------------|-------------|-----------------|--------------|-------------------|--------------|-----------------------|--------------------------|
| Vaccine | Proteins | Vaccine | Proteins | Vaccine | Proteins | Vaccine | Proteins/Polysaccharides |
| <u>Smallpox</u> * | ~200 | Smallpox | ~200 | Diphtheria | 1 | Diphtheria | 1 |
| Total | ~200 | Diphtheria† | 1 | Tetanus | 1 | Tetanus | 1 |
| | | Tetanus‡ | 1 | WC-Pertussis | ~3000 | AC-Pertussis§§ | 2-5 |
| | | WC-Pertussis§ | ~3000 | Polio | 15 | Polio | 15 |
| | | <u>Polio</u> ¶¶ | 15 | Measles¶ | 10 | Measles | 10 |
| | | Total | ~3217 | Mumps# | 9 | Mumps | 9 |
| | | | | <u>Rubella</u> ** | 5 | Rubella | 5 |
| | | | | Total | ~3041 | Hib†† | 2 |
| | | | | | | Varicella# | 69 |
| | | | | | | Pneumococcus§§ | 8 |
| | | | | | | <u>Hepatitis B</u> ¶¶ | 1 |
| | | | | | | Verbar; | |
| | | | | | | Total | 123-126 |

The Problem with Dr. Bob's Alternative Vaccine Schedule

The Message

- Doctors do not understand vaccines
- Public Health agencies and Pharmaceutical companies are not trustworthy
- Vaccine mandates should be eliminated
- Vaccine-preventable diseases are not that bad
- Hide in the herd
- Natural infection is better than vaccination
- Vaccination has eliminated infectious diseases at the price of causing chronic diseases
- Vaccine safety testing is insufficient
- Public health officials make recommendations for the public not for individuals



MIDVALE
SCHOOL FOR
THE GIFTED

What Vaccines *Do* Cause

Lots of local and minor reactions

- Redness, arm/leg swelling at injection site
 - Can be entire limb
 - ~2% of 4th and 5th dose of DTaP
 - Generally self-limited reaction
 - Case reports of bacterial infections
 - Rennels MB, Deloria MA, Pichichero ME, et al. Extensive swelling after booster doses of acellular pertussis-tetanus-diphtheria vaccines. *Pediatrics*. 2000;105:e12.

Fever and Rash with MMR and Varicella Vaccine

- Temp of 103°F or higher in ~ 5% to 15% of MMR recipients
 - 6 to 12 days after vaccine
 - Fever generally lasts 1 to 2 days but may last as long as 5 days
 - Transient rashes in ~ 5% with similar time course
- For varicella vaccine, varicella like rash at site of injection in 3-5%, generalized mild varicella like rash in 3-5% (5-26 days after vaccination)

Anaphylaxis

- Risk is very low
- An analysis of 4 large HMOs found 5 potential cases of anaphylaxis after more than 7 million doses of vaccine (0.65 cases per million doses)
 - Risk of anaphylaxis after vaccination of children and adolescents. Bohlke K, Davis RL, Marcy SM, et al and the Vaccine Safety Datalink Team. Pediatrics. 2003 Oct;112(4):815-20.
- Vaccine components potentially implicated: gelatin, egg protein, neomycin, baker's yeast, the infectious agent.
- Children with a history of severe egg allergy can be immunized with MMR AND influenza vaccine
- Eligible for compensation under Vaccine Injury Compensation Program

Hypotonic, Hyporesponsive episodes

- See above discussion

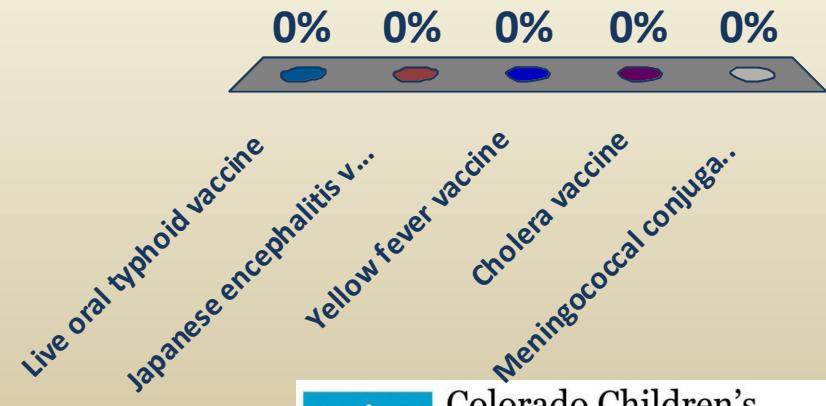


Protracted, Inconsolable Crying

- Thought to be 1 in 100 doses with old whole cell DTP vaccine
- Much less with DTaP
- Has been associated with other vaccines
- No long term sequelae

Which of the following travel vaccines is associated with the rare adverse event of ‘viscerotropic disease’?

- A. Live oral typhoid vaccine
- B. Japanese encephalitis vaccine
- ★ C. Yellow fever vaccine
- D. Cholera vaccine
- E. Meningococcal conjugate vaccine



Yellow Fever Vaccine

- Live attenuated vaccine developed in 1936
- Very effective (100% protective after 4 weeks)
- Indicated for travel to endemic areas as well as certain countries that require “International Certificate of Vaccination”
- Neurotropic disease
 - Encephalitis, usually self-limited
- Viscerotropic disease
 - Resembles wild type yellow fever
 - Case fatality rate 63%
 - ~1 in 250,000 doses
- Risks higher in elderly
- Careful assessment of whom to vaccinate

Death

- From measles, varicella, or polio vaccine strain given to immune compromised patients (extremely rare)
 - Contraindicated in significantly immune compromised
 - Update: vaccine side effects, adverse reactions, contraindications, and precautions. Recommendations of the Advisory Committee on Immunization Practices (ACIP) MMWR Recomm Rep. 1996 Sep 6;45(RR-12):1-35.

Poliomyelitis

- Oral poliovirus vaccine
- 1 case of vaccine associated paralytic poliomyelitis (VAPP) per 2.4 million doses
- Between 250 and 500 cases per year worldwide
- Eligible for compensation under National Childhood Vaccine Injury Act

Febrile Seizures

- Risk is 4 in 10000 doses for MMR and Varivax given together for 12-23 month old infants
 - 9 in 10000 when given as MMRV
 - 1 extra febrile seizure for every 2500 doses
- Slightly elevated risk when flu vaccine given concomitantly with pneumococcal conjugate vaccine in infants
- ACIP recommendation
 - After discussing pros and cons with parents, may give either MMR+V or MMRV at 12-15 months
 - Preference for MMRV at age 5
 - Stocking issues
- Studies regarding flu vaccine and febrile seizures ongoing

Immune Thrombocytopenic Purpura

- MMR, attributable risk is 1 in 40000 doses.
 - Risk of immune thrombocytopenic purpura after measles-mumps-rubella immunization in children. France EK, Glanz J, Xu S, et al and the Vaccine Safety Datalink Team. *Pediatrics*. 2008 Mar;121(3):e687-92.
- No known long term sequelae
- No known severe outcomes
- Chronic?
- Other vaccines? (Tdap, Var, Hep A)
- Eligible for compensation under Vaccine Injury Compensation Program

Intussusception

- RotaShield
- 1 case per 10000 to 12000 infants immunized attributable to vaccine
- Infants were 30-37 times more likely to have intussusception in the 3-7 days following the first dose than unimmunized infants
 - Intussusception among infants given an oral rotavirus vaccine. Murphy TV, Gargiullo PM, Massoudi MS, et al and the Rotavirus Intussusception Investigation Team. *N Engl J Med.* 2001 Feb 22;344(8):564-72.
 - Population-based study of rotavirus vaccination and intussusception. Kramarz P, France EK, Destefano F, et al. *Pediatr Infect Dis J.* 2001 Apr;20(4):410-6.

Intussusception, continued

- Very small increased risk of intussusception with RV1 (5.1 per 100K doses and 1 per 100K doses for RV5) but benefits far outweigh risks
 - Weintraub et al. Risk of intussusception after monovalent rotavirus vaccination N Engl J Med, 370 (2014), pp. 513–519
 - Yih et al. Intussusception risk after rotavirus vaccination in U.S. infants. N Engl J Med. 2014 Feb 6;370(6):503-12.
- Eligible for compensation under Vaccine Injury Compensation Program

Joint aches, arthralgias

- Rubella vaccine
- Occasional joint aches in children
- Rarely, an acute temporary arthritis in adults
 - Adverse events following pertussis and rubella vaccines. Summary of a report of the Institute of Medicine. Howson CP, Fineberg HV. JAMA. 1992 Jan 15;267(3):392-6.
- No risk of chronic arthropathy is apparent
 - Risk of chronic arthropathy among women after rubella vaccination. Vaccine Safety Datalink Team. Ray P, Black S, Shinefield H, et al. JAMA. 1997 Aug 20;278(7):551-6.
- However, chronic arthritis is eligible for compensation under Vaccine Injury Compensation Program







Bell's Palsy

- After an inactivated nasal vaccine given in Switzerland (that is no longer in production)
- Relative risk was quite high (19)
 - Use of the inactivated intranasal influenza vaccine and the risk of Bell's palsy in Switzerland. Mutsch M, Zhou W, Rhodes P, et al. N Engl J Med. 2004 Feb 26;350(9):896-903.
- IOM, 2011, about currently used inactivated influenza vaccines: The evidence favors rejection of a causal relationship between inactivated influenza vaccine and Bell's palsy.

What Vaccines *Might* Cause

SV40 and cancer

- ~100 million Americans may have been exposed to simian virus 40 (SV40) that contaminated the inactivated polio vaccine when it was first introduced
- SV40 is oncogenic in mice, although it is unknown if it is oncogenic in humans
- IOM, 2002: data were “sufficiently flawed” that they could not draw any conclusions
- Several studies since then have suggested that it’s unlikely that there is a link between the SV40 in the old vaccine and cases of cancer, but there are unresolved questions
- No currently licensed vaccines contain SV40

Guillain-Barre Syndrome

- “Swine flu” immunization campaign in 1976-77
- At the time, association was thought to be cause-and-effect
- GBS at a rate of 1 case per 100000 doses over the background rate of 0.87 per million
- Unclear if there is an association with other influenza vaccines
- Most evidence points away from a causal relationship
- Possibly a rate of 1 case per million doses

Guillain-Barre Syndrome

- One case of a man getting GBS after each of three doses of tetanus toxoid
 - Relapsing neuropathy due to tetanus toxoid. Report of a case. Pollard JD, Selby G. J Neurol Sci. 1978 Jun;37(1-2):113-25.
- IOM at the time concluded based on this case that the evidence favored acceptance of a causal relationship between tetanus toxoid containing vaccines and GBS
- Subsequent studies have found no such association
 - The risk of Guillain-Barre syndrome after tetanus-toxoid-containing vaccines in adults and children in the United States. Tuttle J, Chen RT, Rantala H, Cherry JD, Rhodes PH, Hadler S. Am J Public Health. 1997 Dec;87(12):2045-8.

Guillain-Barre Syndrome

- Although there was concern raised with meningococcal conjugate vaccine (Menactra®), the risk does not appear to be elevated

Encephalopathy

- A little history...
- April 19, 1982: the anti-vaccine movement in America is born
- Lea Thompson and “DPT: Vaccine Roulette”
- Hour long documentary aired by Washington, DC, NBC affiliate
- Heartbreaking interviews with parents with parents of children with permanent brain damage following DTP vaccine

Encephalopathy

- Barbara Loe Fisher, Kathi Williams, and Jeff Schwartz form Dissatisfied Parents Together (DPT), later the NVIC
- More media coverage
- Flood of lawsuits claiming DPT caused SIDS, Reye Syndrome, MR, epilepsy, transverse myelitis

Encephalopathy

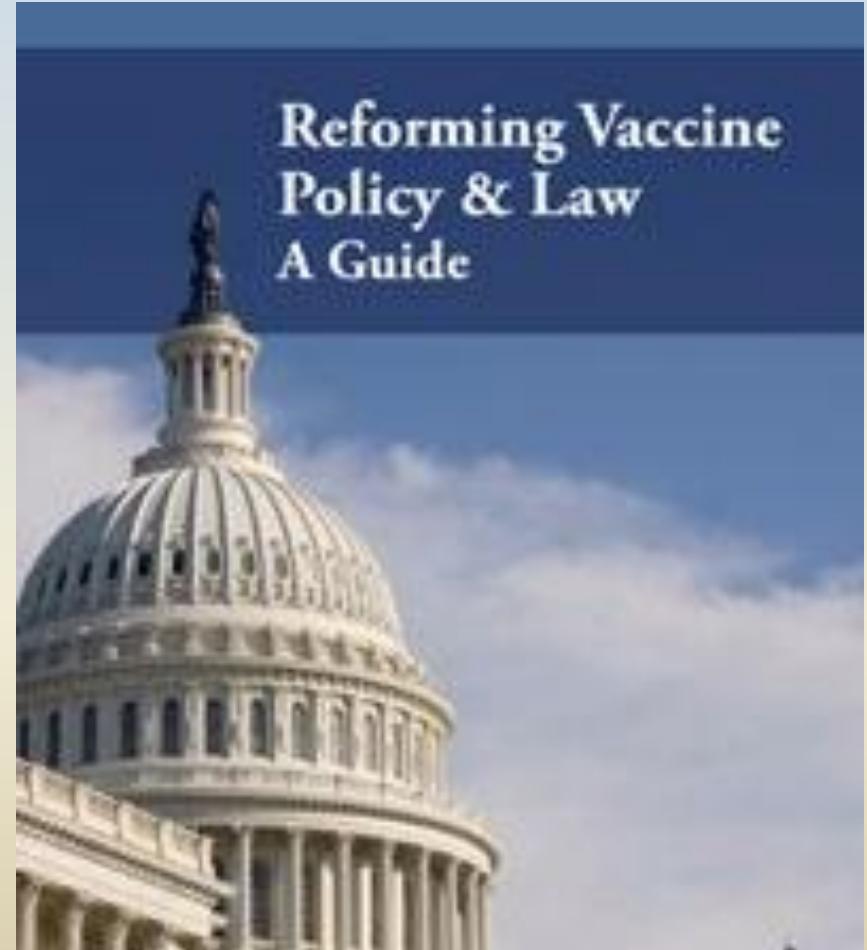
- Price of DTP rose from \$0.19 in 1980 to \$12 in 1986
- Number of polio vaccine makers declined from 3 to 1, of measles vaccine from 6 to 1, and of pertussis vaccine from 8 to 1
- Led to the National Childhood Vaccine Injury Act and the Vaccine Injury Compensation Program
- The less effective DTaP vaccine was created based on all of this too, which is likely playing a role in the current pertussis epidemic

“National Vaccine Information Center”

- Operates on the premise that vaccines have replaced infectious diseases with chronic diseases
- Media savvy, politically connected, and well financed

“National Vaccine Information Center”

- Anti-vaccine group is currently distributing this to state legislators
- Slickly produced, with a mix of real literature used out-of-context, poorly done studies from bogus journals or opinion pieces, making it seem like it's thoroughly researched because it's got 200+ references listed



Let's back up a second...

Did the DTP vaccine really cause encephalopathy in the first place?

- The hypothesis: encephalopathy is a well known complication of wild type pertussis
- IOM, 1994: concluded that there likely *was* a link between the whole cell pertussis vaccine and encephalopathy developing within 7 days

Encephalopathy, continued

- Many studies since that time have failed to establish a causal link
 - Encephalopathy after whole-cell pertussis or measles vaccination: lack of evidence for a causal association in a retrospective case-control study. Ray P, Hayward J, Michelson D, et al and the Vaccine Safety Datalink Group. *Pediatr Infect Dis J.* 2006 Sep;25(9):768-73.
 - Safety and efficacy of acellular pertussis vaccine in Japan, evaluated by 23 years of its use for routine immunization. Kuno-Sakai H, Kimura M. *Pediatr Int.* 2004 Dec;46(6):650-5.
 - Lack of evidence of encephalopathy related to pertussis vaccine: active surveillance by IMPACT, Canada, 1993-2002. Moore DL, Le Saux N, Scheifele D, Halperin SA; Members of the Canadian Paediatric Society/Health Canada Immunization Monitoring Program Active (IMPACT). *Pediatr Infect Dis J.* 2004 Jun;23(6):568-71.

Landmark paper from 2006



De-novo mutations of the sodium channel gene SCN1A in alleged vaccine encephalopathy: a retrospective study

Samuel F Berkovic, Louise Harkin, Jacinta M McMahon, James T Pelekanos, Sameer M Zuberi, Elaine C Wirrell, Deepak S Gill, Xenia Iona, John C Mulley, Ingrid E Scheffer

Summary

Lancet Neurol 2006; 5: 488-92

Published Online
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70446-X

See *Reflection and Reaction*
page 465

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Background Vaccination, particularly for pertussis, has been implicated as a direct cause of an encephalopathy with refractory seizures and intellectual impairment. We postulated that cases of so-called vaccine encephalopathy could have mutations in the neuronal sodium channel $\alpha 1$ subunit gene (*SCN1A*) because of a clinical resemblance to severe myoclonic epilepsy of infancy (SMEI) for which such mutations have been identified.

Methods We retrospectively studied 14 patients with alleged vaccine encephalopathy in whom the first seizure occurred within 72 h of vaccination. We reviewed the relation to vaccination from source records and assessed the specific epilepsy phenotype. Mutations in *SCN1A* were identified by PCR amplification and denaturing high performance liquid chromatography analysis, with subsequent sequencing. Parental DNA was examined to ascertain the origin of the mutation.

Findings *SCN1A* mutations were identified in 11 of 14 patients with alleged vaccine encephalopathy; a diagnosis of a specific epilepsy syndrome was made in all 14 cases. Five mutations predicted truncation of the protein and six were missense in conserved regions of the molecule. In all nine cases where parental DNA was available the mutations arose de novo. Clinical-molecular correlation showed mutations in eight of eight cases with phenotypes of SMEI, in three of four cases with borderline SMEI, but not in two cases with Lennox-Gastaut syndrome.

Interpretation Cases of alleged vaccine encephalopathy could in fact be a genetically determined epileptic encephalopathy that arose de novo. These findings have important clinical implications for diagnosis and management of encephalopathy and, if confirmed in other cohorts, major societal implications for the general acceptance of vaccination.

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Berkovic et al, 2006

- 11 of 14 patients with alleged vaccine encephalopathy had a specific de novo mutation that explained their encephalopathy
- Subsequent studies have had similar findings

What is the name of the condition that most children with alleged DTP encephalopathy likely had?

- Drager Syndrome
- Lesch-Nyhan Syndrome
- Dravet Syndrome
- Leigh Syndrome
- Wernicke's
Encephalopathy

Encephalopathy: Summary

- In other words, the foundation for current anti-vaccination movement in the US is predicated on a mistaken assumption – DTP likely never caused these children's encephalopathy in the first place
- (I have it in the 'maybe' category only because the National Vaccine Injury Compensation Program still considers this eligible for compensation)

Brachial neuritis

- Acute pain and weakness with variable atrophy and sensory loss around the shoulder girdle
- Associated with tetanus toxoid containing vaccines
- IOM concluded the evidence favors a causal relationship
 - Based on case-series reports
 - Brachial neuritis following routine childhood immunization for diphtheria, tetanus, and pertussis (DTP): report of two cases and review of the literature. Hamati-Haddad A, Fenichel GM. Pediatrics. 1997 Apr;99(4):602-3

Brachial Neuritis

- True risk is unknown but thought to be very low
- Eligible for compensation under Vaccine Injury Compensation Program

Alopecia

- Remarkable case of a child who had complete loss of hair after each dose of hepatitis B vaccine (2 times)
 - San Francisco Chronicle, 1994
 - Hair loss after routine immunizations. Wise RP, Kiminno KP, Salive ME. JAMA. 1997 Oct 8;278(14):1176-8.
- Unclear if there truly is a causal relationship

Syncope

- Is it the vaccine or the injection?
- Known to occur in blood donors
 - Graham DT. Prediction of fainting in blood donors. *Circulation*. 1961; 23:901-906.
- Recommendations from ACIP
 - Observe adolescents for 15 minutes after vaccination sitting or lying down
 - Most providers are not following this
- References for syncope after vaccination
 - Braun MM, Patriarca PA, Ellenberg SS. Syncope after immunization. *Arch Pediatr Adolesc Med*. 1997;151(3):255–259, Woo EJ, Ball R, Braun MM.
 - Fatal syncope-related fall after immunization. *Arch Pediatr Adolesc Med*. 2005;159(11):1083.
 - Centers for Disease Control and Prevention (CDC). Syncope after vaccination: United States, January 2005–July 2007. *MMWR Morb Mortal Wkly Rep*. 2008;57(17):457–460.

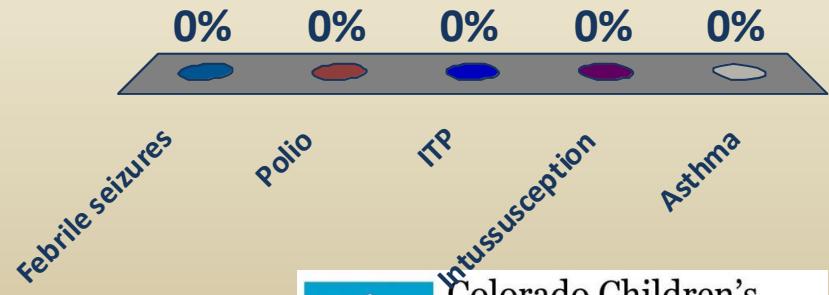


Narcolepsy

- Adjuvanted influenza vaccine (Pandemrix) used in much of Europe
- From Finland: “The risk of falling ill with narcolepsy among those vaccinated in the 4-19 years age group was nine-fold in comparison with those unvaccinated in the same age group.”
- 1 case of narcolepsy per 12000 vaccinated
 - Zarocostas J. WHO backs further probes into possible link between H1N1 vaccine and narcolepsy in children. *BMJ*. 2011 Feb 9;342:d909. doi: 10.1136/bmj.d909.
 - Dauvilliers Y, Montplaisir J, Cochen V, et al Post-H1N1 narcolepsy-cataplexy. *Sleep*. 2010 Nov 1;33(11):1428-30.
- Mechanism not understood, but thought that it may be autoimmune
- No increase in cases in U.S.

Vaccines have been conclusively linked with all of the following except:

- A. Febrile seizures
- B. Polio
- C. ITP
- D. Intussusception
- ★ E. Asthma



Conclusions

- Vaccines are incredibly safe
- There are true significant adverse events we need to be aware of, but they are rare
- Risk of severe adverse events, because of their rarity, is difficult to quantify, but based on the best available evidence, are on the order of 1 in millions
- Benefits of vaccines far outweigh their risks

Do Vaccines Cause That?!

A GUIDE FOR EVALUATING
VACCINE SAFETY CONCERN



Martin G. Myers, M.D. and Diego Pineda

Good Links

- www.nnii.org
- www.cispimmunize.org
- www.cdc.gov/vaccinesafety
- www.vaccinesafety.edu
- www.immunize.org
- www.vaccineinformation.org
- www.vaccine.chop.edu
- www.iom.edu/imsafety

Immunization Info

NATIONAL NETWORK FOR IMMUNIZATION INFORMATION



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Bad Links (that look like Good Links!)

- www.vaccines.net
- www.nvic.org (National Vaccine Information Center)
- www.vaccinationnews.com



Slowly he would cruise the neighborhood, waiting for that occasional careless child who confused him with another vendor.