Common Immunization Myths and Misconceptions:

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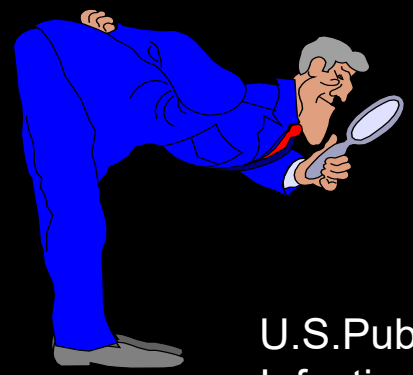
Chief Intelligence and Innovation Officer, Protein Sciences



Disclosures:

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U.S. Army Medical Research and Development Command (Contract DAMD 17-89-C2050): Grant funding

Pasteur-Adventis. Division of Research and Development, Influenza Vaccine Development: Grant funding; Consultant

Biomedical Advanced Research & Development Agency (B16578) Grant funding

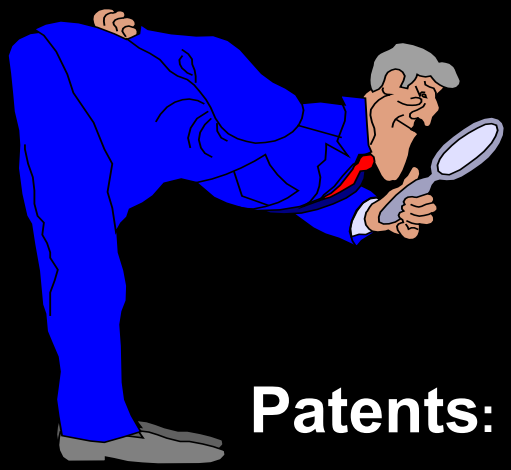
Protein Sciences Corporation, Division of Vaccine Development; Scientific Advisory Board, Patents, Director of Pandemic Influenza

Epivax, Incorporated, Consultant, Scientific Advisory Board, Patents

Chiron Vaccines, Influenza Vaccine Development; Consultant, Grant Funding

PATH: A Catalyst for Golbal Heatth; Sections of Emerging Disease and Influenza Consultant, Grant Funding

XenoPort Pharmaceuticals, my wife works as a pharmaceutical representative



Disclosures:

Patents:

1998: United States Patent: 1998/046262 *Anti-influenza compositions*

2002: United *minidase-supplemente*

2003: United *Recombinan* *emented Influenza Vaccines*

2005: United States Patent: 6,951,649:
Methods of making neuraminidase-supplemented compositions

Background

Parents, patients, and healthcare professionals all have misconceptions about vaccination

- More parents and patients are questioning the safety and effectiveness of vaccines. Your responses to them require knowledge, tact, and time.

- Healthcare providers can miss opportunities to vaccinate by believing false contraindications and following unnecessary rules.

Objectives

This presentation will provide:

- Information that addresses common concerns or misconceptions about vaccination.
- Concerns and misconceptions of patients, parents, and healthcare professionals will be reviewed.
- Links to related evidence-based resources —some are intended as background information for healthcare professionals and others for patients/parents.

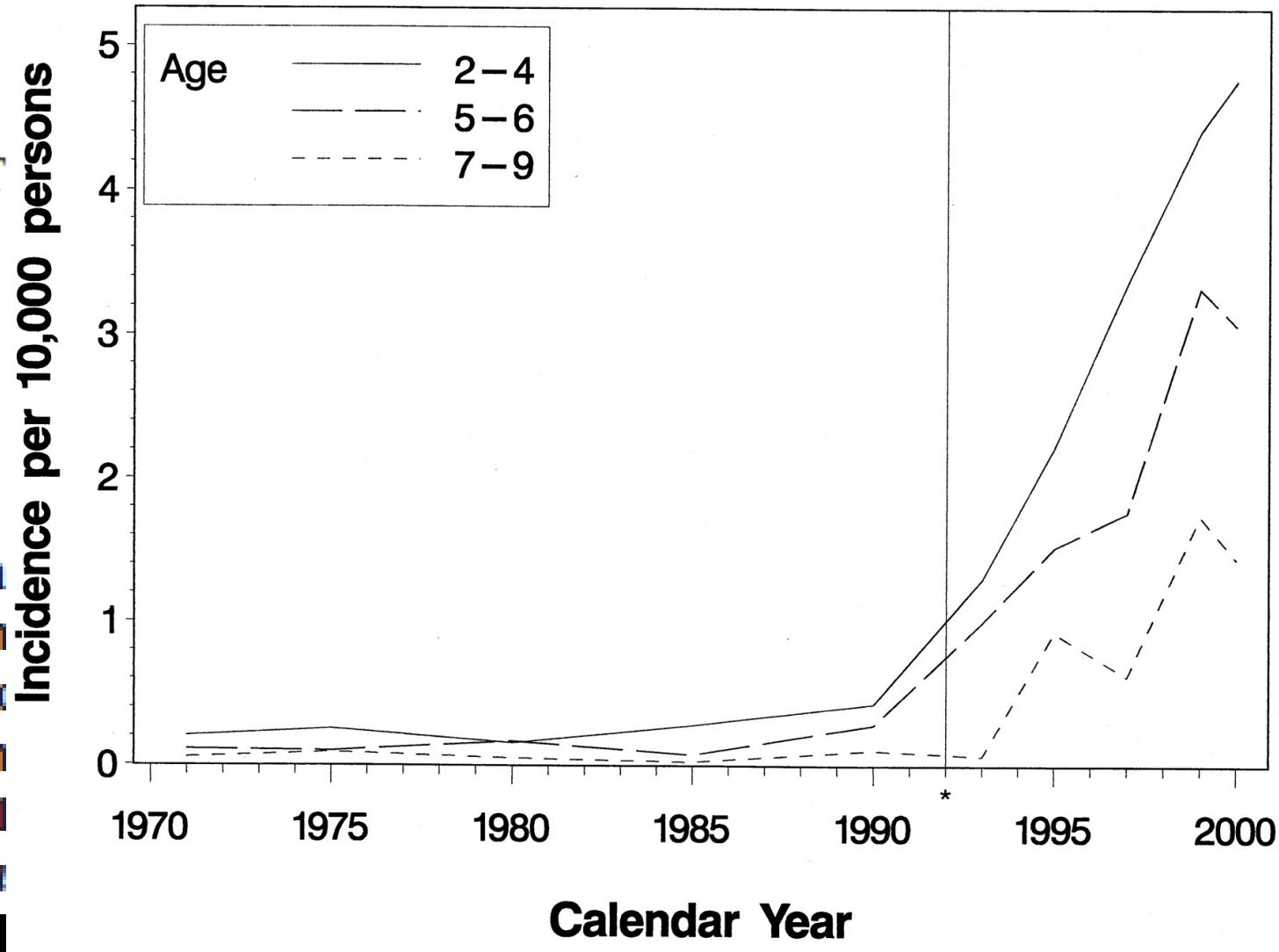
Patient Myths

MYTH: Thimerosal Causes Autism

• The form of mercury found in thimerosal is ethylmercury (EM), not methylmercury (MM). MM is the form that has been shown to damage the nervous system. There is more Mercury in can of tuna than in all infant vaccines combined.

• Despite no evidence of harm, thimerosal was taken out of vaccines as a precaution and “because it can be” (due to single-dose vials)

• Since 2001, with the exception of a influenza vaccine product**, thimerosal has not been used as a preservative** in any routinely recommended childhood vaccines.



PEDIATRICS Vol. 112 No. 3 September 2003

References

- CDC's Vaccine Safety Concerns web page www.cdc.gov/vaccinesafety/concerns

- IAC's collection of thimerosal-related resources www.immunize.org/thimerosal

- NNii's Mercury in Vaccines web page www.immunizationinfo.org/issues/thimerosalmercury

- Institute of Medicine reports on thimerosal www.nap.edu/books/030909237X/html and http://books.nap.edu/catalog/10208.html

MYTH: Ingredients in Vaccines Are Harmful

Aluminum

- Aluminum was used in some vaccines as an adjuvant—an ingredient that improves the immune response. They have been used for this purpose for more than 70 years.

- Aluminum is the most common metal found in nature. It is in the air and in food and drink. Infants get more aluminum through breast milk or formula than vaccines.

- Most of the aluminum taken into the body is quickly eliminated.

MYTH: Ingredients in Vaccines Are Harmful – cont'd

Formaldehyde

- Formaldehyde is used to detoxify diphtheria and tetanus toxins or to inactivate a virus.

- The tiny amount (35-100 μg) is left over from these steps.

- Formaldehyde is also found in products like paper towels, mascara, and carpeting.

- Humans normally have formaldehyde in their blood streams as result of normal metabolism, at levels higher than is found in vaccines (135-180 μg/L).

MYTH
Are H
s

Miscel

• Antibio
bacteria
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• Additiv
lactose,
effective
ucrose,
tay

Vaccine Excipient & Media Summary

Excipients Included in U.S. Vaccines, by Vaccine

This table includes not only vaccine ingredients (e.g., adjuvants and preservatives), but also substances used during the manufacturing process, including vaccine-production media, that are removed from the final product and present only in trace quantities. In addition to the substances listed, most vaccines contain Sodium Chloride (table salt).

Last Updated February 2015

All reasonable efforts have been made to ensure the accuracy of this information, but manufacturers may change product contents before that information is reflected here. If in doubt, check the manufacturer's package insert.

Vaccine	Contains	Source: Manufacturer's P.I. Dated
Adenovirus	sucrose, D-mannose, D-fructose, dextrose, potassium phosphate, plasdone C, anhydrous lactose, micro crystalline cellulose, polacrilin potassium, magnesium stearate, cellulose acetate phthalate, alcohol, acetone, castor oil, FD&C Yellow #6 aluminum lake dye, human serum albumin, fetal bovine serum, sodium bicarbonate, human-diploid fibroblast cell cultures (WI-38), Dulbecco's Modified Eagle's Medium, monosodium glutamate	March 2011
Anthrax (Biothrax)	aluminum hydroxide, benzethonium chloride, formaldehyde, amino acids, vitamins, inorganic salts and sugars	May 2012
BCG (Tice)	glycerin, asparagine, citric acid, potassium phosphate, magnesium sulfate, Iron ammonium citrate, lactose	February 2009
DT (Sanofi)	aluminum potassium sulfate, peptone, bovine extract, formaldehyde, thimerosal (trace), modified Mueller and Miller medium, ammonium sulfate	December 2005
DTaP (Daptacel)	aluminum phosphate, formaldehyde, glutaraldehyde, 2-Phenoxyethanol, Stainer-Scholte medium, modified Mueller's growth medium, modified Mueller-Miller casamino acid medium (without beef heart infusion), dimethyl 1-beta-cyclodextrin, ammonium sulfate	October 2013
DTaP (Infanrix)	formaldehyde, glutaraldehyde, aluminum hydroxide, polysorbate 80, Fenton medium (containing bovine extract), modified Latham medium (derived from bovine casein), modified Stainer-Scholte liquid medium	November 2013
DTaP-IPV (Kinrix)	formaldehyde, glutaraldehyde, aluminum hydroxide, Vero (monkey kidney) cells, calf serum, lactalbumin hydrolysate, polysorbate 80, neomycin sulfate, polymyxin B, Fenton medium (containing bovine extract), modified Latham medium (derived from bovine casein), modified Stainer-Scholte liquid medium	November 2013
DTaP-HepB-IPV (Pediarix)	formaldehyde, gluteraldehyde, aluminum hydroxide, aluminum phosphate, lactalbumin hydrolysate, polysorbate 80, neomycin sulfate, polymyxin B, yeast protein, calf serum, Fenton medium (containing bovine extract), modified Latham medium (derived from bovine casein), modified Stainer-Scholte liquid medium, Vero (monkey kidney) cells	November 2013
DTaP-IPV/Hib (Pentacel)	aluminum phosphate, polysorbate 80, formaldehyde, sucrose, gutaraldehyde, bovine serum albumin, 2-phenoxethanol, neomycin, polymyxin B sulfate, Mueller's Growth Medium, Mueller-Miller casamino acid medium (without beef heart infusion), Stainer-Scholte medium (modified by the addition of casamino acids and dimethyl-beta-cyclodextrin), MRC-5 (human diploid) cells, CMRL 1969 medium (supplemented with calf serum), ammonium sulfate, and medium 199	October 2013
Hib (ActHIB)	ammonium sulfate, formalin, sucrose, Modified Mueller and Miller medium	January 2014
Hib (Hiberix)	formaldehyde, lactose, semi-synthetic medium	March 2012
Hib (PedvaxHIB)	aluminum hydroxphosphate sulfate, ethanol, enzymes, phenol, detergent, complex fermentation medium	December 2010

B

References

- VEC's "Aluminum in Vaccines: What you should know" www.chop.edu/export/download/pdfs/articles/vaccineeducation-center/aluminum.pdf

- IAC's "Adjuvants and Ingredients" web section www.immunize.org/concerns/adjuvants.asp

- NNii's "Aluminum Adjuvants in Vaccines" www.immunizationinfo.org/issues/vaccinecomponents/aluminum-adjuvants-vaccines

- AAP's "Questions and Answers about Vaccine Ingredients" www2.aap.org/immunization/families/faq/vaccineingredien

  - ts.pdf

References cont'd

CDC's "Vaccine Excipient & Media Summary, by Excipient"
www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/B/excipient-table-1.pdf

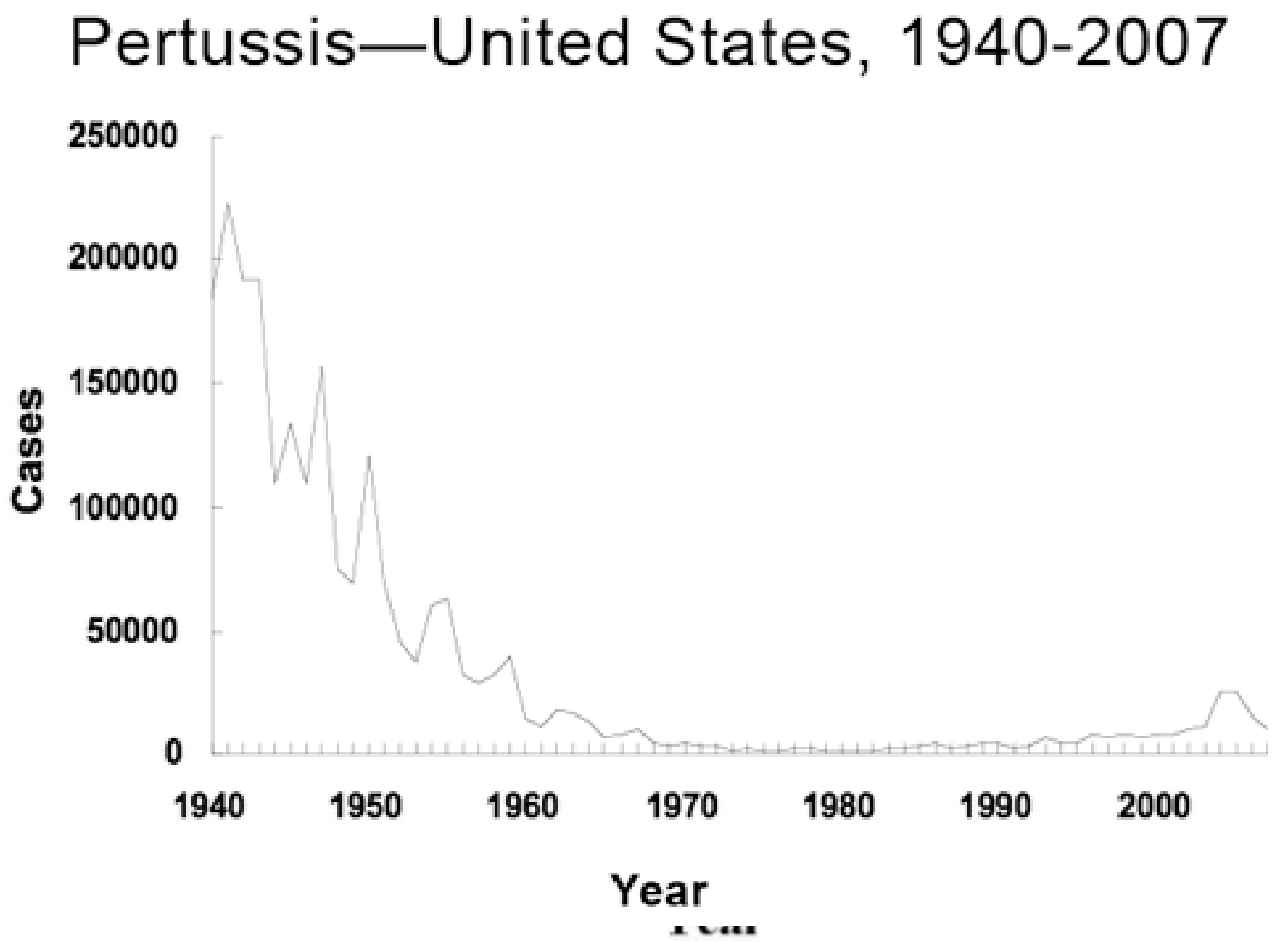
CDC's "Vaccine Excipient & Media Summary, by Vaccine"
www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/B/excipient-table-2.pdf

IAC's Package Inserts web section
www.immunize.org/packageinserts

MYTH: Disease Rates Have Dro r

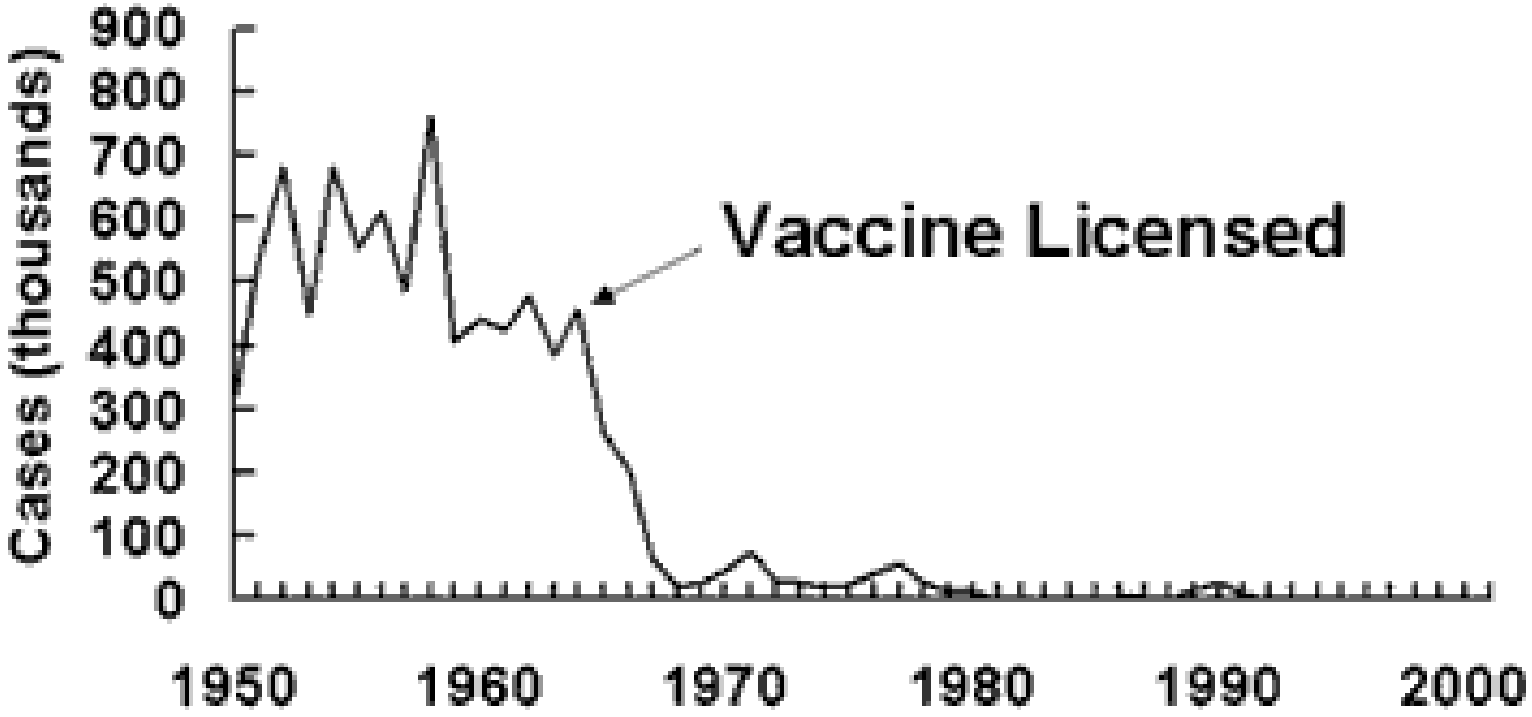
FIGURE 3

Pertussis annual incidence rates in infants aged <1 year by

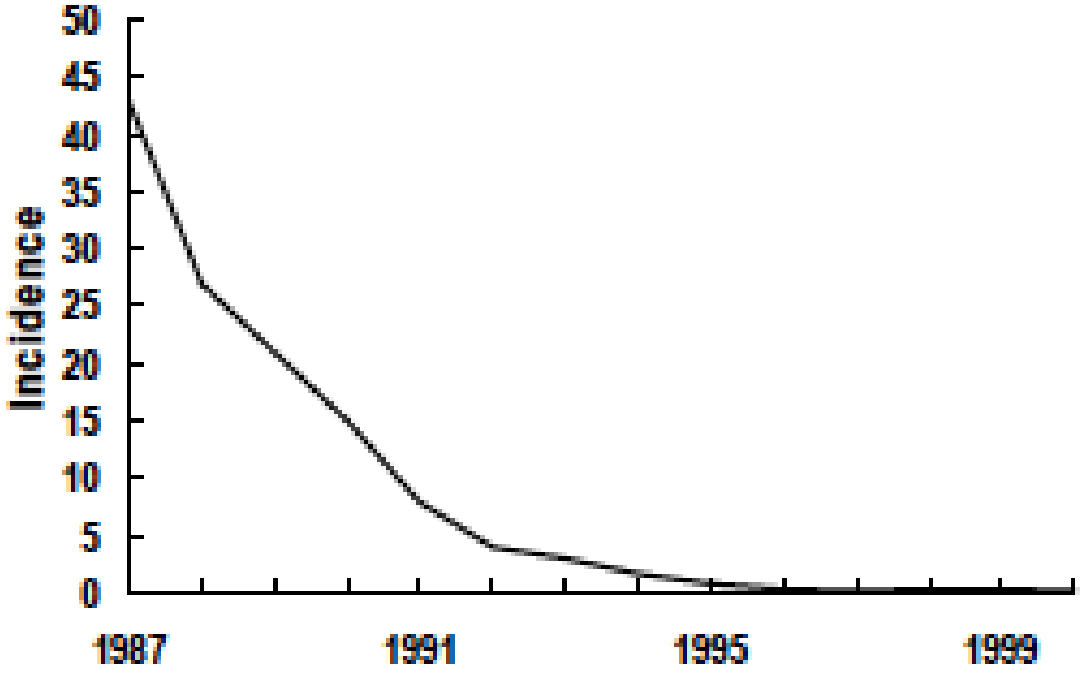


Source: National Epidemiological Surveillance Network.

Measles–United States, 1950-2001



Estimated Incidence* of Invasive Hib Disease, 1987-2000



*Rate per 100,000 children <5 years of age

References

- CDC's "Some Common Misconceptions About Vaccination and How to Respond to Them" www.cdc.gov/vaccines/vac-gen/6mishome.htm
- CDC's "What Would Happen If We Stopped Vaccinations?" www.cdc.gov/vaccines/vacgen/whatifstop.htm
- IAC's "Personal belief exemptions for vaccination put people at risk. Examine the evidence for yourself www.immunize.org/catg.d/p2069.pdf
- NNii's "Vaccine Effectiveness" www.immunizationinfo.org/parents/why-immunize

MYTH: Vaccines Are Not Effective

- Anti-vaccine websites often set up a straw man argument—claiming that experts say that vaccines are 100% effective, and then showing this is not true. No one claims that vaccines are 100% effective, no drug or medical procedure always works.

- Most childhood vaccines are effective when properly administered and all doses are received according to the recommended schedule. (>80%, depending on vaccine)

MYTH: PPSV Vaccine Is Not Effective

An ~ 40,000 cases of invasive pneumococcal disease occuered annually. Case-fatality rates are high, in meningitis (~30%) or bacteremia (~20%).

PPSV is not a general “pneumonia vaccine” as people often think; i.e., it does ***not*** provide protection against all types of pneumonia (viral and bacterial). PPSV is 60–70% effective in preventing serious invasive pneumococcal disease.

References – PPSV

IAC's PPSV web section

www.immunize.org/pneumococcal-ppsv

ACIP's "Prevention of Pneumococcal Disease," April 4, 1997

ftp://ftp.cdc.gov/pub/Publications/mmwr/RR/RR4608.pdf

MYTH: Influenza Vaccines Are Not Effective

- At least two factors play important roles in determining the likelihood that influenza vaccine will protect a person from influenza illness:

1) characteristics of the person being vaccinated
(such as their age and health), and

2) the similarity or "match" between the influenza
virus types in the vaccine and those spreading in the community.

MYTH: Influenza Vaccines Are Not Effective

Many vaccinated people think they “got the flu” from the vaccine when in reality, they had a cold or another viral infection.

Although, Live influenza has RARE secondary contact spread

Flu vaccines will not protect against infection and illness caused by other viruses that can also cause influenza-like symptoms.

References: Influenza Vaccines Are Not Effective

IAC's Influenza web section
www.immunize.org/influenza

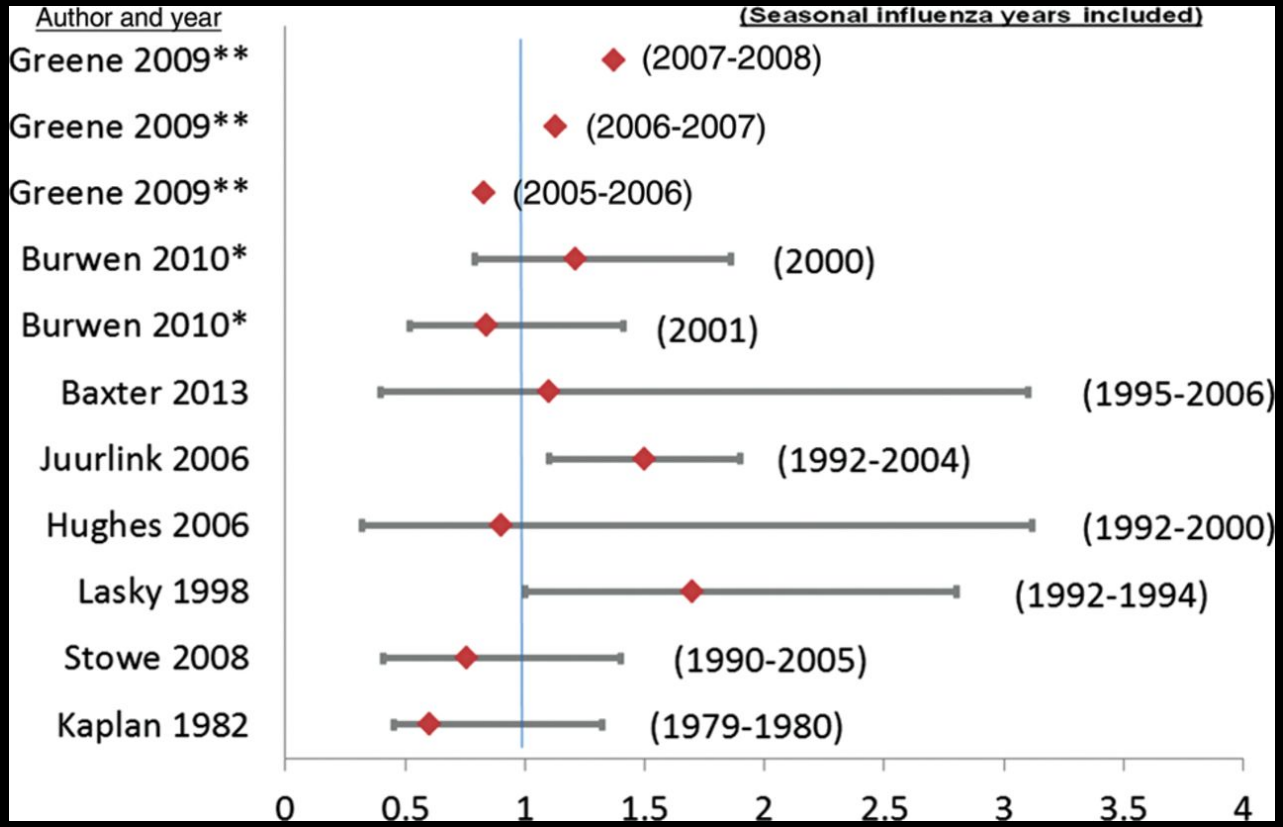
Flu Vaccine Effectiveness: Q&As for Health Professionals
www.cdc.gov/flu/professionals/vaccination/effectivenessqa.htm

Vaccine Effectiveness—How Well Does the Flu Vaccine Work? Q&As for the Public
www.cdc.gov/flu/about/qa/vaccineeffect.htm

Public health groups say flu vaccine is best tool, despite limitations www.cidrap.umn.edu/newsperspective/2011/10/public-health-groups-say-fluvaccine-best-tool-despite-limitations

Influenza Vaccine Causes Guillain-Barre Syndrome

Risk estimates (with 95% confidence intervals) of Guillain-Barré syndrome following influenza vaccines select studies,

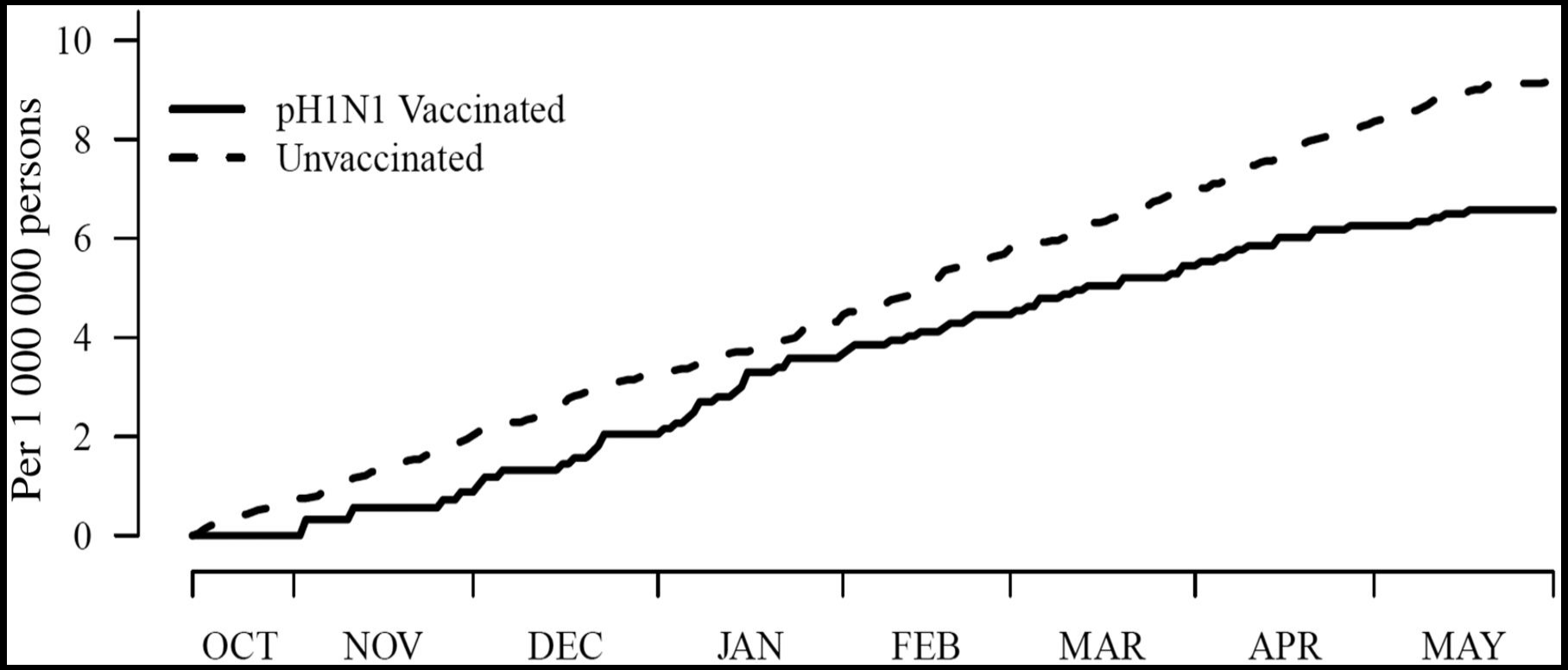


Claudia Vellozzi et al. Clin Infect Dis. 2014;58:1149-1155

Clinical Infectious Diseases

Influenza Vaccine Causes Guillain-Barre Syndrome

Cumulative risk of Guillain-Barré syndrome (GBS) among the 2009 pH1N1 vaccinated and unvaccinated groups by day and all ages, Emerging Infections Program, United States, 15 October 2009–31 May 2010.



Clinical Infectious Diseases

Claudia Vellozzi et al. Clin Infect Dis. 2014;58:1149-1155

PEDIATRICS Volume 137, number 3, March 2016:e20151968

Prevalence of HPV After Introduction of the Vaccination Program in the United States

Lauri E. Markowitz, MD,[a] Gui Liu, MPH,[a] Susan Hariri, PhD,[a] Martin Steinau, PhD,[b] Eileen F. Dunne, MD, MPH,[a] Elizabeth R. Unger, MD, PhD[b]

WHAT THIS STUDY ADDS: This study extends previous observations of quadrivalent HPV vaccine impact and examines cross-protection. Within 6 years of vaccine introduction, there were decreases in national vaccine type HPV prevalence of 64% and 34% among females aged 14 to 19 years and 20 to 24 years, respectively.

BACKGROUND: Si… recommende… vaccinated.

METHODS: HPV … 14 to 34 year… era (2009–20… types (HPV-6… eras. Prevale… according to …

RESULTS: Betwe… 11.5% to 4.3% (adjusted prevalence ratio [aPR]: 0.36 [95% confidence interval (CI): 0.21–0.61]) among females aged 14 to 19 years and from 18.5% to 12.1% (aPR: 0.66 [95% CI: 0.47–0.93]) among females aged 20 to 24 years. There was no decrease in 4vHPV type prevalence in older age groups. Within the vaccine era, among sexually active females aged 14 to 24 years, 4vHPV type prevalence was lower in vaccinated (≥1 dose) compared with unvaccinated females: 2.1% vs 16.9% (aPR: 0.11 [95% CI: 0.05–0.24]). There were no statistically significant changes in other HPV type categories that indicate cross-protection.

CONCLUSIONS: Within 6 years of vaccine introduction, there was a 64% decrease in 4vHPV type prevalence among females aged 14 to 19 years and a 34% decrease among those aged 20 to 24 years. This finding extends previous observations of population impact in the United States and demonstrates the first national evidence of impact among females in their 20s.

Myths: About HPV and the vaccine

- **MYTH:** Having the vaccine at a young age leads to promiscuity.

- **FACT**: There is no evidence that boys and girls who receive the vaccine have sex earlier than those who do not have the vaccine, and nor do they have more sexual partners once they became sexually active.

Myths: About HPV and the vaccine

- **MYTH:** The HPV vaccine causes more serious side effects than other vaccines.

- **FACT:** >187 million doses of the vaccine have been given in more than 130 countries and all adverse reactions are monitored and investigated.
  - All vaccines can have side effects. Common side effects are pain, redness and/or swelling at the site of injection.
  - Very rarely, more serious side effects such as anaphylactic (allergic) reaction can occur, usually if you are allergic to an ingredient in the vaccine such as yeast.

Myths: About HPV and the vaccine

- **MYTH:** The vaccine can give you the virus and cause cancer.

- **FACT:** The vaccine is produced in either recombinant yeast or baculovirus, therefore **cannot** cause cancer or any other HPV-related diseases.

References: HPV vaccine

- The **World Health Organization** directs and coordinates health across the United Nations. It provides leadership on global health matters and evidence-based policy.
- The **Food and Drug Administration** is the regulatory authority for medicines in the USA.
- The **US Center for Disease Control and Prevention** is a world-leading authority on protecting populations from disease and disease control. Their website has comprehensive information about **HPV** and the **vaccine**.
- The **Society of Obstetricians and Gynaecologists of Canada** has put together this website, which provides a wealth of information for teens, adults, parents, teachers and health professionals about **HPV** and the **vaccine**.

Good Resources for Patients

- IAC's Talking About Vaccines

www.immunize.org/concerns

- VEC's handouts on hepatitis A, meningococcal, HPV, influenza, shingles, and Tdap

www.chop.edu/service/vaccine-educationcenter/order-educational-materials

- National Foundation for Infectious Diseases

www.adultvaccination.org

- National Network for Immunization Information

www.immunizationinfo.org

- CDC's web section for adults

www.cdc.gov/vaccines/spec-grps/adults.htm

Good Resources for Patients

- IAC's "Vaccinations for Preteens and Teens, Age 11–19 Years" www.immunize.org/catg.d/p4020.pdf
- IAC's "Vaccinations for Adults" www.immunize.org/catg.d/p4030.pdf
- IAC's website for the public www.vaccineinformation.org
- VEC's "Vaccines and Adults: A Lifetime of Health" www.chop.edu/export/download/pdfs/articles/vaccineeducation-center/vaccines-adults.pdf
- VEC's "Vaccines and Teens: The Busy Social Years" www.chop.edu/export/download/pdfs/articles/vaccineeducation-center/vaccines-and-teens.pdf

Provider Myths

Provider Myths

- Vaccination contraindications and precautions are complicated, and the many new vaccines and their recommendations can cause confusion that leads to misconceptions.

- Providers who are concerned about vaccinating properly frequently err on the side of caution.

- Unfortunately, misconceptions can lead to missed opportunities to vaccinate.

Provider Myths

MYTH

Vaccines can’t be given to people who are sick.

FACT

Mild acute illness with or without fever is not a contraindication to vaccination. Neither is antibiotic treatment, recent exposure to an infectious disease, or convalescing from an illness.

Provider Myths

MYTH

Providers need to check vital signs before vaccinating.

FACT

ACIP does not recommend routinely checking temperature or other vital signs before vaccination. Mild illness is not a reason to withhold vaccination and requiring extra steps can be a barrier to immunization.

Provider Myth

MYTH

Certain vaccines can't be given together.

FACT

All routine vaccines can be given simultaneously (at the same visit, not in the same syringe).

- If 2 live virus vaccines are not given at the same visit, then they need to be separated by at least 4 weeks.

- Inactivated vaccines can be given at the sametime, or any time before or after, another inactivated or live vaccine.

Provider Myths

MYTH

Vaccines can’t be given to breastfeeding women.

FACT

All vaccines can be given to breastfeeding women except smallpox vaccine (yes, even live vaccines, even nasal-spray vaccines!).

Provider Myths

MYTH

Live virus vaccines (zoster, varicella, MMR, and LAIV) should not be given to contacts of pregnant women or to contacts of immunocompromised people.

FACT

False. The only concern is when a person develops a varicella-like rash after receiving varicella or zoster vaccine. Then the vaccinee should avoid close contact with the unvaccinated infant or immunocompromised person.

True: Live polio vaccine was associated with VAPP.

Provider Myths

MYTH

Pregnant women should never get vaccines.

FACT

Pregnant women should not receive LIVE vaccines. Influenza and Tdap are recommended in pregnancy.

HPV vaccine has not been sufficiently studied so should not be administered during pregnancy at this time.

Provider Myths

MYTH

Tdap can’t be given if a person has received Td in the last 5 years.

FACT

There is no "minimum interval" one needs to wait between receiving Td and Tdap. If necessary, it can be given the same day.

References: Provide Myths

- IAC's "ACIP Recommendations" web section
www.immunize.org/acip
- IAC's "Ask the Experts" web section with CDC experts
www.immunize.org/askexperts
- IAC's Vaccine Information Statement (VIS) web section
www.immunize.org/vis
- IAC's Immunization Education Materials web section
www.immunize.org/handouts
- IAC's "Summary of Recommendations for Adult Immunization" www.immunize.org/catg.d/p2011.pdf
- IAC's Pharmacist and Immunization web section
www.immunize.org/pharmacists

Background Resources

- ACIP's “General Recommendations on Immunization”
www.cdc.gov/mmwr/PDF/rr/rr5515.pdf
- CDC's “Pink Book”
www.cdc.gov/vaccines/pubs/pinkbook/index.html
- CDC’s “Guide to Vaccine Contraindications and Precautions”
www.cdc.gov/vaccines/recs/vac-admin/contraindications.htm
- CDC’s “Immunization & Pregnancy”
www.cdc.gov/vaccines/pubs/downloads/f_preg.pdf

Parent Myths

MYTH: MMR causes Autism

Co-occurring Conditions and Change in Diagnosis in Autism Spectrum Disorders

AUTHORS: Heather A. Close, BS,[a] Li-Ching Lee, PhD, ScM,[a] Christopher N. Kaufmann, MHS,[a] and Andrew W. Zimmerman, MD[b]

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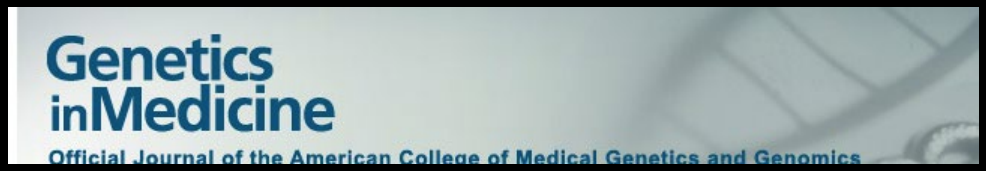
KEY WORDS
autism spectrum disorder, co-occurring conditions, diagnosis change

ABBREVIATIONS
aOR—adjusted odds ratio
ASD—autism spectrum disorder
CI—confidence interval

WHAT'S KNOWN ON THIS SUBJECT: Mixed prevalence rates of co-occurring psychiatric and neurodevelopmental conditions have been reported in children diagnosed with an autism spectrum disorder (ASD). ASD diagnoses remain fairly stable within a continuum, but some do not meet criteria for an ASD diagnosis years after initial diagnosis.

WHAT THIS STUDY ADDS: Co-occurring neurodevelopmental and psychiatric conditions may explain, in part, why the diagnosis of an ASD may change with age.

MYTH: MMR causes Autism



Genetics in Medicine (2009) 11, 111–117; doi:10.1097/GIM.0b013e31818fd762

The prevalence of PTEN mutations in a clinical pediatric cohort with autism spectrum disorders, developmental delay, and macrocephaly

Elizabeth A Varga1,2, Matthew Pastore2, Thomas Prior3, Gail E Herman1,2 and Kim L McBride1,2

1Center for Molecular and Human Genetics, The Research Institute at Nationwide Children's Hospital, Columbus, Ohio
2Departments of Pediatrics, Columbus, Ohio
3Pathology, The Ohio State University, Columbus, Ohio

Mitochondrial dysfunction in autism spectrum disorders: a systematic review and meta-analysis

D A Rossignol, R E Frye

Molecular Psychiatry 2012, 17 (3): 290-314

A comprehensive literature search was performed to collate evidence of mitochondrial dysfunction in autism spectrum disorders (ASDs) with two primary objectives. First, features of mitochondrial dysfunction in the general population of children with ASD were identified. Second, characteristics of mitochondrial dysfunction in children with ASD and concomitant mitochondrial disease (MD) were compared with published literature of two general populations: ASD children without MD, and non-ASD children with MD. The prevalence of MD in the general population of ASD was 5.0% (95% confidence interval 3.2, 6.9%), much higher than found in the general population (≈ 0.01%). The prevalence of abnormal biomarker values of mitochondrial dysfunction was high in ASD, much higher than the prevalence of MD. Variances and mean values of many mitochondrial biomarkers (lactate, pyruvate, carnitine and ubiquinone) were significantly different between ASD and controls. Some markers correlated with ASD severity. Neuroimaging, in vitro and post-mortem brain studies were consistent with an elevated prevalence of mitochondrial dysfunction in ASD. Taken together, these findings suggest children with ASD have a spectrum of mitochondrial dysfunction of differing severity. Eighteen publications representing a total of 112 children with ASD and MD (ASD/MD) were identified. The prevalence of developmental regression (52%), seizures (41%), motor delay (51%), gastrointestinal abnormalities (74%), female gender (39%), and elevated lactate (78%) and pyruvate (45%) was significantly higher in ASD/MD compared with the general ASD population. The prevalence of many of these abnormalities was similar to the general population of children with MD, suggesting that ASD/MD represents a distinct subgroup of children with MD. Most ASD/MD cases (79%) were not associated with genetic abnormalities, raising the possibility of secondary mitochondrial dysfunction. Treatment studies for ASD/MD were limited, although improvements were noted in some studies with carnitine, co-enzyme Q10 and B-vitamins. Many studies suffered from limitations, including small sample sizes, referral or publication biases, and variability in protocols for selecting children for MD workup, collecting mitochondrial biomarkers and defining MD. Overall, this evidence supports the notion that mitochondrial dysfunction is associated with ASD. Additional studies are needed to further define the role of mitochondrial dysfunction in ASD.

CLINICAL REPORT

Comprehensive Evaluation of the Child With Intellectual Disability or Global Developmental Delays

John B. Moeschler, MD, MS, FAAP, FACMG, Michael Shevell, MDCM, FRCP, and COMMITTEE ON GENETICS

ABBREVIATIONS

AAP—American Academy of Pediatrics
CMA—chromosome microarray
CNS—central nervous system
CNV—copy number variant
CT—computed tomography
FISH—fluorescent in situ hybridization
GAA—guanidinoacetate
GDD—global developmental delay
ID—intellectual disability
XLID—X-linked intellectual disability

abstract

FREE

Global developmental de and intellectual disability are relatively common pediatric condit . This report describes the recommended clinical genetics diagnost pproach. The report is based on a review of published reports, mos nsisting edium to large case series of diagnostic tests used, an e propor of those that led to a diagnosis in such patients. Chromosom icroarray is designated as a first-line test and replaces the sta d karyotype and fluorescent in situ hybridization subtelomere tes r the child with intellectual disability of unknown etiology. Fragile X testing remains an important first-line test. The importance of considering testing for inborn errors of metabolism in this population is supported by a recent systematic review of the literature and several case series recently published. The role of brain MRI remains important in certain patients. There is also a discussion of the emerging literature on the use of whole-exome sequencing as a diagnostic test in this population. Finally, the importance of intentional comanagement among families, the medical home, and the clinical genetics specialty clinic is discussed. *Pediatrics* 2014;134:e903–e918

Inborn error metabolic screening in individuals with nonsyndromic autism spectrum disorders

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ABBREVIATIONS

ASD	Autism spectrum disorders
CBCL	Child Behavior Checklist
IEM	Inborn errors of metabolism
SCQ	Social Communication Questionnaire

AIM To perform metabolic testing on 408 patients (age range 3–22y [mean 8.71, SD 4.15], 343 males and 63 females) with nonsyndromic autism spectrum disorders (ASD) to assess the diagnostic yield. In addition, we reviewed our hospital's clinical database of 8500 patients who had undergone metabolic testing to be identified for inborn errors of metabolism (IEM), and described the characteristics of those with IEM and nonsyndromic ASD.
METHOD Neuropsychological evaluation included the Social Communication Questionnaire and Child Behavior Checklist. For metabolic testing/screening, urine samples were analyzed for the diagnosis of cerebral creatine deficiency syndromes, purine and pyrimidine disorders, amino acid metabolism defects, mucopolysaccharidoses, and organic acidurias.
RESULTS The 408 recruited participants fulfilled the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) criteria of ASD. No biochemical evidence of a metabolic disorder was detected in any of the 408 patients studied. Concerning the retrospective evaluation from the 8500 who had metabolic testing, 464 individuals had a diagnosis of an IEM (394 without the diagnosis of ASD and 70 with ASD diagnosis). Only one individual with IEM had a diagnosis of nonsyndromic ASD at the time of the metabolic study; the metabolic testing had revealed diagnosis of urea-cycle disorder.
INTERPRETATION Metabolic testing should be considered in the work-up of individuals with syndromic ASD, but metabolic testing is not cost-effective for individuals with nonsyndromic ASD.

MYTH … tism

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- 12 of 13 … cted the study's interpreta…
- On 2/2/1… er citing the ruling of t… cil that the primary a… esearch was **"dishone… shown a "callous … children involved …**
- 01/2011 … wing Wakefield's work was …

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.

Methods 12 children (mean age 6 years [range 3–10], 11 boys) were referred to a paediatric gastroenterology unit with a history of normal development followed by loss of acquired skills, including language, together with diarrhoea and abdominal pain. Children underwent gastroenterological, neurological, and developmental assessment and review of developmental records. Ileocolonoscopy and biopsy sampling, magnetic-resonance imaging (MRI), electroencephalography (EEG), and lumbar puncture were done under sedation. Barium follow-through radiography was done where possible. Biochemical, haematological, and immunological profiles were examined.

Findings Onset of behavioural symptoms was associ… by the parents, with measles, mumps, and rub… vaccination in eight of the 12 children, with measl… infection in one child, and otitis media in a… . All 1… children had intestinal abnormalities rangi… from lymphoid nodular hyperplasia to a… hoid ul… ration. Histology showed patchy chronic inflam… tion i… in 11 children and reactive ileal lymphoi… perplasia in seven, but no granulomas. Be…viour… disor…s included autism (nine), disintegrativ… sy…sis (one), a… possible postviral or vaccinal encephalitis … o). There were no focal neurological ab…malities and … and EEG tests were normal. Abno…al laboratory results …ere significantly raised urinary …ethylmal…c acid compared with age-matched contro… (p=…003), low haemoglobin in four children, a… low s…m IgA in …r children.

Interp…tation …e ident… associated gastrointestinal dis…se and …evelopmental regression in a group of previ…ly …mal ch…n, which was generally associated in time … possible environmental triggers.

Lancet 199… **351:** 637–41
See Commentary page

Inflammatory Bowel Disease Study Group, University Departments of Medicine and Histopathology (A J Wakefield FRCS, A Anthony MB, J Linnell PhD, A P Dhillon MRCPath, S E Davies MRCPath) **and the University Departments of Paediatric Gastroenterology** (S H Murch MB, D M Casson MRCP, M Malik MRCP, M A Thomson FRCP, J A Walker-Smith FRCP,), **Child and Adolescent Psychiatry** (M Berelowitz FRCPsych), **Neurology** (P Harvey FRCP), **and Radiology** (A Valentine FRCR), **Royal Free Hospital and School of Medicine, London NW3 2QG, UK**

Correspondence to: Dr A J Wakefield

Introduction

We saw several children who, after a pe…d of apparent normality, lost acquired skills, includ…g com…nication. They all had gastrointestinal …mptoms, …luding abdominal pain, diarrhoea, and …ating and, i…some cases, food intolerance. We d…scribe… clinical f…dings, and gastrointestinal featur… of these chi…en.

Patients and meth…ds

12 children, cons…tively …rred to … department of paediatric gastr…terology … a hi…y of a pervasive developmental …der with loss …ired skills and intestinal symptoms …arrh… abdominal …in, bloating and food intolerance), were inve…gated. All children were admitted to the ward f…week, accomp…ed by their parents.

Clinical investigations

… took histori… including details of immunisations and e…osure to infect…s diseases, and assessed the children. In 11 cas… the histor…as obtained by the senior clinician (JW-S). Neur… and psychiatric assessments were done by consultant staff (PH, MB) with HMS-4 criteria.[1] Developmental …s included a review of prospective developmental records from …arents, health visitors, and general practitioners. Four children did not undergo psychiatric assessment in hospital; all had been assessed professionally elsewhere, so these assessments were used as the basis for their behavioural diagnosis.

After bowel preparation, ileocolonoscopy was performed by SHM or MAT under sedation with midazolam and pethidine. Paired frozen and formalin-fixed mucosal biopsy samples were taken from the terminal ileum; ascending, transverse, descending, and sigmoid colons, and from the rectum. The procedure was recorded by video or still images, and were compared with images of the previous seven consecutive paediatric colonoscopies (four normal colonoscopies and three on children with ulcerative colitis), in which the physician reported normal appearances in the terminal ileum. Barium follow-through radiography was possible in some cases.

Also under sedation, cerebral magnetic-resonance imaging (MRI), electroencephalography (EEG) including visual, brain stem auditory, and sensory evoked potentials (where compliance made these possible), and lumbar puncture were done.

Laboratory investigations

Thyroid function, serum long-chain fatty acids, and cerebrospinal-fluid lactate were measured to exclude known causes of childhood neurodegenerative disease. Urinary methylmalonic acid was measured in random urine samples from eight of the 12 children and 14 age-matched and sex-matched normal controls, by a modification of a technique described previously.[2] Chromatograms were scanned digitally on computer, to analyse the methylmalonic-acid zones from cases and controls. Urinary methylmalonic-acid concentrations in patients and controls were compared by a two-sample *t* test. Urinary creatinine was estimated by routine spectrophotometric assay.

Children were screened for antiendomyseal antibodies and boys were screened for fragile-X if this had not been done

RETRACTED

G Model
JVAC 15366 1–7
ARTICLE IN PRESS
Vaccine xxx (2014) xxx–xxx
Contents lists available at ScienceDirect
Vaccine

The findings were summarized as:

- There was no relationship between vaccination and autism
- There was no relationship between vaccination and Autism Spectrum Disorder
- There was no relationship between autism and the MMR vaccine

Mercury

evidence for increased risk of developing autism or ASD following MMR, Hg, or thimerosal exposure when grouped by condition (OR: 0.90, 95% CI: 0.83 to 0.98; $p = 0.02$) or grouped by exposure type (OR: 0.85, 95% CI: 0.76 to 0.95; $p = 0.01$). Findings of this meta-analysis suggest that vaccinations are not associated with the development of autism or autism spectrum disorder. Furthermore, the components of the vaccines (thimerosal or mercury) or multiple vaccines (MMR) are not associated with the development of autism or autism spectrum disorder.

References: MYTH: MMR causes Autism

• IAC's "MMR vaccine does not cause autism. Examine the evidence!"
www.immunize.org/catg.d/p4026.pdf
• IAC's "Clear Answers & Smart Advice about Your Baby's Shots" by Ari Brown, MD, FAAP
www.immunize.org/catg.d/p2068.pdf
• CDC's "MMR Vaccine"
www.cdc.gov/vaccinesafety/Vaccines/MMR/index.html
• The Fraud Behind the MMR Scare (IAC web section)
www.immunize.org/bmj-deer-mmr-wakefield
• IOM Report: "MMR Vaccine and Autism"
www.nap.edu/catalog.php?record_id=10101

References: MYTH: MMR causes Autism

- IAC's "Evidence Shows Vaccines Unrelated to Autism" www.immunize.org/catg.d/p4028.pdf
- IAC's "Decisions in the Omnibus Autism Proceeding"

www.immunize.org/catg.d/p4029.pdf

- VEC's "Vaccines and Autism: What you should know" www.chop.edu/export/download/pdfs/articles/vaccineeducation-center/autism.pdf
- "Vaccines and Autism: A Tale of Shifting Hypotheses" by Paul Offit, MD and Jeffery Gerber, MD www.journals.uchicago.edu/doi/pdf/10.1086/596476

References: MYTH: MMR causes Autism

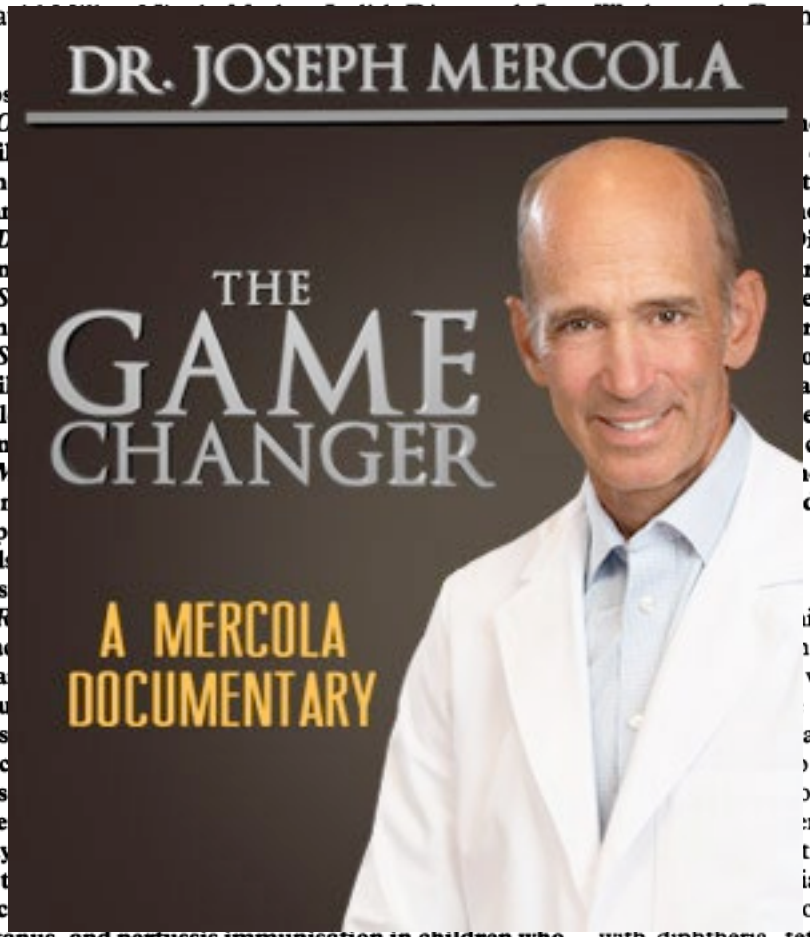
- "Fitness to Practice Panel Hearing" report from the U.K.'s General Medical Council regarding Dr.Andrew Wakefield www.neurodiversity.com/wakefield_gmc_ruling.pdf

- The Lancet retraction http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(97)11096-0/abstract

"How a zealot's word led us astray on autism" by Arthur Caplan, PhD www.msnbc.msn.com/id/35218819/ns/healthhealth_Care

Pertussis immunisation and serious acute neurological illnesses in children

Da… …n Ross



Abs… …(95% confidence interval 1·6 to …e number of cases associated with chil… …extremely small and statistically illn… …ther possible agents or predispos- im… …ot be excluded.

***D*… …iphtheria, tetanus, and pertussis con… …re occasions be associated with the *S*… …evere acute neurological illnesses sch… …rious sequelae. Some cases may *S*… …or have other causes. The role of chil… …as a prime or concomitant factor in foll… …ese illnesses cannot be determined con… …case. The balance of possible risk *M*… …efits from pertussis immunisation tion… …d use of the vaccine.**

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Correspondence to:
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BMJ 1993;307:1171-6

…ildhood encephalopathy study was …1976 after reports questioning the …vaccine[1,2] had led to serious loss of … immunisation programme and a …acceptance rates for this vaccine.[3,4] …examine the causes and outcome of …ological illnesses in young children …rence to the possible role of pertus- …tiological agent.[5] The results showed …iation between the onset of certain …ological illnesses and immunisation **tetanus, and pertussis immunisation in children who had died or had any dysfunction in comparison with** with diphtheria, tetanus, and pertussis vaccine in the previous seven days.[5-7] Despite three years of active

DPT vaccine is Dangerous

MMWR

Recommendations and Reports

March 28, 1997 / 46(RR-7);1-25

Persons using assistive technology might not be able to fully access information in this file. For assistance, please send e-mail to: mmwrq@cdc.gov. Type 508 Accommodation in the subje
e-mail.

Pertussis Vaccination: Use of Acellular Pertussis Vaccines Among Infants and Young Childre
Recommendations of the Advisory Committee on Immunization Practices (ACIP)

Summary

J Pharmacol Pharm

doi: 10.4103/0976-500X.92514

Diphtheria, pertussis (whooping cough), and tetanus vaccine induced recurrent seizures and acute encephalopathy in a pediatric patient: Possibly due to pertussis fraction

Mahendra K. Patel, Tejas K. Patel, and C. B. Tripathi

Author information ► Copyright and License information ►

study is … tudy conducte … following DPT as:

- 1:310,000 doses, 95% confidence interval 1:50,000 to 1:18,000,000.

MYTH: Giving an infant multiple vaccines can overwhelm the immune system

• Babies are exposed to immunological challenges at the time of birth. As babies pass through the birth canal and breathe, they ***are immediately colonized with trillions of bacteria***. Healthy babies constantly make antibodies against these bacteria and viruses.

• Though children receive more vaccines than in the past, today's vaccines contain fewer antigens than previous vaccines.

- Smallpox vaccine alone contained 200 proteins; the 11 currently recommended routine vaccines contain fewer than 130 immunologic components.

References

- VEC's "Too Many Vaccines? What you should know"

www.chop.edu/export/download/pdfs/articles/vaccineeducation-center/too-many-vaccines.pdf

- FAQs about Multiple Vaccinations and the Immune System

www.cdc.gov/vaccinesafety/Vaccines multiplevaccines.html

MYTH: It's better to space out vaccines using an alternative schedule

- Delaying vaccines increases the time children will be susceptible to diseases.
  - SSPE and other complications of measles occur if infection is in the first 18 months of life. In 2011, there were more than 1200 cases reported in the US. Most among children <5 years of age
  - There is no evidence that spreading out the schedule decreases the risk of adverse reactions.
- Requiring many extra appointments for vaccinations increases the stress for the child and may lead to a fear of visits to the clinic.

References

• “The Problem With Dr Bob's Alternative Vaccine Schedule” by Paul Offit, MD, and Charlotte Moser
www.immunize.org/concerns/offit_moser2009.pdf

• AAP’s “Adhering to Vaccine Schedule is Best Way to Protect Children from Disease”
www.immunize.org/aap/fisher.pdf

• VEC’s “Too Many Vaccines? What you should know”
www.chop.edu/export/download/pdfs/articles/vaccineeducation-center/too-many-vaccines.pdf

• IOM Report: “Multiple Immunizations and Immune Dysfunction” www.nap.edu/catalog.php?record_id=10306

• “Parental Refusal of Pertussis Vaccination Is Associated with an Increased Risk of Pertussis Infection in Children”
(Glanz et al, Pediatrics, June 2009)
http://pediatrics.aappublications.org/content/123/6/1446.abstract

MYTH: Natural infection is better than immunization

• Natural infection, in many diseases does cause better immunity than vaccination.

• However, the price paid for natural disease can include paralysis, permanent brain damage, liver failure, liver cancer, deafness, blindness, pneumonia, or death.

References

- “Natural Infection vs. Immunization” by Paul Offit, MD www.chop.edu/service/vaccine-education-center/hottopicsnatural-infection-vs-immunization.html
- NNii’s “Exposure Parties” www.immunizationinfo.org/exposure_parties.cfm
- Photos of people with vaccine-preventable diseases www.immunize.org/photos
- Real-life accounts of people who have suffered or died from vaccine-preventable diseases www.immunize.org/reports

MYTH: Abortions Are Required to Produce Vaccines

- Production of *varicella, rubella, rabies, adenovirus, and hepatitis A vaccines* involves growing viruses in human cell culture.

- Two human cell lines provide these cultures; they were developed from two legally aborted fetuses in the 1960s. With known Congenital Rubella Syndrome

- The donor fetuses were not aborted for the purpose of obtaining these cells.

- The same cell lines have been used for 35 years — no new fetal tissue is required. WI-38 and MRC-5

References

- IAC's web page about ethical and religious objections to vaccination

www.immunize.org/concerns/religious.asp

- NNii's "Human Fetal Links with Some Vaccines"

www.immunizationinfo.org/issues/vaccinecomponents/human-fetal-links-some-vaccines

Religious Objections

- There is no direct command or directive In the Old or New Testaments or Holy Quran, that says, "*Do not vaccinate yourself or your children*"

- However, there are scriptures and principles from which some religious groups derive that unspoken directive.

Religious Objections

- The Bible teaches that there are clean and unclean animals and that God's people are not to put the unclean into their bodies (Deuteronomy 14).
- Bible teaches that "*Ye shall not eat of anything that dieth of itself*"; (Deuteronomy 14:21) and "*that flesh with the life thereof, which is the blood thereof, shall ye not eat*". (Genesis 9:4)
- “Vaccines are often made of, or embodies, fetuses or eggs of said unclean creatures. The process of creating the vaccine often causes said creatures to die in the process. Many vaccines are made in or of the blood of diseased animals.”

Religious Objections

We must be very careful with pharmaceutical drugs. Pharmacy comes from the Greek word *pharmakeia* means witchcraft, sorcery. These are the main meanings:

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Rank	Biologic	Expression System	Company	2010 Worldwide Sales in Millions	Approved Indication
1	Enbrel	CHO	Amgen	6,808	RA. ankylosing spondylitis, psoriasis, PA, juvenile rheumatoid arthritis
2	Humira	CHO	Abbott	6,548	RA. ankylosing spondylitis, juvenile rheumatoid arthritis, Crohn's disease, PA. psoriasis
3	Remicade	Murine Myeloma	Johnson & Johnson	6,478	Psoriasis, ulcerative Myeloma colitis, ankylosing spondylitis, Crohn's disease. PA. RA
4	Avastin	CHO	Roche	6,193	Colorectal cancer, breast cancer, brain cancer, renal cell cancer, non·small cell lung cancer
5	Rituxin	CHO	Biogen-Idec	6,088	Non·Hodgkin's lymphoma, RA, chronic lymphocytic leukemia

Data *Source: Public Biotech 2010 – the numbers. Nature Biotechnology*

try.

Sc chemicals. It is prudent an prescribes for you. M toid arthritis. I was told it er immune system and teach it not to attack itself. What they did NOT tell me is that IT is CREATED using aborted fetal tissue. As soon as she learned that, she went off the medication. You cannot trust THEM (whoever THEY are) to give you all of the information, you must search it out for yourself

Religious Objections

- Parents are to care for and be responsible for their children. (1 Tim 5:8) Parents, not the government, make decisions for their children. **The Comprehensive Child Health Immunizations Act of 1993 made known the fact that there are risks to vaccinations by stating "Vaccine information should be simplified to ensure that parents understand the benefits and *risks".***

MYTH: VAERS Data Prove that Vaccines Are Dangerous

VAERS data cannot “prove” anything

- Anyone can report anything and are encouraged to do so!
- Reports include many non-serious reactions.
- The number of reported adverse events is influenced by publicity.
- VAERS is properly used to detect early warning signals and generate hypotheses.

References

- Vaccine Adverse Events Reporting System (VAERS) www.vaers.hhs.gov
- CDC's "Why it's Important to Monitor Vaccine Safety" www.cdc.gov/vaccinesafety/Vaccine_Monitoring/Index.html
- NNii's "Monitoring Vaccine Safety" www.immunizationinfo.org/parents/why-immunize/monitoring-vaccine-safety
- NNii's "Vaccine Safety: Cause or Coincidence?" www.immunizationinfo.org/issues/vaccine-safety/cause-orcoincidence
- WHO's "Causality assessment of adverse events following immunization" www.who.int/vaccine_safety/causality/en

Good Resources for Providers Talking to Parents

- IAC's Responding to Vaccine Concerns web section
www.immunize.org/concerns

- IAC's Talking with Parents web section
www.immunize.org/concerns/comm_talk.asp

- Vaccine Education Center (at the Children's Hospital of Philadelphia)
www.vaccine.chop.edu

- AAP's immunization website
www.aap.org/immunization

- National Network for Immunization Information
www.immunizationinfo.org

Good Resources for Parents

- IAC's handouts for communicating with parents
www.immunize.org/handouts/discussing-vaccines-parents.asp

- IAC's website for the public
www.vaccineinformation.org

- CDC's web section about provider resources for parents
www.cdc.gov/vaccines/spec-grps/hcp/conversations.htm

- CDC's "Parents Guide to Childhood Immunization"
www.cdc.gov/vaccines/pubs/parents-guide

- Vaccine Education Center (at CHOP)
www.vaccine.chop.edu

- Every Child By Two's websites: www.ecbt.org and
www.vaccinateyourbaby.org

- National Network for Immunization Information
www.immunizationinfo.org

Mandatory Vaccination Violates Civil Rights

- Massachusetts enacted the first mandatory vaccination law in the U.S. in 1809. (Smallpox)

- Vaccination laws have been found to be constitutional in U.S. courts. Seminal case was *Jacobson v.Massachusetts* in 1905.

- All states offer medical exemptions, 47 allow religious exemptions, and 20 allow philosophical exemptions. 22 allow school entrance without vaccination

- Many states mandate that Parents need to be aware that if they don't vaccinate their children, they are putting them, and their contacts, at risk of serious disease.

Association Between Vaccine Refusal and Vaccine-Preventable Diseases in the United States

A Review of Measles and Pertussis FREE

Varun K. Phadke, MD[1]; Robert A. Bednarczyk, MS, PhD[2,3]; Daniel A. Salmon, MPH, PhD[4]; Saad B. Omer, MBBS, MPH, PhD[2,3,5,6]

JAMA. 2016;315(11):1149-1158. doi:10.1001/jama.2016.1353.

Conclusions and Relevance A substantial proportion of the US measles cases in the era after elimination were intentionally unvaccinated. The phenomenon of vaccine refusal was associated with an increased risk for measles among people who refuse vaccines and among fully vaccinated individuals. Although pertussis resurgence has been attributed to waning immunity and other factors, vaccine refusal was still associated with an

References

- IAC's "What if you don't immunize your child?" www.immunize.org/catg.d/p4017.pdf
- IAC's "Decision to Not Vaccinate My Child" (declination form) www.immunize.org/catg.d/p4059.pdf
- "Personal belief exemptions for vaccination put people at risk" www.immunize.org/catg.d/p2069.pdf
- AAP's "Refusal to Vaccinate" form www.aap.org/immunization/pediatricians/pdf/Refusal to Vaccinate.pdf
- All Star Pediatric's sample vaccine policy statement www.immunize.org/aap/pediatrics_vaccine_letter.pdf
- VaccineEthics.org – University of Pennsylvania www.vaccineethics.org/issue_briefs/requirements.php

Don’t Worry About Every Possible Question

- Be able to recommend good websites and handouts for patients/parents.
- Be aware of major vaccine-critical groups and individuals and become familiar with their websites.
- Be ready to answer the most common questions — many concerns haven’t changed in over 200 years!
- Remember, it’s acceptable to say you’ll look into a question and get back to the patient with more information.
- It’s worth your time — people respect the opinion of their healthcare providers.

The National Childhood Vaccine Injury Act (NCVIA) of 1986