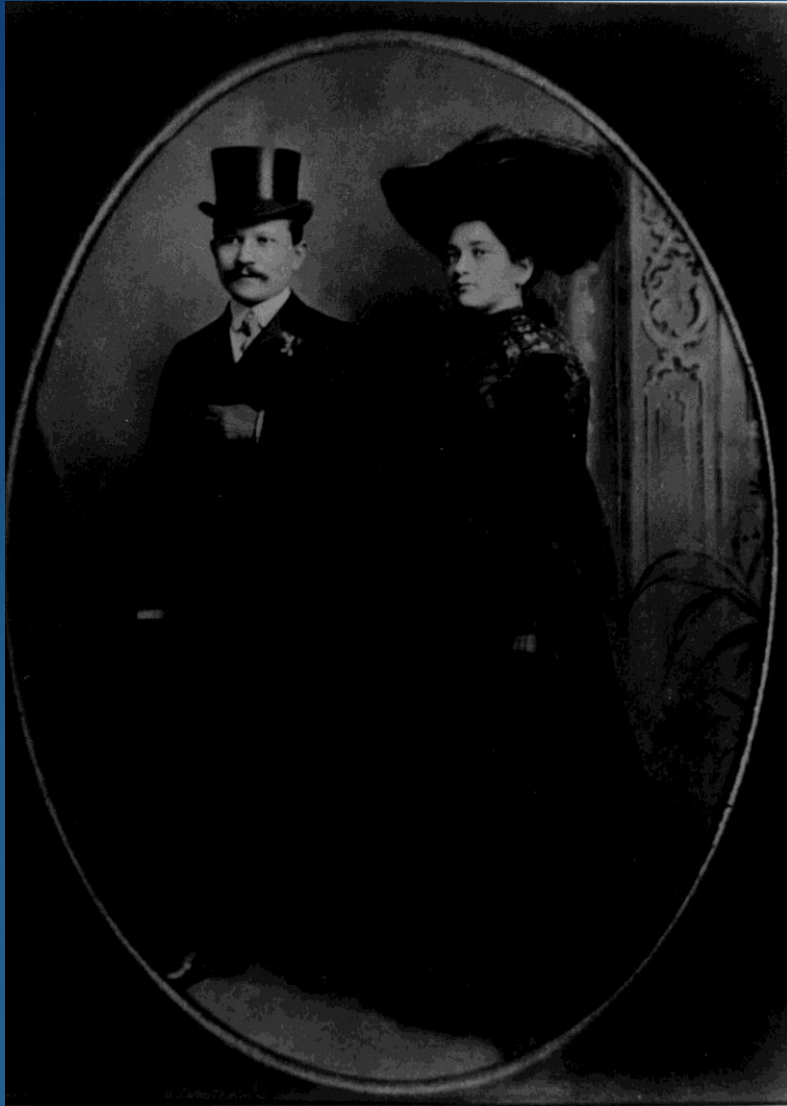




A Brief [Personal] History of ~~Time~~ Immunizations

THE MAKING OF AN IMMUNIZATION CHAMPION AT KAISER PERMANENTE

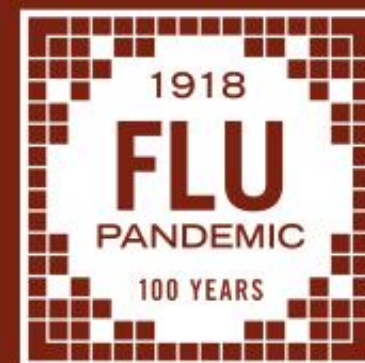
Irene S Landaw, MD



1890's



1919



WE REMEMBER. WE PREPARE.



1959



Smallpox Rash - Distribution



World Health Organization (WHO)

WebMD

Smallpox Vaccine and Eczema Don't Mix

Combination Can Cause Severe, Possibly Deadly Infection

By Salynn Boyles

FROM THE WEBMD ARCHIVES

Sept. 9, 2002 -- As many as half of all Americans are poor candidates for smallpox vaccination due to a rare, but potentially fatal, skin infection caused by the vaccine, health officials report. They conclude that mass immunization against smallpox in the absence of an identified bioterrorist attack may do more harm than good.

Immunologist Donald Leung and colleagues report that smallpox vaccination poses a threat to people with a history of the skin condition *eczema*, with the risk being particularly great for children. Being in

Today on WebMD

- Baby's Bathing Routine: A good one helps halt eczema flares
- Need Help: Getting your eczema under control?
- Your Diet: Does it affect your eczema?
- Be Choosy: And be educated when shopping for cosmetics.

QUARANTINE.jpg SMALLPOX VACCI... smallpox-rediff.webp POLIO CRUTCHES.jpg POLIO HEADLINE.jpg POLIO SHOT.jpg



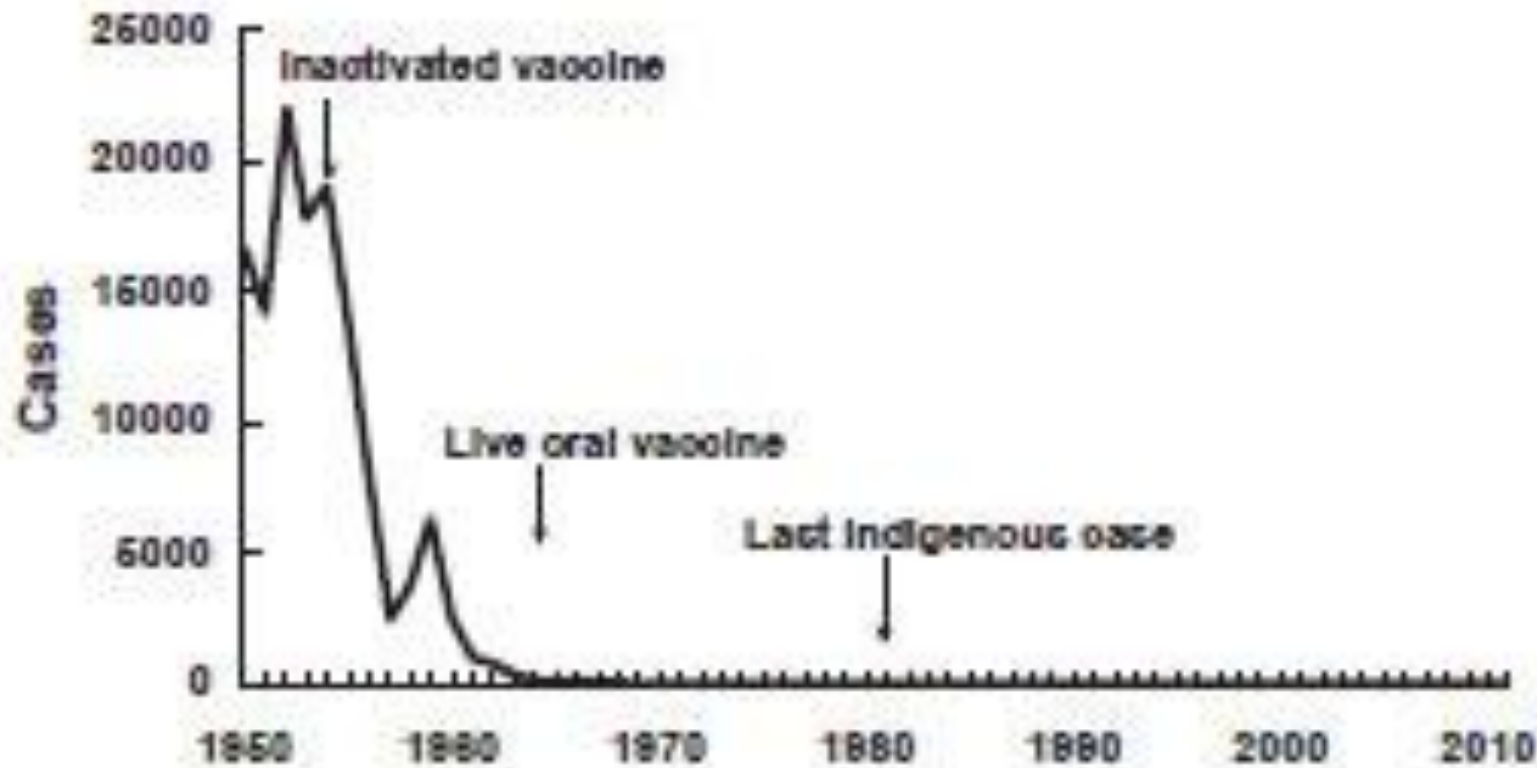
1959



1955



1961



1952: 21,000 US Paralytic cases
1955: Inactivated Vaccine (Salk)
1960: 2,525 Paralytic Cases
1961: Live Oral Vaccine (Sabin)
1961: 61 Paralytic Cases
1979: Last US Indigenous Polio
1980-1999: 165 Cases, 95% VAPP
1993: Last Imported Case
1999: Last Indigenous VAPP
2000: Oral Polio Vaccine discontinued in US

1981



CDC
CENTERS FOR DISEASE CONTROL
AND PREVENTION

MMWR
MORBIDITY AND MORTALITY
WEEKLY REPORT

June 5, 1981 / Vol. 30 / No. 21

- 249 Dengue Type 4 Infections in U.S. Travelers to the Caribbean
- 250 *Pneumocystis* Pneumonia — Los Angeles
- 252 Measles — United States, Five Weeks
- 253 Risk-Factor-Prevalence Survey
- 259 Surveillance of Childhood Lead Poisoning — United States
- 261 Quarantine Measures

Pneumocystis Pneumonia — Los Angeles

In the period October 1980–May 1981, 5 young men, all active homosexuals, were treated for biopsy-confirmed *Pneumocystis carinii* pneumonia at 3 different hospitals in Los Angeles, California. Two of the patients died. All 5 patients had laboratory-confirmed previous or current cytomegalovirus (CMV) infection and candidal infection. Case reports of these patients follow.

Patient 1: A previously healthy 33-year-old man developed *P. carinii* pneumonia in March 1981 after a 2-month history of fever associated with oral mucosal candidiasis, leukopenia, and CMV viremia. The serum complement level in October 1980 was 256; in May 1981 it was 32. The patient's condition deteriorated despite courses of treatment with trimethoprim-sulfamethoxazole, pyrimethamine, and acyclovir. He died May 3, and postmortem examination confirmed *P. carinii* pneumonia, but no evidence of neoplasia.



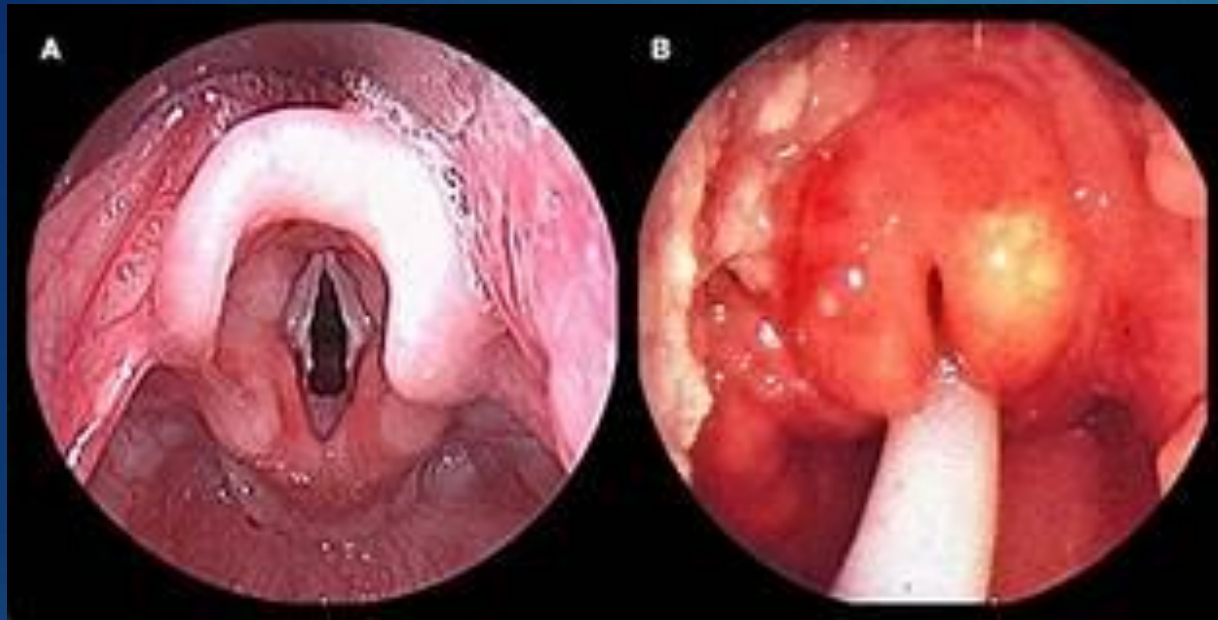
1981



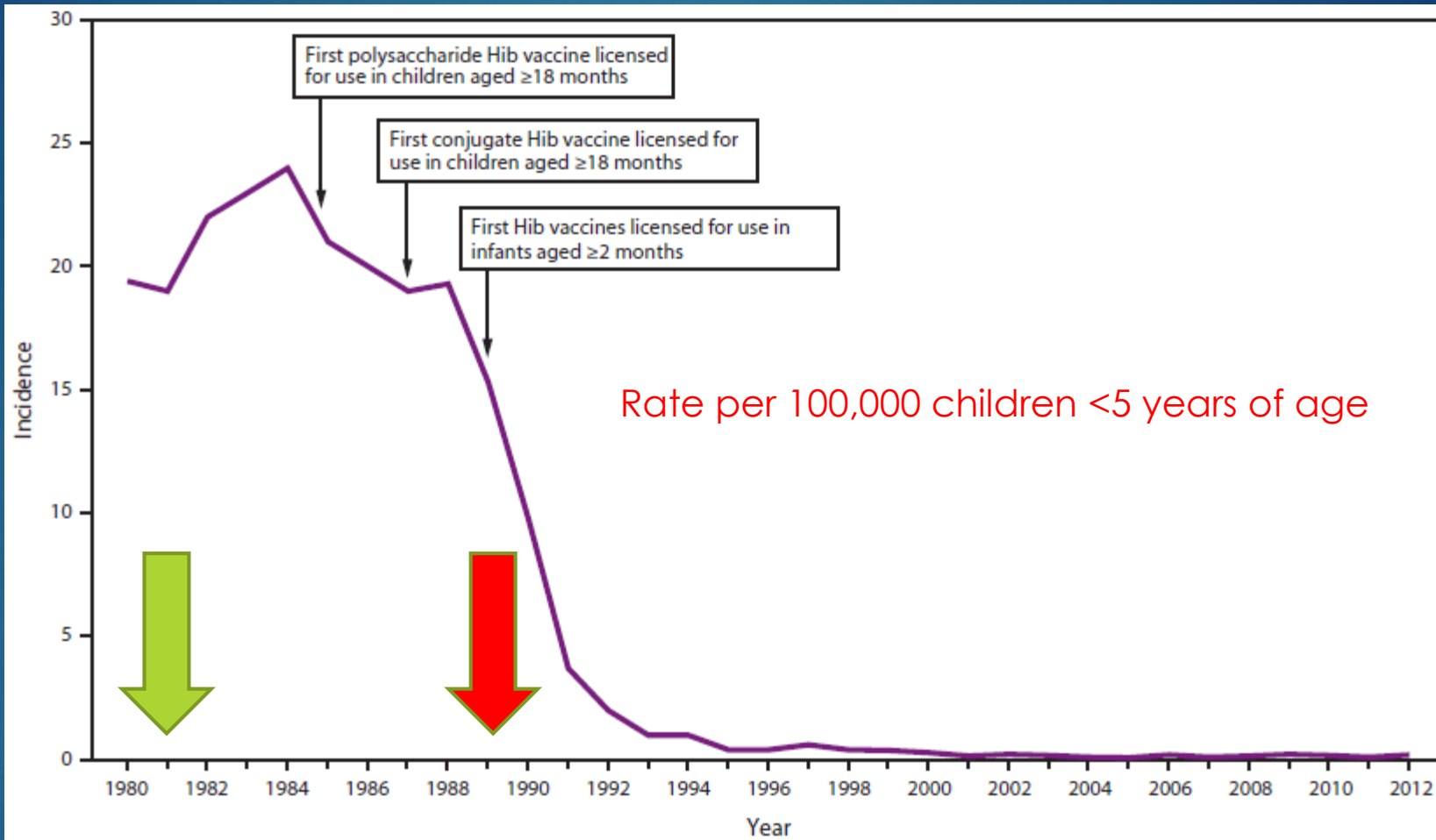
1991-1994



1998



Haemophilus Influenzae Type B Infections



Haemophilus b Conjugate Vaccines for Prevention of Haemophilus influenzae Type b Disease Among Infants and Children Two Months of Age and Older Recommendations of the ACIP

INTRODUCTION

Three *Haemophilus b* conjugate vaccines are currently licensed for administration to children greater than or equal to 15 months of age in the United States. Recently, the Food and Drug Administration approved the use of HbOC (October 4, 1990) and PRP-OMP (December 13, 1990) for routine administration to infants beginning at 2 months of age. This statement a) summarizes available information about *Haemophilus b* conjugate vaccines, b) offers guidelines for use of HbOC and PRP-OMP for infants for prevention of Hib disease, and c) advises how to use conjugate vaccines for older children. It should be noted that HbOC and PRP-OMP have different schedules for administration, which are discussed below.

Immunology of Hib

The polyribosylribitol phosphate (PRP) capsule of Hib is a major virulence factor for the organism. Antibody to PRP is the primary contributor to serum bactericidal activity, and increasing levels of antibody are associated with decreasing risk of invasive Hib disease. The human immune response to PRP resembles the murine response to T-cell independent antigens: B cells provide the primary response without a contribution from T-helper cells. In contrast to T-cell dependent antigens, T-cell independent antigens are characterized by a) induction of a poor antibody response in less than 18-month-old infants and children, b) a variable and quantitatively smaller antibody response than that seen with T-cell dependent antigens, c) production of a higher proportion of immunoglobulin M (IgM), and d) inability to induce a booster response.

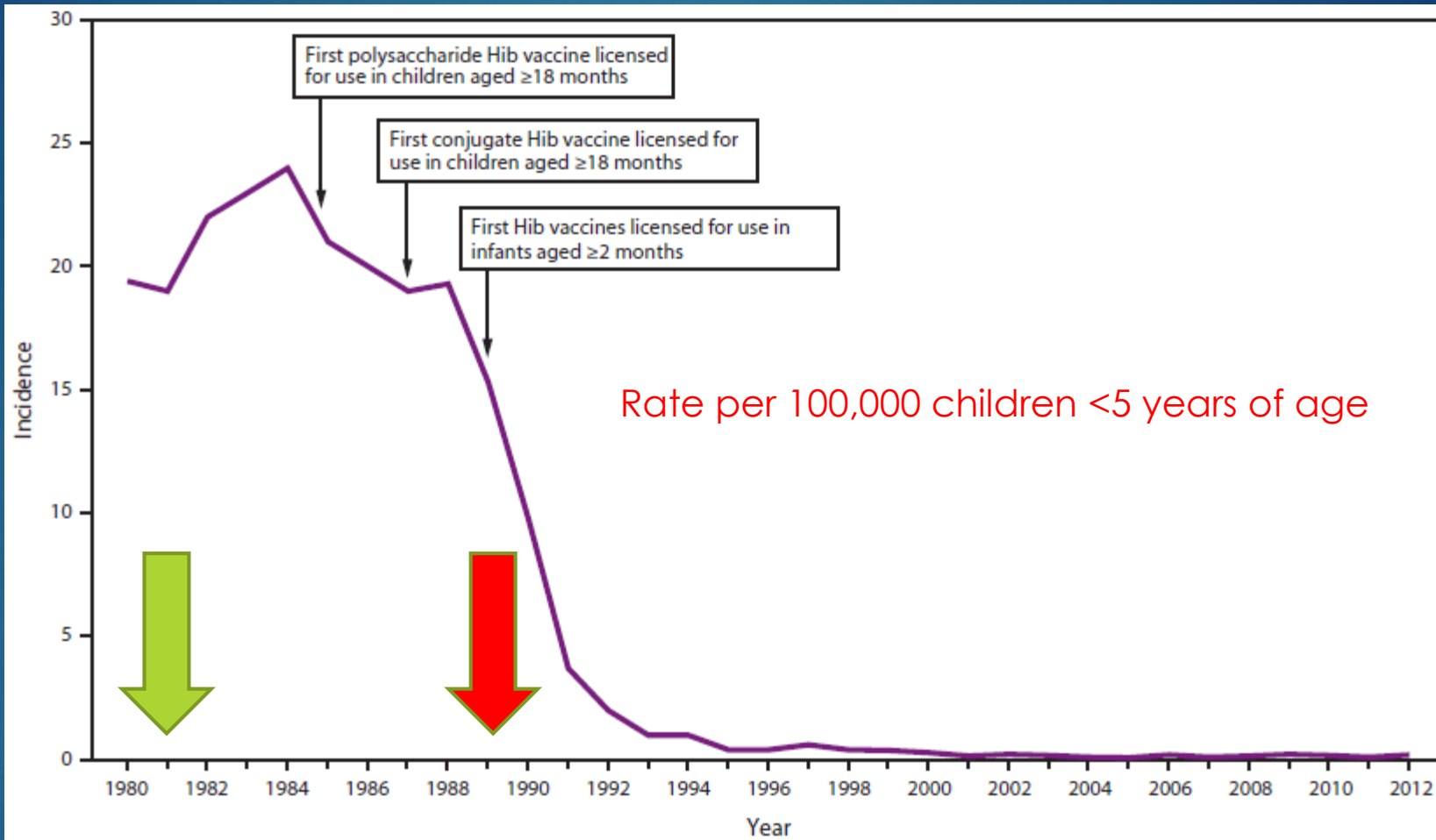
POLYSACCHARIDE VACCINES

Vaccines derived from PRP alone (polysaccharide vaccines) were developed in the 1970s. After demonstration of safety, immunogenicity, and induction of serum bactericidal activity, an efficacy of 90% (95% confidence interval (CI) = 50%-95%) was shown for one dose of vaccine given to children 18-71 months old in a large trial in Finland. However, the vaccine was ineffective for infants 3-17 months of age (2). Beginning in 1985, several PRP vaccines were licensed for use in the United States for children greater than or equal to 18 months of age, and a series of post-licensure case-control studies demonstrated variable efficacy. Four of five studies showed efficacy in the range of 41%-88%, and one study showed no efficacy (3).

CONJUGATE VACCINES

Covalent linkage (conjugation) of PRP with T-cell dependent protein antigens was evaluated in an attempt to overcome the T-cell independent characteristics of PRP. At present three different *Haemophilus b* conjugate vaccines are licensed for use with older children -- HbOC,

Haemophilus Influenzae Type B Infections



KAISER PERMANENTE VACCINE STUDY CENTER CLINICAL TRIALS

1988

Praxis HbOC Trial - Phase III

-25,000 enrolled
-31 sites

1990

Lederle Post Licensure Surveillance of Hemophilus Disease – Phase IV

-Study Population 250,000
-31 sites

Lederle HDTP Trial – Phase III

1991

Lederle ADTP/HbOC Trial – Phase II

-400 enrolled
-7 sites

1992

Merck Varicella Trial 1076 – Phase II

Postmarketing Evaluation of Lederle DTaP (ACEL-IMUNE) – Phase IV

Merck Varicella Trial 004-007 – Phase II

Chiron APDT Trial V8P1 - Phase III

1993

Postmarketing Evaluation of Lederle HDTP (TETRAMUNE) - Phase IV

-Surveillance population - 20,000
-31 sites

Merck Varicella 10 Year Persistence Trial 1076 – Phase IV

Merck Varicella Trial 1133 - Phase III

SmithKline HHDTP Trial 212616/003 – Phase II

1994

Chiron APDT Trial V8P1 Amendment 2 – Phase III

Merck Varicella Trial 1134 – Phase II

-Start Date 05/94
-600 enrolled
-6 sites

Lederle ADTP/HbOC Trial 91-2 – Phase II

Lederle ADTP/HbOC Trial 91-5 – Phase III

SmithKline DTPa-HB Trial 222074/001 - Phase II

1995

Lederle Pneumococcal Trial D118-P7 – Phase II

Merck Varicella Persistence Trial 004/007 – Phase IV

-Start Date - 07/95
-2 sites
-Enrolled 150

Lederle Pneumococcal Efficacy Trial D118-P8 - Phase III

-Start Date- 10/95
-38,000 enrolled
-21 sites

Postmarketing Evaluation of Short Term Safety of Merck Varicella Vaccine- Phase II

1996

SmithKline Varicella Trial 208133/135 – Phase II

1997

Chiron Kindergarten V8P1 Amendment 6 Trial - Phase III

Merck VAQTA (Hep A vaccine) Post-Marketing Trial – Phase IV

-Start date - 01/97
-Enrollment - 10,000
-31 sites

Wyeth Lederle D118-P16 Pneumococcal Bridging Trial – Phase III

Merck Varicella Persistence Trial 1133, 1134 – Phase IV

SmithKline DTaP/HepB/Hib 045/027 Trial – Phase III

Merck MMRV 008 – Phase II

1998

Merck MMRV 009 - Phase II

Nabi 1356 – Staphylococcus Type A Vaccine- Phase III

1999

Wyeth Lederle D118-P16 Amendment 1 – Booster dose of Pneumococcal Vaccine Phase III

KAISER PERMANENTE VACCINE STUDY CENTER CLINICAL TRIALS

1998

Wyeth Lederle D118-P8 Pneumococcal Vaccine in Children Between 1 and 9 years of age – Phase III

Merck MMRV 011 – Phase III

NAVA DTaP Evaluation of Manufacturing Lots – Phase IV

NAVA Post-Marketing Expanded Safety Trial of NAVA DTaP – Phase IV

SmithKline Beecham APV 123 - Phase III

2000

Merck 012 - IND 7068

Comparison of the Safety, Tolerability, and Immunogenicity of Three Consistency Lots of Frozen Measles, Mumps, Rubella and Varicella Vaccine (MMRV) in Healthy Children

Aviron Flumist - IND 6216

A Prospective, Randomized, Double Blinded, Placebo-Controlled Trial to Assess the Safety of Frozen FluMist in Healthy Children and Adolescents

2001

Wyeth D139 - P2

A Phase III Randomized Double-Blind Trial To Compare The Immunogenicity Of Three Unique Lots Of 9-Valent Pneumococcal Meningococcal Group C Saccharide Conjugate Combination Vaccine In Infants.

Wyeth D139-P3

A Phase III Randomized Study To Evaluate The Safety Of The 9-Valent Pneumococcal, Meningococcal Groups C Saccharide-CRM 197 Conjugate Combination Vaccine Compared To Licensed 7-Valent Pneumococcal Conjugate Vaccine (Prenar™) Administered To Healthy Infants

2002

Aventis M5A03 - IND 8502

Lot –Consistency and Bridge Study of HCP 20/20/5/3 DT-mIPV/PRP-T(Pentacel) in Infants and Toddlers – Protocol M5A03

Merck 016 - IND 7068

A Comparison of the Safety and Tolerability and Immunogenicity of Refrigerator Stable Measles, Mumps, Rubella, and Varicella Combination vaccine ProQuad™ (Refrigerated) versus ProQuad™ (Frozen) in Healthy Children

Merck 006 – IND not listed in protocol Product number = V260

Safety and Efficacy of Pentavalent (G1,G2,G3,G4, and P1) Human-Bovine Reassortant Rotavirus Vaccine in Healthy Infants

DMID Smallpox

A Multicenter, Double Blind, Randomized Dose-Response Study of Dryvax Vaccine Against Smallpox in Previously Vaccinated Adults (DMID protocol 02-007)

DMID Smallpox

A Phase I/II Study to Evaluate the Safety and Preliminary Efficacy of Various Concentrations of Aventis Pasteur's Smallpox Vaccine, USP (APSV) IN Vaccinia-Naïve Adults (Protocol DMID 02-009)

2003

GSK 047 – IND 10663

Open, randomized, phase II, clinical trial to compare the immunogenicity and safety of a booster dose of GSK Biologicals' DTaP-IPV vaccine (Infanrix® -IPV) co-administered with a booster dose of Merck and Company's MMR®II, to that of separate injections of GSK Biologicals' DTaP vaccine (Infanrix®), Aventis Pasteur's IPV (IPOL®) and MMR®II administered as booster doses to healthy children 4 to 6 years of age –

Chiron V14P39 – IND 6426

A Phase 3, Randomized, Controlled, Single - blind Study to Evaluate the Safety and Tolerability of Menjugate in Healthy Children, Adolescents, and Adults.

Aventis M5A07 – IND 8502

Immunogenicity Assessment of Pentacel™ (Hybrid CP_{20/20/5/3}DT-mIPV//PRP-T) when Given at Different Times from or Concurrently with a Pneumococcal Conjugate Vaccine

KAISER PERMANENTE VACCINE STUDY CENTER CLINICAL TRIALS

Aventis P3T10 – IND 3397

Safety And Immunogenicity Of DAPTACEL® (CP_{10/5/5/3}DT Aventis Pasteur 5-Component Pertussis Vaccine in Combination with Tetanus And Diphtheria Toxoids Adsorbed) Administered as a 5th Dose with IPV and MMR in 4- To 6- Year Old Children Previously Immunized with Pentacel™ (HCP_{20/20/5/3} DT-mIPV//PRP-T

2004

Chiron V59P4 – IND 11278

A Phase 2, Randomized, Double-Blind, Multi-Center Trial to Evaluate the Safety and Immune Response of Different Formulations of Chiron Meningococcal ACWY Conjugate Vaccine With or Without Aluminum Phosphate Adjuvant Administered to Healthy Toddlers 12 to 16 Months of Age and to Assess the Safety and Immunogenicity of a Single-Dose of Licensed Meningococcal Polysaccharide Vaccine, Menomune® when Administered to Children 3-5 Years of Age (Open Label)

GSK 232 – IND 3200

A Phase IIIb, open, randomized, controlled, multicenter study of the immunogenicity and safety of GlaxoSmithKline Biologicals' inactivated hepatitis A vaccine (Havrix®) [720 EI.U/0.5 mL dose] administered on a 0, 6-month schedule concomitantly with GlaxoSmithKline Biologicals' DTaP vaccine (Infanrix®) and Aventis Pasteur's Haemophilus b conjugate (Tetanus Toxoid Conjugate) vaccine (ActHIB®) in healthy children 15 months of age

Aventis TDC01 – IND 11474

Immunogenicity and Safety of Canadian Manufactured Tetanus and Diphtheria Toxoids Adsorbed (Td) for Adult Use Vaccine compared with U.S. Manufactured Tetanus and Diphtheria Toxoids Adsorbed for Adult Use Vaccine in Persons 60 Years of Age and Older and Immunogenicity and Safety of Canadian Td Vaccine in Persons 11 through 59 Years of Age

GSK 040 – IND 5505

A double-blind, randomized, controlled study to evaluate the immunogenicity and safety of GlaxoSmithKline Biologicals' herpes simplex candidate vaccine (gD2-AS04) in healthy HSV seronegative and seropositive female subjects aged 10 – 17 years.

MedImmune MI-CP111 – IND 9204

A Randomized, Double Blind Trial To Assess the Safety and Relative Efficacy Of CAIV-T Against Inactivated Influenza Vaccine In Children 6-59 Months Of Age

2005

GSK 048 – IND 10663

A phase III, open (double-blind for consistency lots), randomized, single center, with satellite sites, clinical trial of the safety, immunogenicity and consistency of three manufacturing lots of GSK Biologicals' DTaP-IPV candidate vaccine compared to that of separate injection of GSK Biologicals' DTaP vaccine (Infanrix) and...

...Aventis Pasteur's IPV vaccine (IPOL) administered as booster dose to healthy children 4 to 6 years of age, each co-administered with Merck and Company's MMR vaccine (M-M-R II)

2006

Merck ProQuad

An Open, Randomized, Multicenter Study of the Safety, Tolerability, and Immunogenicity of ProQuad™ Given Concomitantly with a Fourth Dose of PREVNAR™ and a Third Dose of IPOL™ in Healthy Children 12 to 15 Months of Age (Merck 019-00)

MBL Cdiff MAB

A Phase II Randomized, Double-Blind, Placebo Controlled Study of the Clinical Effectiveness of a Human Monoclonal Antibody to Clostridium difficile Toxin A [GS-CDA1] and a Human Monoclonal Antibody to Clostridium difficile Toxin B [MDX-1388] in Patients being Treated for Clostridium difficile Associated Disease (MBL Protocol No. CA-GCDX-06-02)

Novartis MenACWY

A Phase 3, Randomized, Observer-Blind, Controlled, Multi-Center Study to Evaluate the Lot to Lot Consistency of Novartis Meningococcal ACWY Conjugate Vaccine when One Dose is Administered to Healthy Adolescents 11-18 Years of Age and to Compare the Safety and Immunogenicity of...

KAISER PERMANENTE VACCINE STUDY CENTER CLINICAL TRIALS

...Novartis Meningococcal ACWY Conjugate Vaccine with that of Licensed Meningococcal ACWY Conjugate Vaccine (Menactra™) when One Dose is Administered to Healthy Subjects 11-55 Years of Age (Novartis V59P13)

MBL Cdiff MAB

A Phase II Randomized, Double-Blind, Placebo-Controlled Study of the Clinical Effectiveness of a Human Monoclonal Antibody to Toxin A [CDA1] in Patients being Treated for Clostridium difficile Associated Diarrhea (CDAD) (CA-CDA1-05-02 Version 1)

2007

Novartis MenACWY V59P14

A Phase III, Open Label, Randomized, Parallel Group, Multi Center Study to Evaluate the Safety and Immunogenicity of Novartis Meningococcal ACWY Conjugate Vaccine When Administered with Routine Infant Vaccinations to Healthy Infants (Novartis V59P14)

Novartis MenACWY V59P21

A Phase 3, Open-Label, Randomized, Multi-Center Study to Evaluate the Safety and Immunogenicity of Proquad Vaccine when Administered Concomitantly with Novartis Meningococcal ACWY Conjugate Vaccine to Healthy Toddlers (Novartis Protocol No. V59P21)

Protein Sciences FluBIOk

Evaluation of the Safety and Reactogenicity of FluBIOk, Trivalent Recombinant Baculovirus-Expressed Hemagglutinin Influenza Vaccine, and Comparison of the Immunogenicity, Efficacy and Effectiveness of FluBIOk to a Licensed Egg-Grown Influenza Vaccine in Adults Aged 50 to 64 (Protocol No. PSC06)

GSK Fluarix

A Phase III, Single-Blind, Randomized Study to Evaluate the Immunogenicity and Safety of Fluarix (GSK Biologicals) Compared with Fluzone (Aventis Pasteur/Sanofi) Administered Intramuscularly in Children (6 months and older) (GlaxoSmithKline Biologicals Protocol No. 104858)

2008

GSK 054

Immunogenicity of GlaxoSmithKline Biologicals' MMRV Vaccine vs. ProQuad, when Co-administered with Hepatitis A and Pneumococcal Conjugate Vaccines to Children 12-14 Months of Age (GlaxoSmithKline Biologicals Protocol No. 110058 [MMRV-054]) PRI

Sanofi Td517

2008 Safety and Immunogenicity of Tdap Vaccine Compared to DTaP Vaccine as Fifth Dose Booster in Children 4 to 6 Years of Age (Sanofi Pasteur Protocol No. Td517)

GSK 062 MenACWY

A Phase II, Open, Multi-Center Study to Evaluate the Long-Term Antibody Persistence at 1 Year, 3 Years and 5 Years After the Administration of One or Two Doses of GlaxoSmithKline (GSK) Biologicals' Meningococcal Serogroups A, C, W-135, Y-Tetanus Toxoid Conjugate (MenACWY-TT) Vaccine in Healthy Toddlers at 9-12 Months of Age, and to Evaluate the Safety and Immunogenicity of a Booster Dose of MenACWY-TT Administered 5 Years Post-Primary Vaccination (GlaxoSmithKline Biologicals Protocol No. 112021) [MENACWY-TT-062 EXT: 055 Y1, 3, 5]

GSK 059 MenACWY

A phase II, open, controlled, multi-center study to evaluate the long-term antibody persistence at 1 year, 3 years and 5 years after the administration of one dose of GlaxoSmithKline (GSK) Biologicals' meningococcal serogroups A, C, W-135, Y-tetanus toxoid conjugate (MenACWY-TT) vaccine versus one dose of sanofi-pasteur's meningococcal serogroups A, C, W-135 and Y-diphtheria toxoid conjugate vaccine (Menactra®) in healthy adolescents/adults aged 10-25 years and to evaluate the safety and immunogenicity of a booster response to MenACWY-TT vaccine administered at 5 years post-primary vaccination with MenACWY-TT or Menactra® (GlaxoSmithKline Biologicals Protocol No. 111670 [MenACWY-TT-059 EXT:052 Y1, 3, 5]) GSK 59

Safety and immunogenicity of heptavalent pneumococcal CRM₁₉₇ conjugate vaccine in infants and toddlers

HENRY R. SHINEFIELD, MD, STEVEN BLACK, MD, PAULA RAY, MPH, IH CHANG, PHD, NED LEWIS, MPH, BRUCE FIREMAN, MA, JILL HACKELL, MD, PETER R. PARADISO, PHD, GEORGE SIBER, MD, ROBERT KOHBERGER, PHD, DACE V. MADORE, PHD, FRANK J. MALINOWSKI, MD,* ALAN KIMURA, MD, PHD,† CHINH LE, MD, IRENE LANDAW, MD, JANET AGUILAR, MD AND JOHN HANSEN, BA

Objectives. The objectives of this study were (1) to determine the safety and immunogenicity of heptavalent pneumococcal CRM₁₉₇ conjugate (PNCRM7) vaccine in infants and (2) to determine the effect of concurrent hepatitis B immunization during the primary series and the effect of concurrent diphtheria and tetanus toxoid and acellular pertussis [DTaP (ACEL-IMUNE)] and conjugate CRM₁₉₇ *Haemophilus influenzae* type b [HbOC (HibTITER) immunization at time of the booster dose on the safety and immunogenicity of PNCRM7 and these other concurrently administered vaccines.

Methods. This was a randomized double-blinded study in 302 healthy infants in the Northern California Kaiser Permanente (NCKP) Health Plan. Infants received either PNCRM7 vaccine or meningococcal group C conjugate vaccine as a control at 2, 4 and 6 months of age and a booster at 12 to 15 months of age. Study design permitted the evaluation of immunology and safety of concurrent administration of routine vaccines. Antibody titers were determined on blood samples drawn before and 1 month after the primary series and the booster dose.

Results. After the third dose of PNCRM7 geometric mean concentrations (GMCs) ranged from 1.01 for serotype 9V to 3.72 $\mu\text{g/ml}$ for serotype 14. More than 90% of all subjects had a post-third dose titer of $\geq 0.15 \mu\text{g/ml}$ for all serotypes, and the

percentage of infants with a post-third dose titer of $\geq 1.0 \mu\text{g/ml}$ ranged from 51% for type 9V to 89% for type 14. After the PNCRM7 booster dose, the GMCs of all seven serotypes increased significantly over both post-Dose 3 and pre-Dose 4 antibody levels. In the primary series there were no significant differences in GMCs of pneumococcal antibodies between the subjects given PNCRM7 alone or concurrently with hepatitis B vaccine. At the toddler dose concurrent administration of PNCRM7 and DTaP and HbOC resulted in a near conventional threshold for statistical significance of a post-Dose 4 GMC for serotype 23F [alone 6.75 $\mu\text{g/ml}$ vs. concurrent 4.11 $\mu\text{g/ml}$ ($P = 0.057$)] as well as significantly lower antibody GMCs for *H. influenzae* polyribosylribitol phosphate, diphtheria toxoid, pertussis toxin and filamentous hemagglutinin. For all antigens there were no differences between study groups in defined antibody titers that are considered protective.

Conclusion. We conclude that PNCRM7 vaccine was safe and immunogenic. When this vaccine was administered concurrently at the booster dose with DTaP and HbOC vaccines, lower antibody titers were noted for some of the antigens when compared with the antibody response when PNCRM7 was given separately. Because the GMCs of the booster responses were all generally high and all subjects achieved similar percentages above predefined antibody titers, these differences are probably not clinically significant.

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 associated by the parents, with measles, mumps, and rubella vaccination in eight of the 12 children, with measles infection in one child, and otitis media in another. All 12 children had intestinal abnormalities ranging from lymphoid nodular hyperplasia to atrophic ulceration. Histology showed patchy chronic inflammation in 11 children and reactive ileal lymphoid hyperplasia in seven, but no granulomas. Behavioural disorders included autism (nine), disintegrative psychosis (one), and possible postviral or vaccinal encephalitis (two). There were no focal neurological abnormalities and MRI and EEG tests were normal. Abnormal laboratory results were significantly raised urinary methylmalonic acid compared with age-matched controls (p=0.03), low haemoglobin in four children, and low serum IgA in four children.

Interpretation We identify associated gastrointestinal disease and developmental regression in a group of previously normal children, which was generally associated in time to possible environmental triggers.

Lancet 1998; **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 FRCS), **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 period of apparent normality, lost acquired skills, including communication. They all had gastrointestinal symptoms, including abdominal pain, diarrhoea, and bloating and, in some cases, food intolerance. We describe the clinical findings, and gastrointestinal features of these children.

Patients and methods

12 children, consecutively referred to the department of paediatric gastroenterology with a history of a pervasive developmental disorder with loss of acquired skills and intestinal symptoms (diarrhoea, abdominal pain, bloating and food intolerance), were investigated. All children were admitted to the ward for 1 week, accompanied by their parents.

Clinical investigations

We took histories including details of immunisations and exposure to infectious diseases, and assessed the children. In 11 cases the history was obtained by the senior clinician (JW-S). Neurological and psychiatric assessments were done by consultant staff (PH, MB) with HMS-4 criteria.¹ Developmental assessments included a review of prospective developmental records from parents, 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

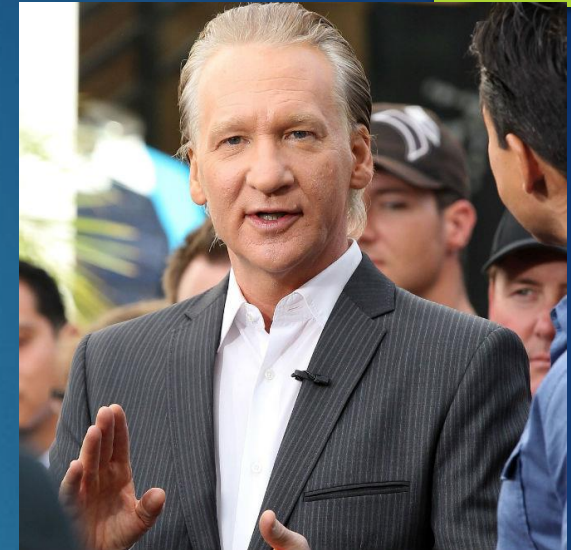
Thyroid function, serum long-chain fatty acids, and cerebrospinal-fluid lactate were measured to exclude known causes of childhood neurodegenerative disease. Urinary methylmalonic acid was measured in random urine samples from eight of the 12 children and 14 age-matched and sex-matched normal controls, 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



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Famous experts on vaccine safety



"Something is there with vaccines, because they're not tested in some ways the way other medicines are, and they're just taken for granted and mandated in some states. And people do get sick from it."



"I, as a parent of a child who has autism, am concerned..."

And I want to know the truth."

- Robert De Niro





AUTISM'S **FALSE** PROPHETS

BAD SCIENCE, RISKY MEDICINE,
AND THE SEARCH FOR A CURE

PAUL A. OFFIT

DEADLY CHOICES

— HOW THE —
ANTI-VACCINE
— MOVEMENT —
THREATENS
— **US ALL** —

PAUL A. OFFIT, M.D.

BAD ADVICE

Or Why Celebrities, Politicians,
and Activists Aren't Your Best Source
of Health Information



PAUL A. OFFIT, M.D.

Anti Vaccine Pseudo Science

The 4 most dreaded words in the English language: "I've done my research."



Leave the cows alone.

Ohio: 27 out of 28 persons who contracted the mumps were vaccinated for the mumps.

Princeton: 7 out of 7 students who contracted meningitis were vaccinated for meningitis.

San Diego: 5 out of 5 persons who contracted whooping cough were vaccinated for the whooping cough.

Herd immunity doesn't work.

Question the vaccines, not the unvaccinated.


Age of Autism



HIDDEN DANGERS OF VACCINATIONS

Information Session

Monday, Dec. 3 7-8 p.m.




YOU WILL LEARN:

- How to **AVOID** vaccine-related injuries in your child!
- The most common **SIDE-EFFECTS** of vaccines.
- Why **MANY** Canadians are saying "**NO**" to vaccines.
- The **SECRET INGREDIENTS** to watch for in many vaccines.
- **HOW** to **INCREASE** your child's natural immunity.

Held at:

Life Chiropractic and Whiplash Centre
80 Guelph St. Georgetown, Ontario
905-873-1871 www.painfree.ca

Guest Speaker: Cynthia Simmons, HD. Dr. of Homeopathy and Health coach
Former Pharmaceutical Clinical Research Consultant



Cynthia Simmons, HD

What's an Immunization Champion to Do?



Analyze the Problems

Barriers to Immunization

- Physical barriers

- Waiting time
- Distance
- Discomfort



- Psychological barriers

- Discourtesy
- Endangered privacy



- Changing Schedules
- Prompts
- Data (new/returning)
- Reminders
- MD/LVN/RN Time
- Commitment

IDENTIFY AND ELIMINATE MISSED OPPORTUNITIES

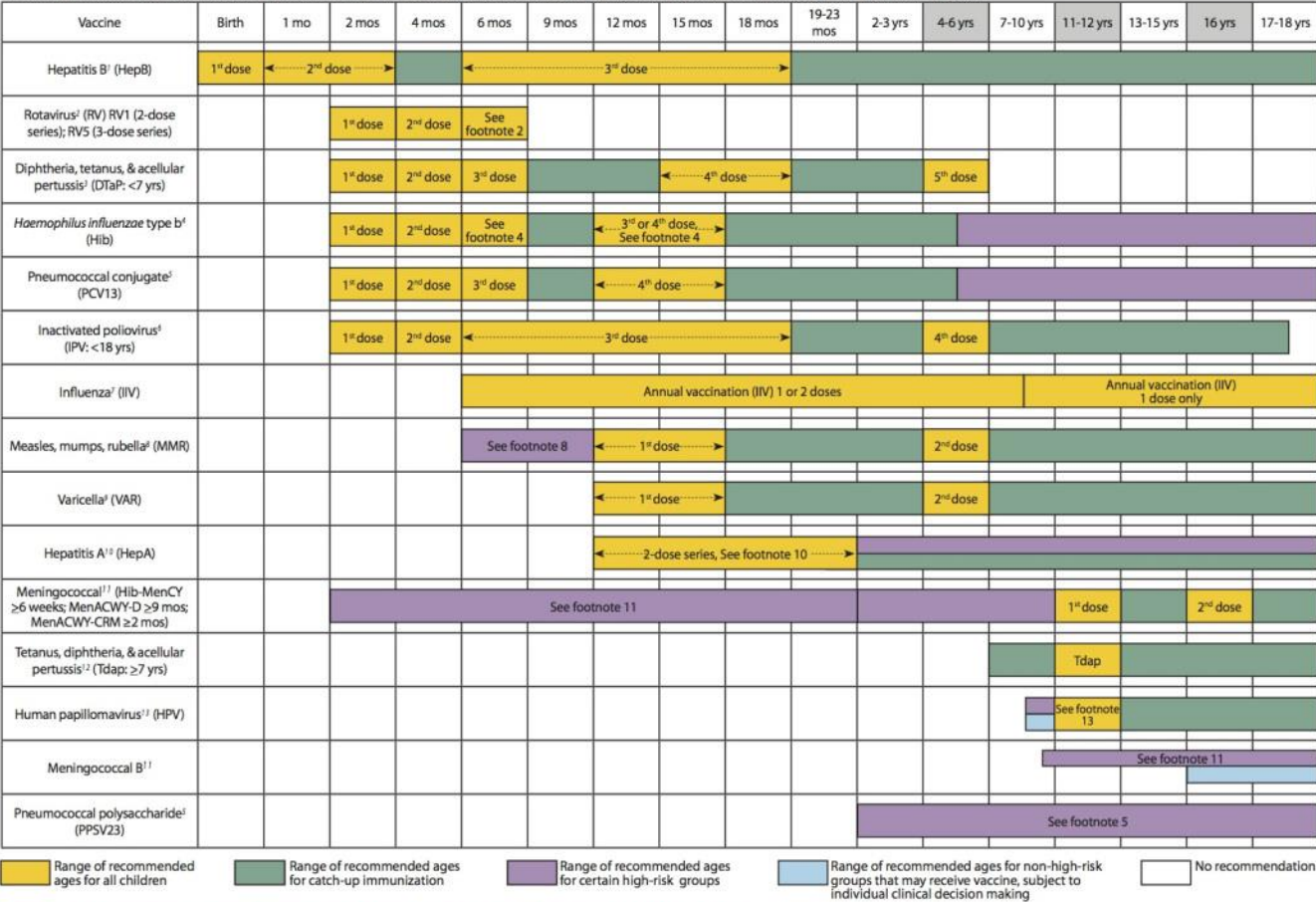
- Language
- Cultural Barriers
- Gender ?

2017 Childhood Immunization Schedule

Figure 1. Recommended Immunization Schedule for Children and Adolescents Aged 18 Years or Younger—United States, 2017.

(FOR THOSE WHO FALL BEHIND OR START LATE, SEE THE CATCH-UP SCHEDULE [FIGURE 2]).

These recommendations must be read with the footnotes that follow. For those who fall behind or start late, provide catch-up vaccination at the earliest opportunity as indicated by the green bars in Figure 1. To determine minimum intervals between doses, see the catch-up schedule (Figure 2). School entry and adolescent vaccine age groups are shaded in gray.



NOTE: The above recommendations must be read along with the footnotes of this schedule.

TABLE 3. Recommended schedule for routine active vaccination of infants and children*

Vaccine	At birth (before hospital discharge)	1–2 months	2 months†	4 months	6 months	6–18 months	12–15 months	15 months	4–6 years (before school entry)
Diphtheria-tetanus- pertussis [‡]			DTP OPV	DTP OPV	DTP OPV**			DTaP/DTP†	DTaP/DTP OPV
Polio, live oral									
Measles-mumps- rubella							MMR		
<i>Haemophilus</i> <i>influenzae</i> type b conjugate HbOC/PRP-T ^{§,} PRP-OMP							Hib ^{††} Hib ^{††}		
Hepatitis B*** Option 1 Option 2									

*See Table 4 for the recommended immunization schedule for infants and children up to their seventh birthday who do not begin the vaccination series at the recommended times or who are >1 month behind in the immunization schedule.

† Can be administered as early as 6 weeks of age.

‡ Two DTP and Hib combination vaccines are available (DTP/HbOC [TETRAMUNE™]; and PRP-T [ActHIB™, OmniHIB™] which can be reconstituted with DTP vaccine produced by Connaught).

† This dose of DTP can be administered as early as 12 months of age provided that the interval since the previous dose of DTP is at least 6 months. *Diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP)* is currently recommended only for use as the fourth and/or fifth doses of the DTP series among children aged 15 months through 6 years (before the seventh birthday). Some experts prefer to administer these vaccines at 18 months of age.

**The American Academy of Pediatrics (AAP) recommends this dose of vaccine at 6–18 months of age.

†† The AAP recommends that two doses of MMR should be administered by 12 years of age with the second dose being administered preferentially at entry to middle school or junior high school.

§ HbOC: [HibTITER®] (Lederle Praxis). PRP-T: [ActHIB™, OmniHIB™] (Pasteur Merieux). PRP-OMP: [PedvaxHIB®] (Merck, Sharp, and Dohme). A DTP/Hib combination vaccine can be used in place of HbOC/PRP-T.

|| After the primary infant Hib conjugate vaccine series is completed, any of the licensed Hib conjugate vaccines may be used as a booster dose at age 12–15 months.

*** For use among infants born to HBsAg-negative mothers. The first dose should be administered during the newborn period, preferably before hospital discharge, but no later than age 2 months. Premature infants of HBsAg-negative mothers should receive the first dose of the hepatitis B vaccine series at the time of hospital discharge or when the other routine childhood vaccines are initiated. (All infants born to HBsAg-positive mothers should receive immunoprophylaxis for hepatitis B as soon as possible after birth.)

††† Hepatitis B vaccine can be administered simultaneously at the same visit with DTP (or DTaP), OPV, Hib, and/or MMR.

1989

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IDENTIFY AND ELIMINATE MISSED OPPORTUNITIES

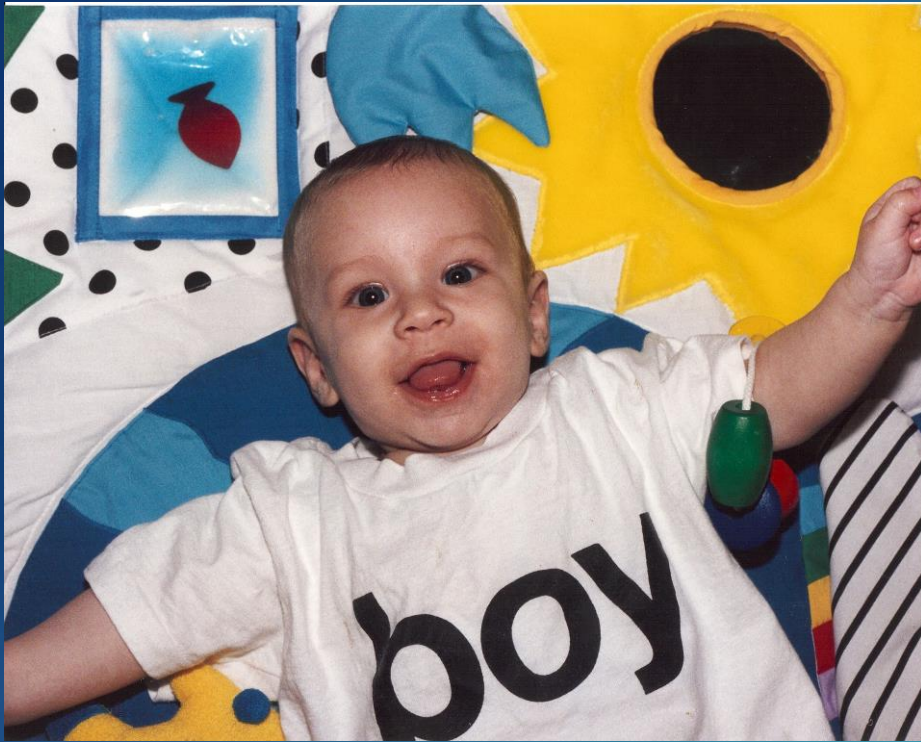
- Language
- Cultural Barriers
- Gender ?

Teens and Preteens



SPECIAL CONSIDERATIONS

- Activities/Schedules
- Consent
- Fainting
- HPV Relation to Gender & **SEX**



2007 ACIP

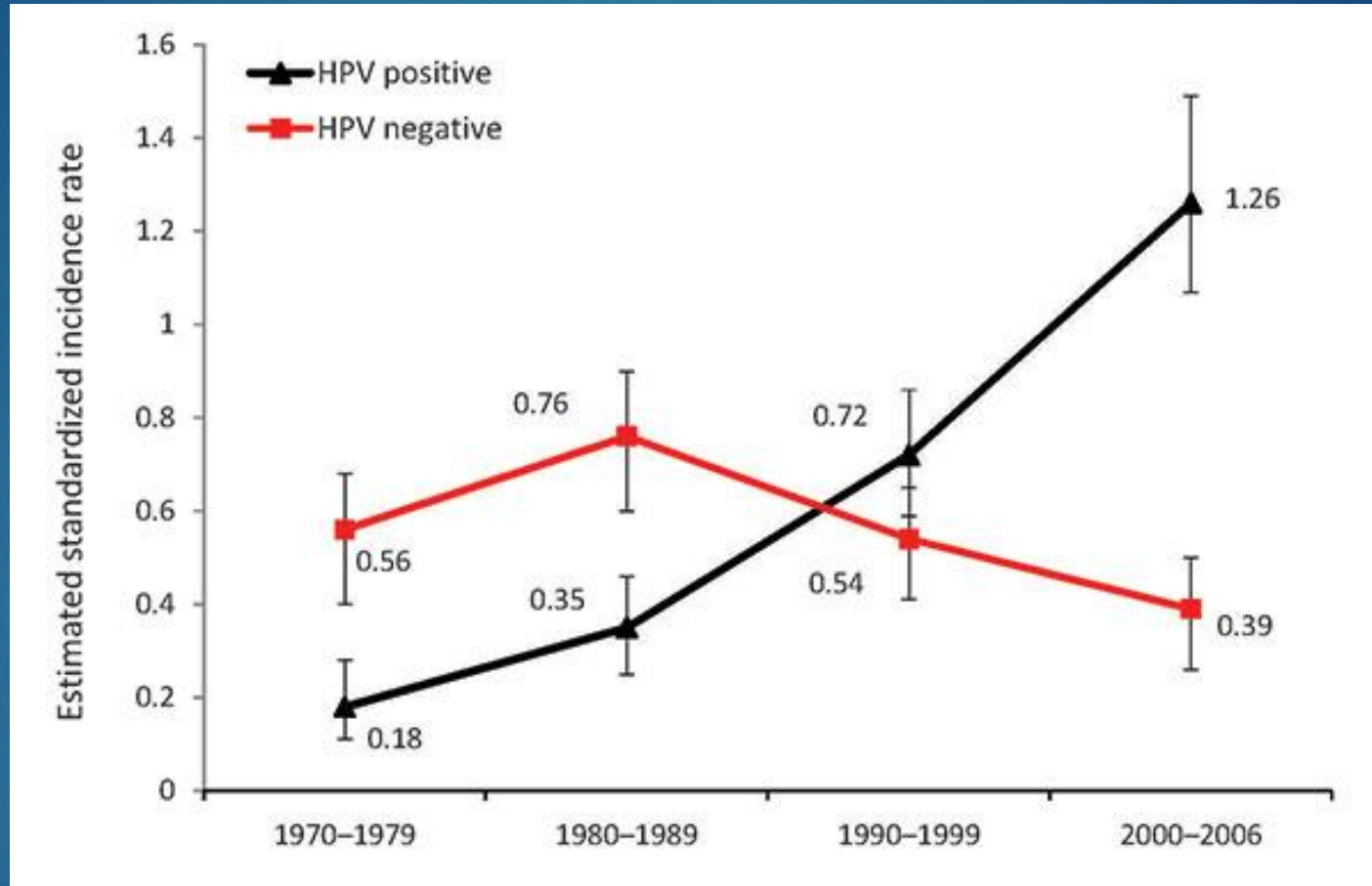
Quadrivalent HPV vaccine is not licensed for use among males. Although data on immunogenicity and safety are available for males aged 9–15 years, no data exist on efficacy in males at any age. Efficacy studies in males are under way.



2011 ACIP

Adding male vaccination to female-only vaccination becomes more cost-effective when all HPV-associated health outcomes are included in the model and vaccine coverage of females is low

HPV Related Oropharyngeal Cancers



Epidemics are effective treatments for Vaccine Hesitancy




NOW WHAT????



AUTISM'S **FALSE** PROPHETS

BAD SCIENCE, RISKY MEDICINE,
AND THE SEARCH FOR A CURE

PAUL A. OFFIT



A mother's kiss: Too many, too soon?

The average healthy adult human mouth is home to more than 600 unique species of bacteria and a very high number of viruses. Every milliliter of saliva contains over 100 million bacteria.

Every time a mother kisses her baby, the baby's immune system is exposed to magnitudes more antigens than are present in the entire US childhood immunization schedule.

A well-functioning immune system is a marvel, protecting against countless viruses and bacteria even in the youngest children. It can handle the challenge presented by the US immunization schedule and it can handle the even-greater challenge from every mother's kiss.

Do not worry about 'too many, too soon'.
Vaccinate your baby on time, every time.

www.tinyurl.com/kiss-antigens

Refutations to Anti-Vaccine Memes

"Now, here, you see, it takes all the running you can do just to keep in the same place. If you want to get somewhere else, you must run at least twice as fast!"

- Red Queen from *Through the Looking Glass*



2012: AB 2109
Advice before Exemption

2015: SB 277
No Personal Belief Exemptions

2019?: SB 276
Review Medical Exemptions

KAISER PERMANENTE

PEDIATRICS



Communication, Not Confrontation



KP PEDIATRICS COMMUNICATION CURRICULUM

1. Relax, Don't Debate
2. Clear Recommendations
3. We All Want the Same Thing
4. Words Matter

Protection, Protection, Protection

By the Winner of the NATIONAL BOOK CRITICS CIRCLE AWARD

EULA BISS

ON IMMUNITY

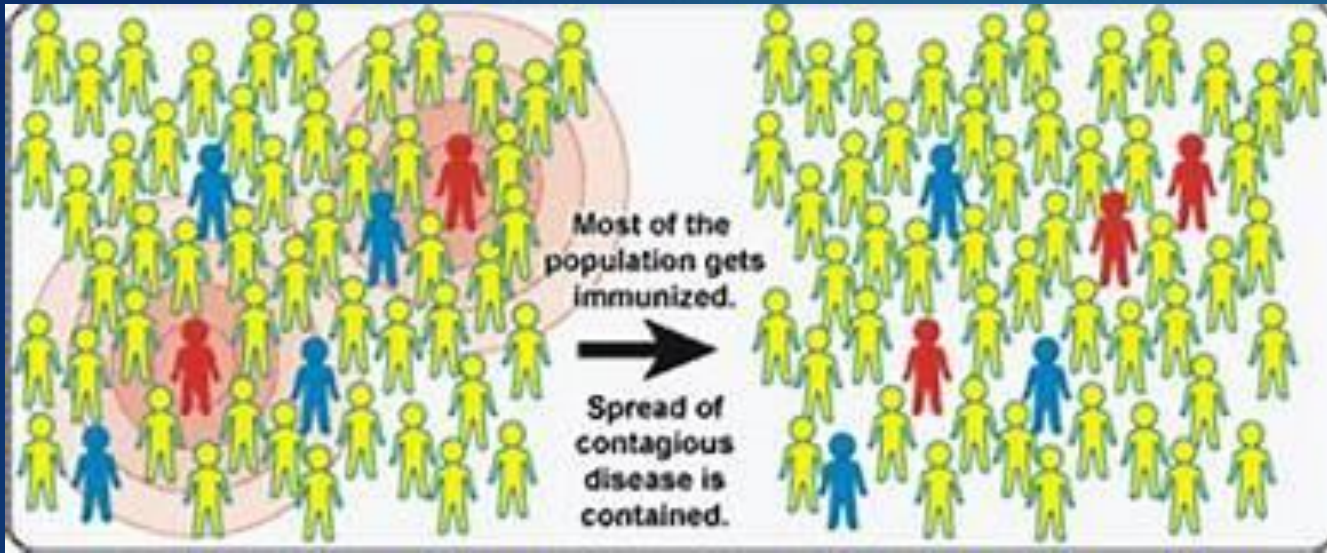
AN INOCULATION

"Biss is telling us the story of our country—one we never saw coming."

—Chicago Tribune, on *Notes from No Man's Land*

VACCINE HESITANT PARENTS: What I learned

- It's not crazy to doubt doctors or pharma (& not about my Ego!)
- They've never seen these diseases,&their [grand] parents have forgotten
- We agree on most choices
- We make Risk/Benefit analyses unconsciously all the time
- It feels riskier to do SOMETHING than NOTHING**
- Belief trumps Science**
- "Nature" can be Cruel
- Vaccines are not *UNnatural*. They bend nature to our purpose
- DON'T TALK ABOUT THE HERD!!!**



It is not my responsibility to vaccinate my child to protect immune compromised people through herd immunity. First and foremost, my responsibility is to my child.

**I will not set my child
on fire to keep someone
else warm.**

What parent would knowingly risk their child's life for the sake of the herd? Would you? My child is not a human shield. Secondly, herd immunity is a myth. We do not have vaccine induced herd immunity and never have.

Anonymous



Community Protection: For **ALL** our Kids





Thank You!