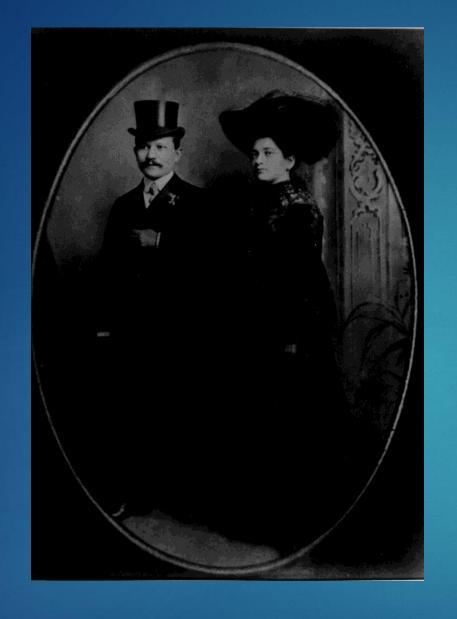


A Brief [Personal] History of Time Immunizations

THE MAKING OF AN IMMUNIZATION CHAMPION AT KAISER PERMANENTE

Irene S Landaw, MD

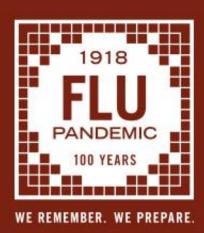


1890's











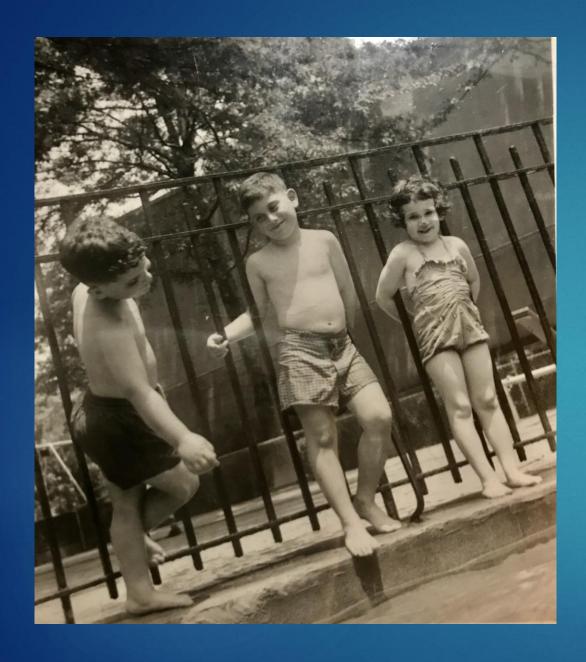


Smallpox Rash - Distribution



World Health Organization (WHO)













Polio Shots Given botte Today ... 12,000 in Area

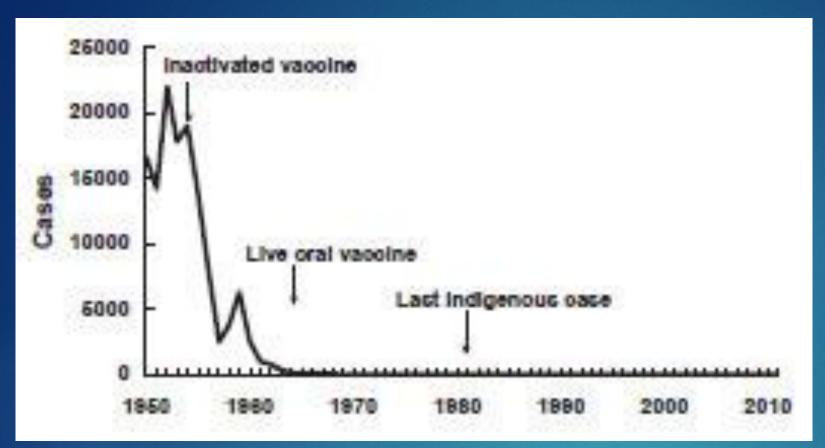
Compress Award Compre



Rusk Urges Lay Interest In Policies







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

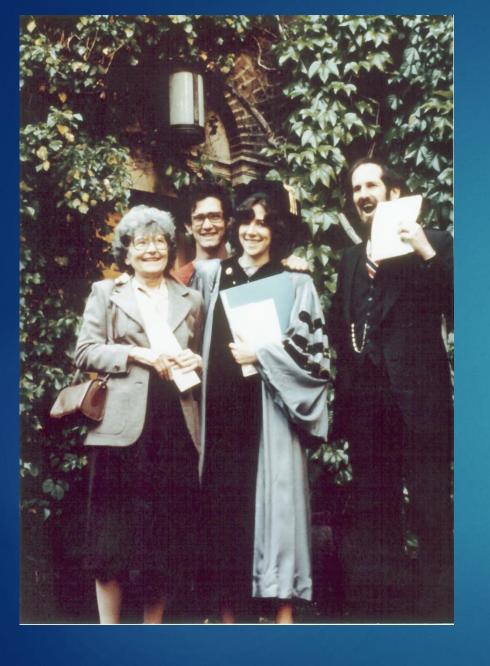
1980-1999: 165 Cases, 95% VAPP

1993: Last Imported Case

1999: Last Indigenous VAPP

2000: Oral Polio Vaccine

discontinued in US



1981



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

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

Pneumocystis Pneumonia — Los Angeles

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

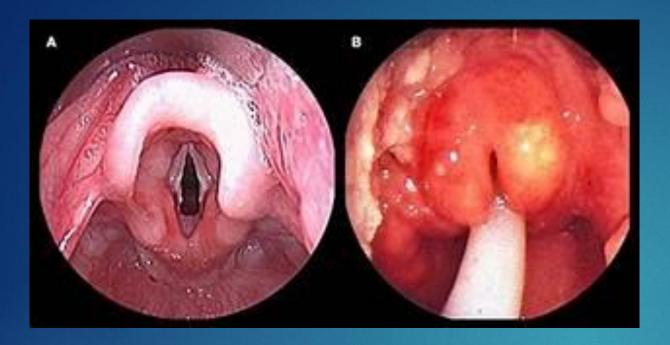
Patient 1: A previously healthy 33-year-old man developed P. carinii pneun oral mucosal candidiasis in March 1981 after a 2-month history of fever assoc elevated liver enzymes, leukopenia, and CMV viruria. The serum compleme CMV titer in October 1980 was 256; in May 1981 it was 32. The patient's deteriorated despite courses of treatment with trimethoprim-sulfamethoxa stamidine, and acyclovir. He died May 3, and postmortem examinati





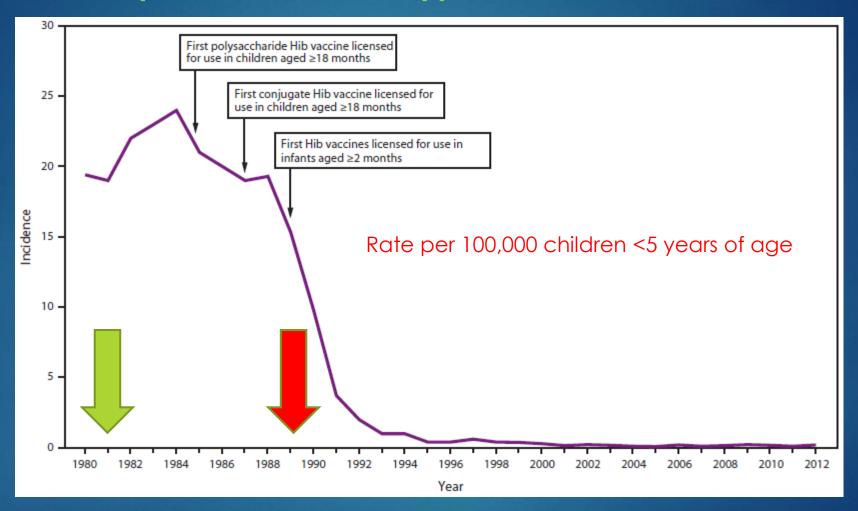


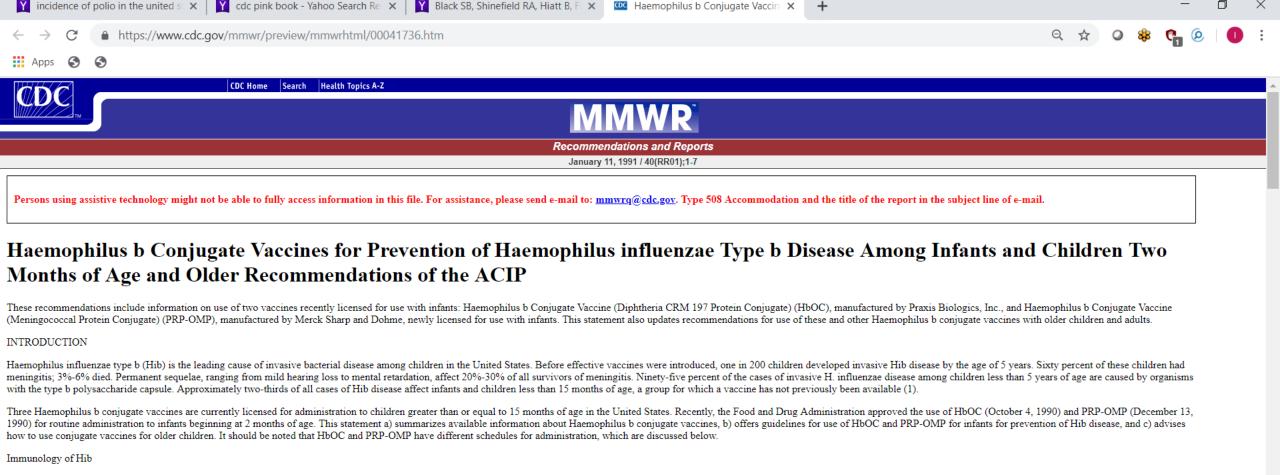
1991-1994





Haemophilus Influenzae Type B Infections





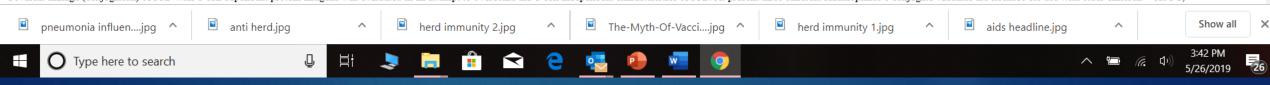
The polyribosylribitol phosphate (PRP) capsule of Hib is a major virulence factor for the organism. Antibody to PRP is the primary contributor to serum bactericidal activity, and increasing levels of antibody are associated with decreasing risk of invasive Hib disease. The human immune response to PRP 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

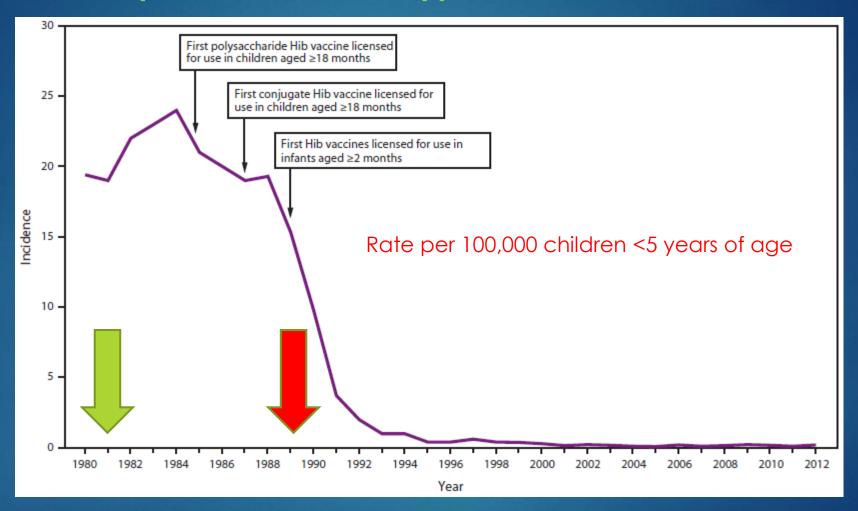
Vaccines derived from PRP alone (polysaccharide vaccines) were developed in the 1970s. After demonstration of safety, immunogenicity, and induction of serum bactericidal activity, an efficacy of 90% (95% confidence interval (CI) = 50%-95%) was shown for one dose of vaccine given to children 18-71 months 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



1988 Praxis HbOC Trial - Phase III	Merck Varicella Trial 1133 - Phase III	Postmarketing Eva of Merck Varicella
-25,000 enrolled -31 sites	SmithKline HHDTP Trial 212616/003 – Phase II	<u>1996</u>
<u>1990</u>	1994	<u>SmithKline Varicelle</u>
Lederle Post Licensure Surveillance of	Chiron APDT Trial V8P1 Amendment 2 – Phase	1997
		Chiron Kindergarte
-Study Population 250,000 -31 sites	Merck Varicella Trial 1134 – Phase II	Phase III
	-Start Date 05/94 -600 enrolled	Merck VAQTA (H
<u>Lederle HDTP Trial – Phase III</u>	-6 sites	Marketing Trial -
1991		-Start date -
Lederle ADTP/HbOC Trial – Phase II	<u>Lederle ADTP/HbOC Trial 91-2 – Phase II</u>	-Enrollment - -31 sites
-400 enrolled	Lederle ADTP/HbOC Trial 91-5 – Phase III	01 31103
-7 sites		Wyeth Lederle D11
1992	SmithKline DTPa-HB Trial 222074/001 - Phase II	<u>Bridging Trial – Pha</u>
Merck Varicella Trial 1076 – Phase II		
Postmarketing Evaluation of Lederle DTaP		Merck Varicella Pe Phase IV
(ACEL-IMUNE) – Phase IV	Lederle Pneumococcal Trial D118-P7 – Phase II	THE PERSON NAMED IN COLUMN 2 IN COLUMN 2
		SmithKline DTaP/He
Merck Varicella Trial 004-007 – Phase II	Merck Varicella Persistence Trial 004/007 –	<u>Phase III</u>
Chiron APDT Trial V8P1 - Phase III	Phase IV -Start Date - 07/95	Merck MMRV 008 -
	-2 sites	1998
<u>1993</u>	-Enrolled 150	Merck MMRV 009
Postmarketing Evaluation of Lederle HDTP		Nabi 1356 – Staphy
(TETRAMUNE) - Phase IV		Phase III
-Surveillance population - 20,000	-Start Date- 10/95	1999
-31 sites	-38,000 enrolled	Wyeth Lederle D11
Merck Varicella 10 Year Persistence Trial 1076	Ol sites	Booster dose of Pne

-21 sites

- Phase IV

lluation of Short Term Safety Vaccine- Phase II

<u>a Trial 208133/135 – Phase II</u>

en V8P1 Amendment 6 Trial -

01/97 10,000

8-P16 Pneumococcal se III

ersistence Trial 1133, 1134 –

epB/Hib 045/027 Trial – Phase II

- Phase II lococcus Type A Vaccine-8-P16 Amendment 1 – **Booster dose of Pneumococcal Vaccine Phase** Ш

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 (Prevnar™) Administered To Healthy Infants

2002

Aventis M5A03 - IND 8502

Lot –Consistency and Bridge Study of HCP 20/20/5/3 DT-mllPV/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

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 PentacelTM (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 El.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

200!

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 coadministered 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 abd Immunogenicity of...

...Novartis Meningococcal ACWY Conjugate Vacine with that of Licensed Meningcoccal ACWY Conjugate Vaccine (MenactraTM) 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 Reactogenciity 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
Coadministered with Hepatitis A and
Pneumococcal Conjugate Vaccines to
Children 12-14 Months of Age (GlaxoSmithKline
Biologicals Protocol No. 110058 [MMRV-054])
PRI

Sanofi Td517

2008Safety 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 Evaulate 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, Ytetanus toxoid conjugate (MenACWY-TT) vaccine versus one dose of sanofi-pasteur's meningococcal serogroups A, C, W-135 and Ydiphtheria 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 PNCRM7and 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 $3.72 \mu g/ml$ for serotype 14. More than 90% of all subjects had a post-third dose titer of $\geq 0.15 \mu g/ml$ for all serotypes, and the

percentage of infants with a post-third dose titer of ≥1.0 µg/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 PN-CRM7 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 μg/ml vs. concurrent 4.11 μg/ml (P = 0.057)] as well as significantly lower antibody GMCs for H. influenzæ 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 associate by the parents, with measles, mumps, and rub vaccination in eight of the 12 children, with meas infection in one child, and otitis media in ag All children had intestinal abnormalities lymphoid nodular hyperplasia to a ration. Histology showed patchy chronic inflat in 11 children and reactive ilea seven, but no granulomas. Be vioural diso s included autism (nine), disintegrative sy sis (one), a possible o). There were no postviral or vaccinal encephalitis focal neurological ab malities and and EEG tests were normal. Abnor al laboratory results are significantly raised urinary acid compared with age-03), low haemoglobin in four matched contro

Internation e idem associated gastrointestinal dia se and evelopmental regression in a group of previously amarom. It, which was generally associated in time of 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 Frocs, A Anthony MB, J Linnell Pao, A P Dhillon Merchah, S E Davies MRCParb) 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 part tof apparent normality, lost acquired skills, including communication. They all had gastrointestinal amptoms, uluding abdominal pain, diarrhoea, and to taing and, it some cases, food intolerance. We during the clinical fillings, and gastrointestinal feature of these children.

Patients and metions

12 children, conscrivel, a red to 3' department of paediatric gastra derology a hi cey of a pervasive developmental or der with loss accorded skills and intestinal symptoms arriva abdominate in, bloating and food intolerance); were invocated. All children were admitted to the ward for layeck, accompanyed by their parents.

nical investigations

took historia including details of immunisations and consure to infect us diseases, and assessed the children. In 11 case the history as obtained by the senior clinician (JW-S). Neuron of all psychiatric assessments were done by onsultant saff (PH, MB) with HMS-4 criteria. Developmental way 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 zones from cases 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

THE LANCET • Vol 351 • February 28, 1998

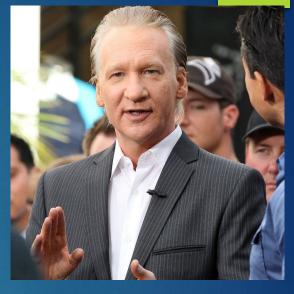


<u>This Photo</u> by Unknown Author is licensed under CC BY-NC

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



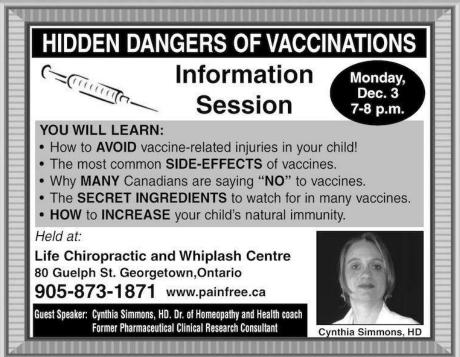
PAUL A. OFFIT, M.D.

Anti Vaccine Pseudo Science

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







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.

Vaccine	Birth	1 mo	2 mos	4 mos	6 mos	9 mos	12 mos	15 mos	18 mos	19-23 mos	2-3 yrs	4-6 yrs	7-10 yrs	11-12 yrs	13-15 yrs	16 yrs	17-18 y
Hepatitis B ¹ (HepB)	1"dose	⋖ 2 nd (dose >		<		3 rd dose										
Rotavirus ² (RV) RV1 (2-dose series); RV5 (3-dose series)			1º dose	2 nd dose	See footnote 2												
Diphtheria, tetanus, & acellular pertussis ³ (DTaP: <7 yrs)			1*dose	2 nd dose	3 rd dose			∢ 4 ⁿ d	ose>			5 th dose					
Haemophilus influenzae type b' (Hib)			1ª dose	2 rd dose	See footnote 4			otnote 4									
Pneumococcal conjugate ^s (PCV13)			1º dose	2 nd dose	3 rd dose		≺ 4 th (dose>									
Inactivated poliovirus ⁶ (IPV: <18 yrs)			1#dose	2 nd dose			3 rd dose		>			4 th dose					
Influenza ⁷ (IIV)							An	inual vaccina	tion (IIV) 1 o	or 2 doses				An	nual vaccina 1 dose o	ition (IIV) nly	
Measles, mumps, rubella ^a (MMR)					See foo	tnote 8	≺ 1 ^g (iose>				2 nd dose			- 10		
Varicella ^g (VAR)							≺ 1¤c	lose>				2 nd dose					
Hepatitis A ¹⁸ (HepA)							∢ 2-∢	dose series, S	ee footnote	10>							
Meningococcal ¹¹ (Hib-MenCY ≥6 weeks; MenACWY-D ≥9 mos; MenACWY-CRM ≥2 mos)						See foo	tnote 11							1 st dose		2 nd dose	
Tetanus, diphtheria, & acellular pertussis¹² (Tdap: ≥7 yrs)														Tdap			
Human papiliomavirus ¹³ (HPV)														See footnote 13			
Meningococcal B ¹¹															See footr	ote 11	
Pneumococcal polysaccharide ^s (PPSV23)													5	ee footnote	5		

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

JUST THE FOOTNOTES! (2017)

notes — Recommended Immunization Schedule for Children and Adolescents Aged 18 Years or Younger, UNITED STATES, 2017 For further guidance on the use of the vaccines mentioned below see: www.cdc.gov/vaccines/hcp/acin-recs/index.html.

vaccine recommendations for persons 19 years of age and older, see the Adult Immunization Schedule.

- For information on contraindications and precautions for the use of a vaccine and for additional information regarding that vaccine, vaccination providers should consult the ACIP General
- For information containable may be activately as the properties of the suce of a version was contained as a final production on an information of the production of the produc
- internation for devenues with primary and secondary immunodificancies, see fails to University of persons with primary and secondary immunodificancies, in General Recommendations on immunozation (ACPI), available at view.occ.gov/immunodificancies, see fails of University of Secondary immunodificancies, in Sinchedificancies, and immunozation (ACPI), available at view.occ.gov/immunoficancies, in Sinchedificancies, and immunozation (ACPI), available at view.occ.gov/immunoficancies, in Sinchedificancies, and immunozation (ACPI), available at view.occ.gov/immunoficancies, in Sinchedificancies, in Sinchedificancies
- ne Injury Compensation Program (VICP) is a no-fault alternative to the traditional legal system for resolving vaccine injury petitions. Created by the National Childhood Vaccin

- positive mothers, administer HepB vaccine and 0.5 ml of hepatitis B immune globulin (HBIG) within 12 hour
- For infants weighing less than 2,000 grams, adminis Determine mother's HBsAq status as soon as possible

- 6 weeks after the first dose. The final (third or fourth) no earlier than age 24 weeks

Rotavirus (RV) va-

RV1 [Rotarix] and RV5 [Ro

Administer a series of RV v

- within 24 hours of birth. For infants born to hepatitis B surface antigen (HBsAg)-
- brith. These finants should be tested for flosing and libody to HBsAg (anti-HBs) at age 9 through 12 months eferably at the next well-child visit) or 1 to 2 months er completion of the HepB series if the series was
- and, if mother is HBsAg-positive, also administer HBIG to infants weighing 2,000 grams or more as soon as possible,

- Catch-up vaccination:

- Catch-up vaccination: ses following the birth dose: The maximum age for th
- infants aged 15 weeks, 0 The maximum age for the months, 0 days. For other catch-up guid. Diphtheria and tetanus to
- IPV (Kinrix, Quadracel): 4:

- except for pneumococcal polysaccharide vaccine (PPSV23). For more information: see www.l
 - Catch-up vaccination:

 If dose 1 was administered at ages 12 through 14 mon administer a second (final) dose at least 8 weeks after dose 1, regardless of Hib vaccine used in the primary

 - If the first dose was administered at age 7 through 11 months, administer the second dose at least 4 weeks late and a third (and final) dose at age 12 through 15 months or 8 weeks after second dose, whichever is later. If first dose is administered before the first birthday and second close administered at younger than 15 month
 - For unvaccinated children aged 15-59 months,
 - 3. If any dose in the seri
 - For unvaccinated children aged 15–59 months, administer only 1 dose. For other catch-up guidance, see Figure 2. For catch-up guidance related to Mentillbirs, see the meningocota waccine footnotes and also MiWIF February 28, 2014 / 63(RR01):1-13, available at www.cdc.gov/mmwr/PDF/m of RV vaccine should
 - Children aged 12 through 59 months who are at increas risk for Hib disease, including chemotherapy recipients and those with anatomic or functional asplenia (including
 - sickle cell disease), human immunodeficiency virus (HIV infection, immunoglobulin deficiency, or early componen complement deficiency, who have received either no doses or only 1 dose of Hib vaccine before age 12 months should receive 2 additional doses of Hib vaccine, 8 week

 - transplant, regardless of vaccination history; doses should
 - be administered at least 4 weeks apart. A single dose of any Hib-containing vaccine should be tered to unimmunized* children and adolescent 15 months of age and older undergoing an elective splenectomy; if possible, vaccine should be administered at least 14 days before procedure.
 - S years or older. However, 1 dose of Hib vaccine should dministered to unimmunized* persons aged 5 s or older who have anatomic or functional asplenia

- Injury Act of 1986, it provides compensation to people found to be injured by certain vaccine/For further guidance on the use of the vaccines mentioned below, see: www.cdc.gov/vaccines/hcp/acip-recs/index.html
 - (including sickle cell disease) and unimmunized* persons 5 through 18 years of age with HIV infection.

 - prior to PPSV23 vaccination if possible. For children aged 2 through 5 years with any of cyanotic congenital heart disease and cardiac chronic lung disease (including asthma if treat
 - nephrotic syndrome; diseases associated with including malignant neoplasms, leukemias, lyn and Hodgkin disease; solid organ transplantati
 - of 3 doses of PCV13 was received previous?

 2. Administer 2 doses of PCV13 at least 8 we 3 doses of PCV13 was received previousl

 - dose of PCV13. For children aged 6 through 18 years who have or functional asplenia; congenital or acquired immunodeficiencies; HIV infection; chronic rer nephrotic syndrome; diseases associated with including malignant neoplasms, leukemias, lym and Hodgkin disease; generalized malignancy;
 - 1. If neither PCV13 nor PPSV23 has been rec ously, administer 1 dose of PCV13 now and PPSV23 at least 8 weeks later.

- - 2. If PCV13 has been received previously but PPSV23
 - ister 1 dose of PCV13 at least 8 weeks after the mos
 - For children aged 6 through 18 years with chronic hea and cardiac failure), chronic lung disease (including asthma if treated with high-dose oral corticosteroi
 - For further guidance on the use of the vaccines mentioned below, see: www.cdc.gov/vaccines/hcp/acip-recs/index.html. Influenza vaccines. (Minimum age: 6 months for inacti-Catch-up vaccination: vated influenza vaccine [IIV], 18 years for recombinan
 - Administer influenza vaccine annually to all children beginning at age 6 months. For the 2016–17 season use of live attenuated influenza vaccine (LAIV) is not
 - vaccine for the first time or who have not previously received ≥2 doses of trivalent or quadrivalent influenza vaccine before July 1, 2016. For additional guidance follow dosing guidelines in the 2016-17 ACIP influenza vaccine recommendations (see MMWR August 26,
 - For the 2017–18 season, follow dosing guidelines in the 2017–18 ACIP influenza vaccine recommendations.
- 2017-18 ACIP Influenza vaccine recommendations. For persons aged 9 years and older:

 Administer 1 dose.

 Measles, mumps, and rubella (MMRI) vaccine, (Minimum age: 12 months for routine vaccination).

 Routine vaccination:

 Administer a 2-dose series of MMRI vaccine at ages 12 descriptions. The personal contraction of the property of the propert
 - through 15 months and 4 through 6 years. The second dose may be administered before age 4 years, provided at Administer 1 dose of MMR vaccine to infants aged 6 through 11 months before departure from the United States for international travel, These children should b evaccinated with 2 doses of MMR vaccine, the first at age

 - have had 2 doses of MMR vaccine; the minimum interval

Varicella (VAR) vaccine, (Minimum age: 12 months) Administer a 2-dose series of VAR vaccine at ages 12

through 15 months and 4 through 6 years. The second dose may be administered before age 4 years, provided at least 3 months have elapsed since the first dose, if the second dose was administered at least 4 weeks after the risk conditions, see 'Menin vaccination of persons with other persons at increased

- If the first dose is administered at age 16 years or order, a booster dose is not needed.
 For other catch-up guidance, see Figure 2.
 Clinical discretion:
 Young adults aged 16 through 23 years (preferred age
- For any person aged 2 years
- aready received the Heap For further guidance on the use of the vaccines mentioned below, see; www.cdc.gov/vaccines/hcp/acip-recs/index.html

infection is desired. Catch-up vaccination:

- **HIV** infection — Children 14 months and aider who have not received a Special populations Sweeks apart. If Menactra is administered to a chil Administer 2 doses of Hep/ when splenia (including sickle cell disease) or HIV infection, do not administer Menactra until age 2 years and at least 4 weeks after the completion of
 - o Children with persistent complement component doses at least 12 weeks apart.

o All high-risk children

- [Menveo], 9 months for Men
- at age 11 through 12 years.
- Meningococcal B vaccination of persons with high-risk conditions and other persons at increased risk of disease: Children with anatomic or functional asplenia (including sickle cell disease) or children with persistent complemen omponent deficiency (includes persons with inherited or hronic deficiencies in C3, C5-9, properdin, factor D, factor

o Children with anatomic or functional asplenia or

a complete series. Administer 2 primary doses at

- doses at least 1 month apart, or a 3-dose series of frumenba, with the second dose at least 1-2 months
- For children who travel to or reside in countries in which neningococcal disease is hyperendemic or epidemic, including countries in the African meningitis belt or the
- belt or the Hajj because it does not contain serogroup

For children at risk during an outbreak attributable to a

Komstream Land
 Komstream Complete an age and formulation-appropriate series of MenHibrix, Menactra, or Menveo.

range is 16 through 18 years) who are not at increase risk for meningococcal disease may be vaccinated with a 2-dose series of either Bexsero (0, ≥1 month) or Trumenba

If the first dose is administered at age 13 through 15 years

18 years, with a minimum interval of at least 8 week

- the first. The two MenB vaccines are not interchangeable the same vaccine product must be used for all dose For MenACWY booster doses among persons with high-risk conditions, refer to MMWR 2013:62(RR02):1-22, at MMWR June 20: 2014 / 63(24):527-530, at www.cdc.or
- 5324 pdf, and MMWR November 4, 2016 /65(43):1189-1194. at www.cdc.gov/mmwr/volumes/6
- wr/pdfs/mm6543a3.pdf. For other catch-up recommendations for these persons and complete information on use of meningococcal vaccines, including guidance related to vaccination of persons at increased risk of infection, see meningococcal MMWR.
- If Menactra is to be administered to a child at high risk for meningococcal disease, it is recommended that Menactra be given either before or at the same time as DTaP. 12. Tetanus and diphtheria toxoids and acellular pertuss

 - and Adacel

 Mouther succhasion:
 Administer I dose of Idap vaccine to all adolescents aged
 11 through 12 years.
 Talap may be administered regardless of the interval since
 the last teatura and diphthreis taxouid-containing vaccine.
 Administer I dose of Idap vaccine to pregnant
 adolescent during wach pregnancy ligerelately during
 the object of the processing interval of the Idap of Persons aged 7 years and older who are not fully
 - immunized with DTaP vaccine should receive Tdap vaccine as 1 dose (preferably the first) in the catch-up series; if additional doses are needed, use Td vaccine. Fo children 7 through 10 years who receive a dose of Tdag as part of the catch-up series, an adolescent Tdap vaccin dose at age 11 through 12 years may be administered.
 - Persons aged 11 through 18 years who have not received Tdap vaccine should receive a dose, followed by tetanus and diphtheria toxoids (Td) booster doses every 10 year Inartwertent closes of FITaP varrings
 - If administered inadvertently to a child aged 7 through
 10 years, the dose may count as part of the catch-up
 series. This dose may count as the adolescent Tdap dose,
 - adolescent Tdap booster.
 For other catch-up guidance, see Figure 2.

- For sergogroup 8: Administer a 2-dose series of Bescero, with doses at least 1 month apart, or a 3-dose series of Trumenba, with the second dose at least 15 months after the first and the third dose at least 6 months after

 Administre a 2-dose series of Hi years for 4vHPV [Gardasil] and 9vHPV [Gardasil 9])
 - Routine and catch-up vaccination Administer a 7-dose series of HPV vaccine on a schedul of 0.6-12 months to all adolescents aged 11 or 12 year
 - pased on age at administration of the first dose.
 - ecommended immunization schedule is 2 doses of HF raccine at 0. 6-12 months.
 - vaccine at 0, 0-12 months.

 For persons intilating vaccination at age 15 years or older, the recommended immunization schedule is 3 does of HPV vaccine at 0, 1-2, 6 months.

 A vaccine dose administered at a shorter interval should be readministered at the recommended interval.

 In a 2-dose schedule of HPV vaccine, the minimum

 - 12 weeks between the second and third dose, and 5 dose is administered at a shorter interval, it should b

Special populations: For children with history of sexual abuse or assault.

- administer HPV vaccine beginning at age 9 years. Immunocompromised persons*, including those should receive a 3-dose series at 0. 1–2, and 6 month
- after initiating the vaccination series, no intervention i until after the pregnancy. Pregnancy testing is not
- ee MMWR December 16, 2016;65(49):1405-1408.

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	DTP	DTP			DTaP/DTP1	DTaP/DTP
Polio, live oral	1 1		OPV	OPV	OPV**	l .			OPV
Measles-mumps- rubella Haemophilus influenzae type b conjugate							MMR		
PRP-OMP ^{§§} Hepatitis B*** Option 1 Option 2							Hib11		

^{*}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.

⁵ 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).

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

¹¹ 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.

⁵⁵ 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.

11 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.)

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

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.

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?

Teens and Preteens





SPECIAL CONSIDERATIONS

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



2007 ACIP

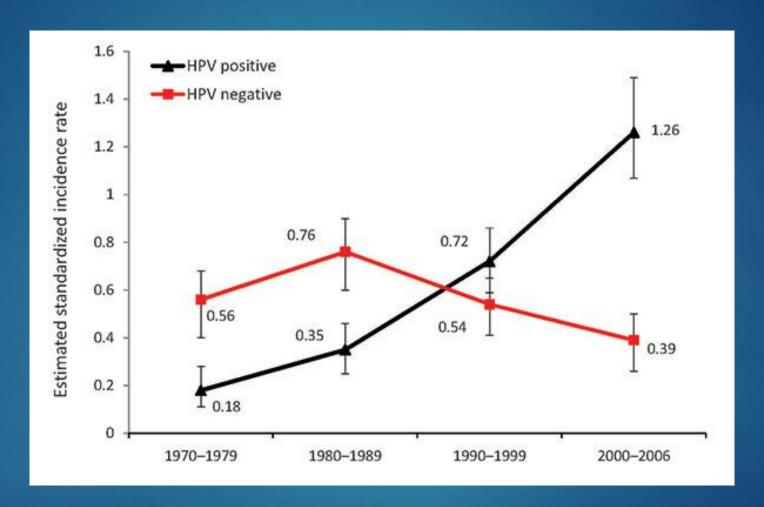
Quadrivalent HPV vaccine is not licensed for use among males. Although data on immunogenicity and safety are available for males aged 9–15 years, no data exist on efficacy in males at any age. Efficacy studies in males are under way.



2011ACIP

Adding male vaccination to female-only vaccination becomes more cost-effective when all HPVassociated 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



www.tinyurl.com/kiss-antigens

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

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



Communication, Not Confrontation

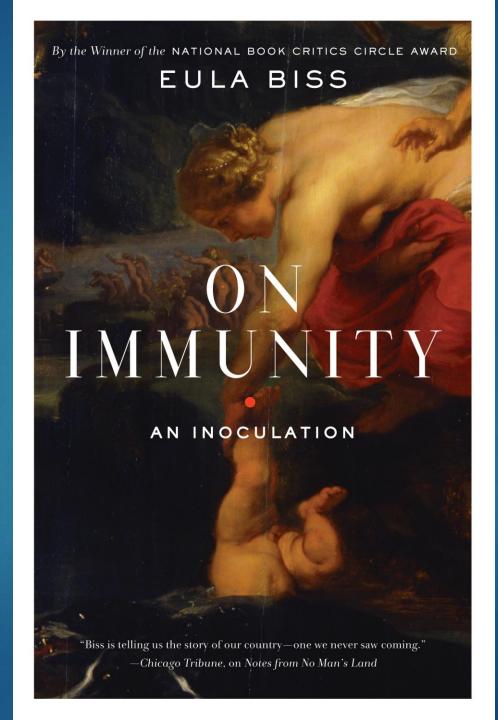




KP PEDIATRICS COMMUNICATION CURRICULUM

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

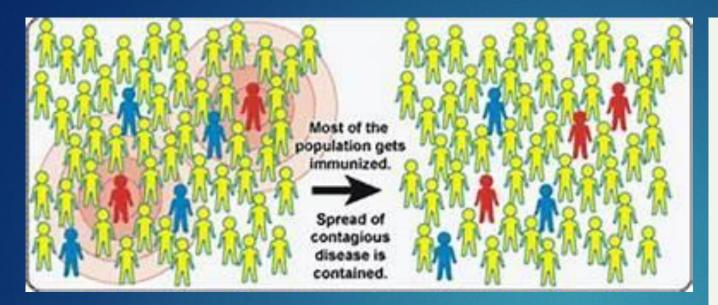
Protection, Protection, Protection



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.

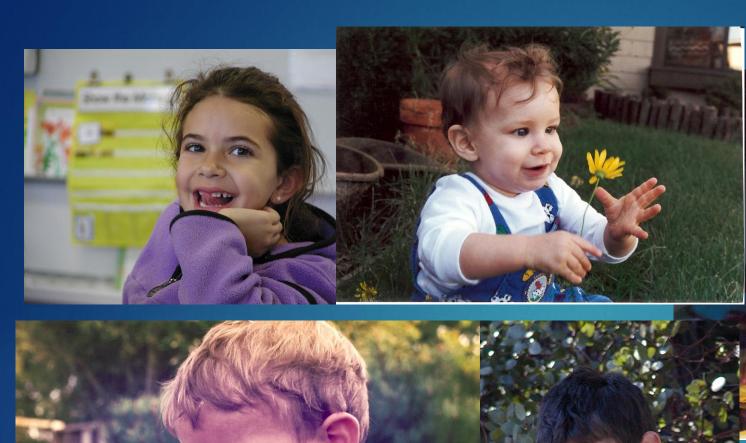
I will not set my child on fire to keep someone else warm.

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!