Immunization Updates

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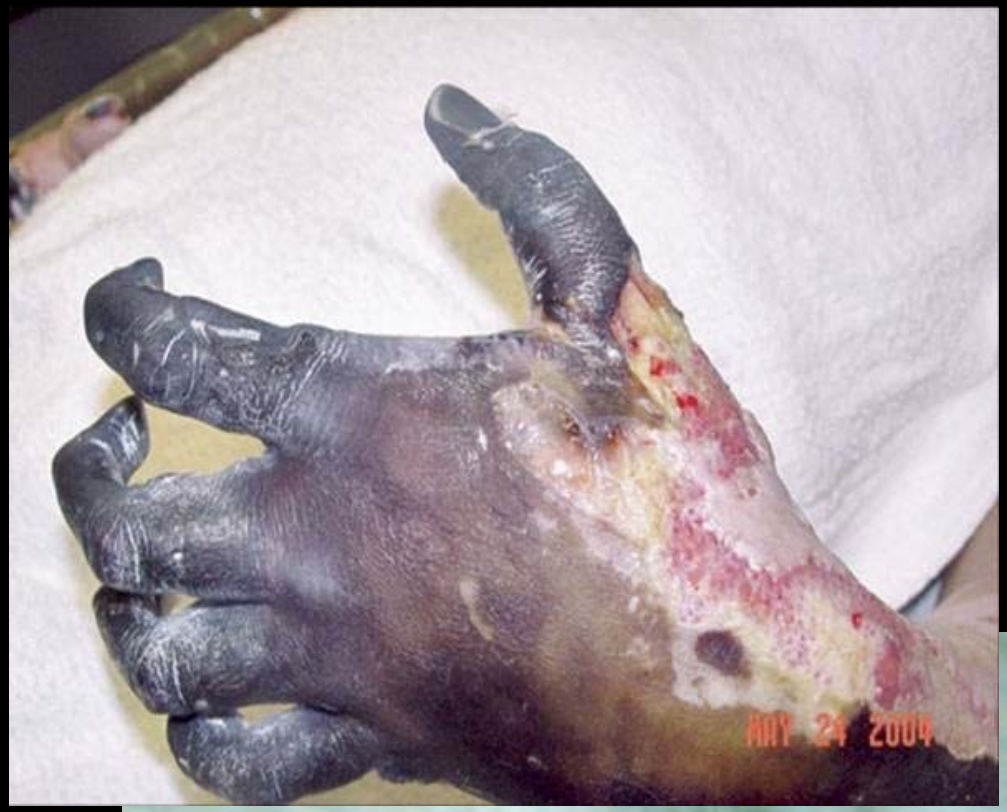
Disclosures

- William Atkinson is a federal government employee with no financial interest or conflict with the manufacturer of any product named in this presentation
- The speaker will discuss the off-label use of meningococcal conjugate vaccines, pneumococcal conjugate vaccine and zoster vaccine
- The speaker will not discuss a vaccine not currently licensed by the FDA

What Else is New in Immunization

- Meningococcal conjugate vaccine revaccination
- PCV13
- Tdap
- Zoster and PPSV23
- Thimerosal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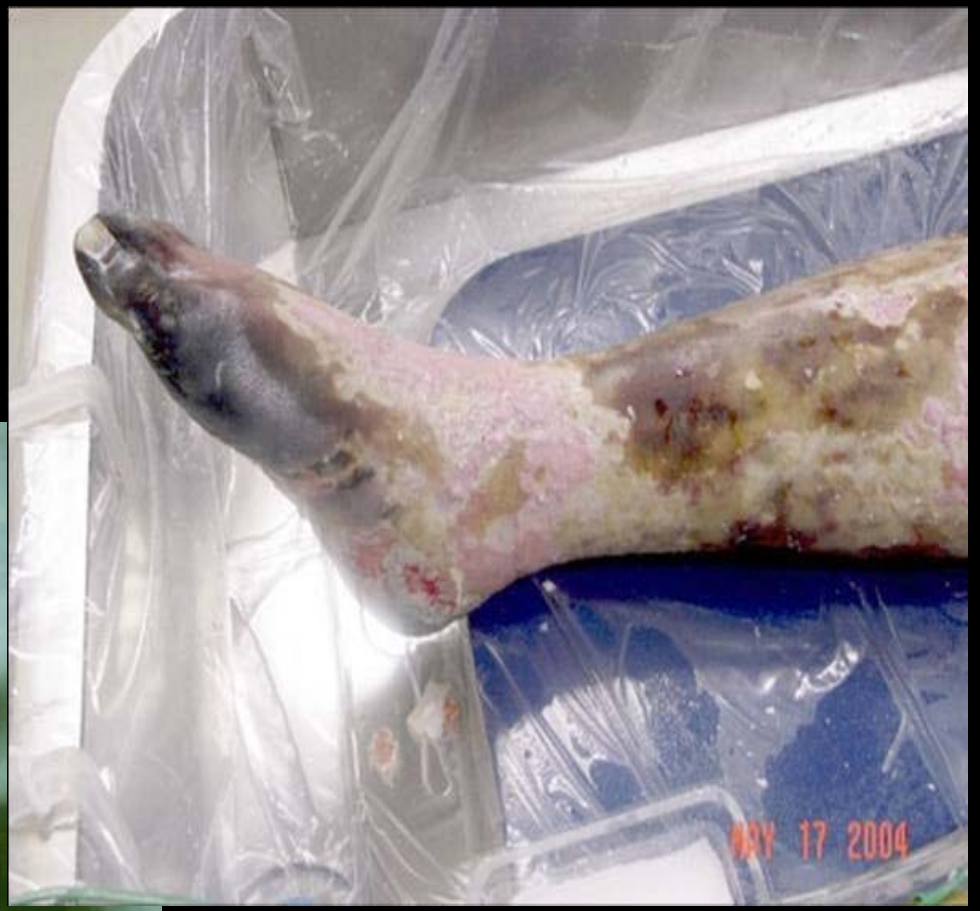
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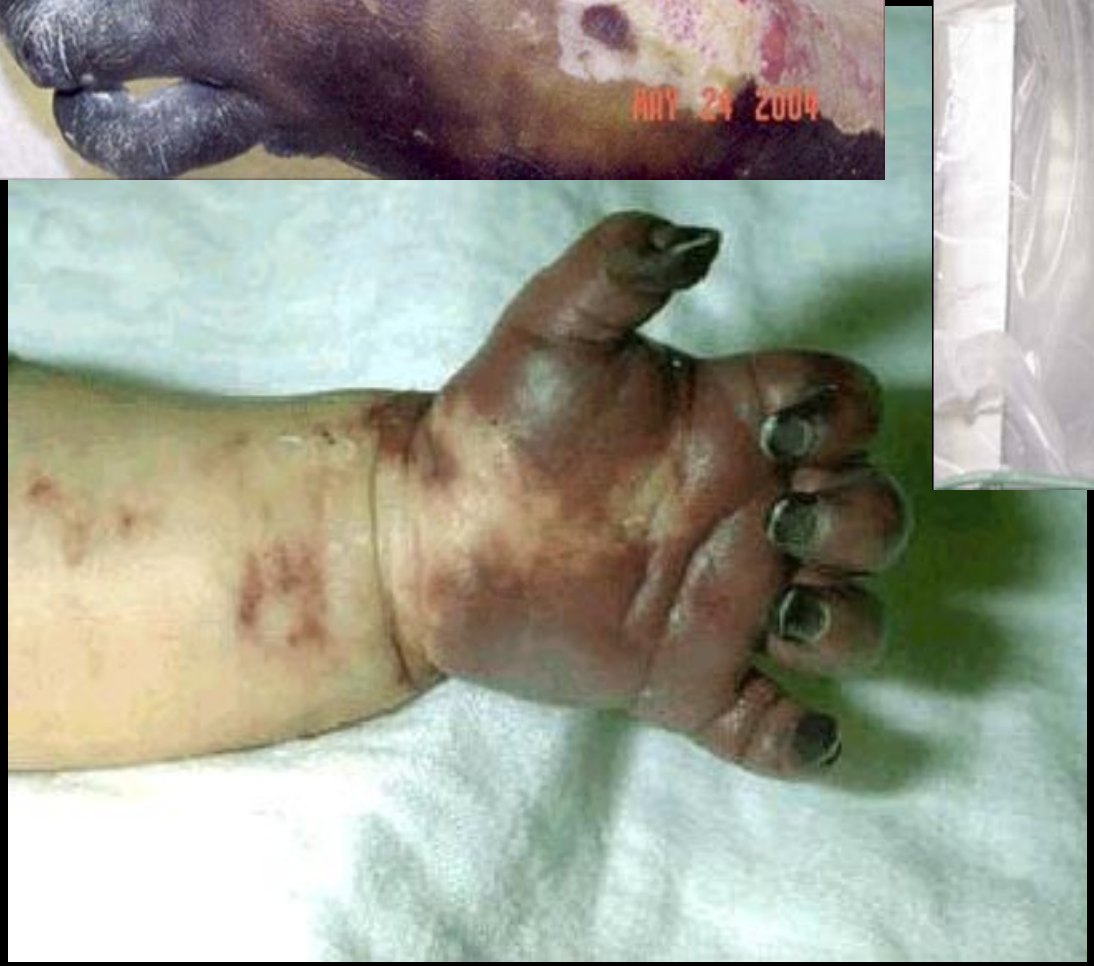


Meningococcal Conjugate Vaccine (MCV4) Issues

- Inadequate response to a single dose of MCV4
  - routine 2-dose primary series
- Waning immunity following 1 dose of MCV4
  - revaccination of some MCV4 recipients
- Routine vaccination of infants

Persons at Highest Risk of Meningococcal Disease or Suboptimal Vaccine Response

- Complement deficiency
  - very high antibody titer required to compensate for complement deficiency
- Asplenia
  - evidence of suboptimal response
- HIV infection
  - evidence of suboptimal response
- Single dose primary series may not be sufficient to confer protection for persons with these high-risk conditions

New MCV4 Recommendations*

- Administer 2 doses of MCV4 at least 8 weeks apart to children aged 2 through 10 years with persistent complement component deficiency and anatomic or functional asplenia, and 1 dose every 5 years thereafter
- Persons with Human Immunodeficiency Virus (HIV) infection who are vaccinated with MCV4 should receive 2 doses at least 8 weeks apart

*These recommendations are provisional until published in Morbidity and Mortality Weekly Report (MMWR). Publication anticipated in December 2010.

New MCV4 Recommendations*

- Persons with complement component deficiency, asplenia and HIV who previously received 1 dose should receive a booster dose at the earliest opportunity

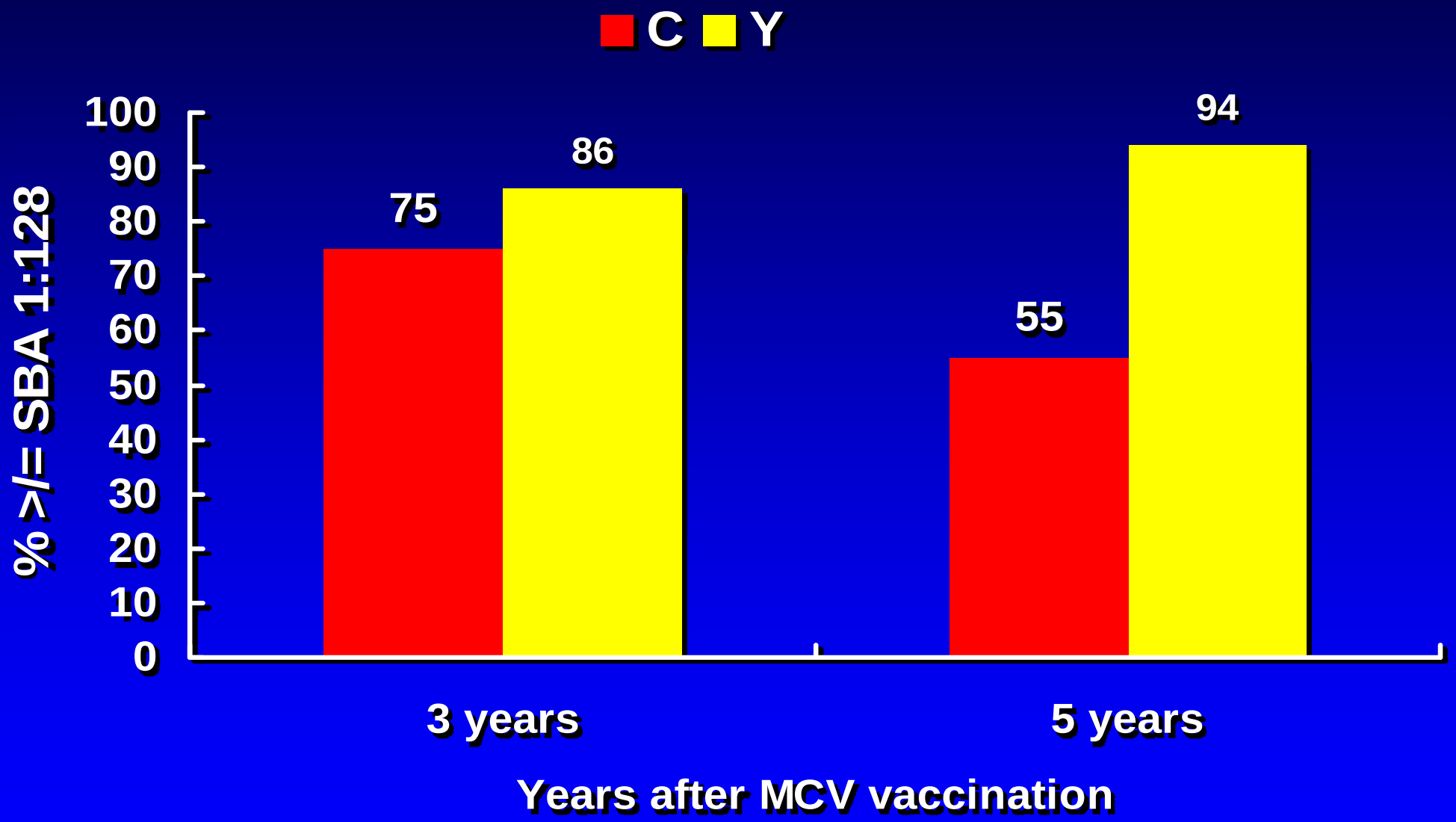
*These recommendations are provisional until published in Morbidity and Mortality Weekly Report (MMWR). Publication anticipated in December 2010.

Meningococcal Conjugate (MCV) Revaccination

- In its 2005 recommendations for MCV, ACIP made no recommendation about revaccination pending the availability of additional data
- Serologic data are now available from the manufacturer that show significant decline in antibody 3-5 years after vaccination although few "breakthrough" cases have been reported

MMWR 2009;58(No. 37):1042-3

Seroprotection Rates Following MCV Vaccination



MMWR 2009;58(No. 37):1042-3

MCV Revaccination Recommendations*

- High-risk persons who recommended for revaccination in 2009
  - persistent complement component deficiency
  - anatomic or functional asplenia
  - microbiologists with prolonged exposure to *Neisseria meningitidis*
  - frequent travelers to or persons living in areas with high rates of meningococcal disease

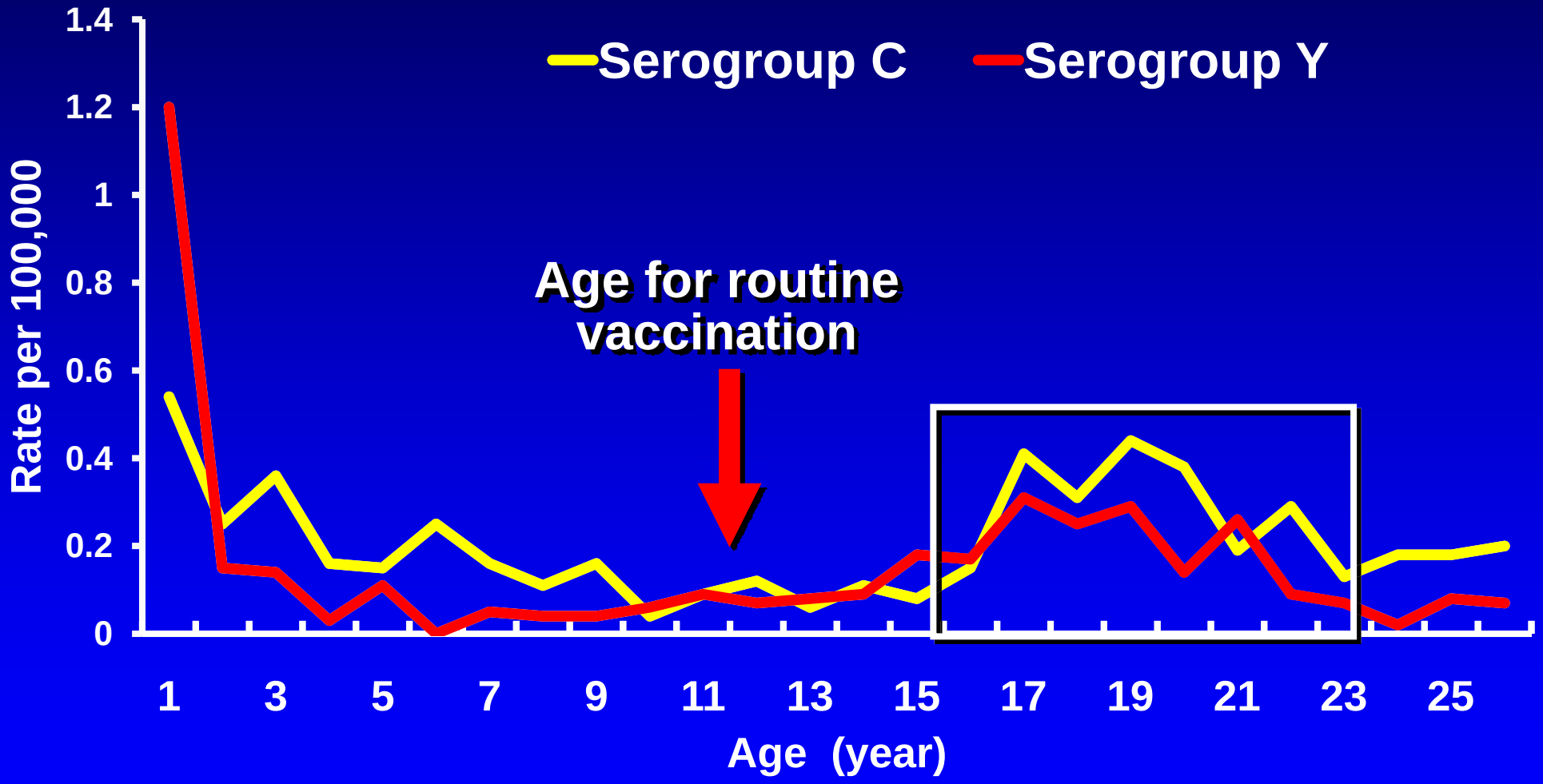
*off-label recommendation. *MMWR* 2009;58(No. 37):1042-3

Meningococcal Revaccination Recommendations

- Revaccination with meningococcal vaccine should continue every 5 years as long as the person remains at increased risk*
  - MCV for persons 2 through 55 years of age
  - MPSV for persons 56 years and older

*off-label recommendation. *MMWR* 2009;58(No. 37):1042-3

Rates of Meningococcal Disease (C and Y) by Age, 1999-2008



Active Bacterial Core surveillance (ABCs), 1998-2008

New MCV4 Recommendations*

- ACIP believes that ALL adolescents need to be adequately protected during the years of increased incidence (17-22 years of age)

New MCV4 Recommendations*

- New recommendations
  - administer MCV4 at age 11 through 12 years with a booster dose at age 16 years
  - administer 1 dose at age 13 through 18 years if not previously vaccinated
  - for persons vaccinated at age 13 through 15 years administer a 1-time booster dose 5 years after the first dose

*These recommendations are provisional until published in Morbidity and Mortality Weekly Report (MMWR). Publication anticipated in December 2010.


MenCYW-135 Liquid
Conjugate Component
MENVEO®
Novartis Vaccines
NDC 46028-208-01
℞ Only
MenA Lyo Conjugate
Component
MENVEO®
Novartis Vaccines
NDC 46028-208-01
℞ Only

Menveo MCV Vaccine

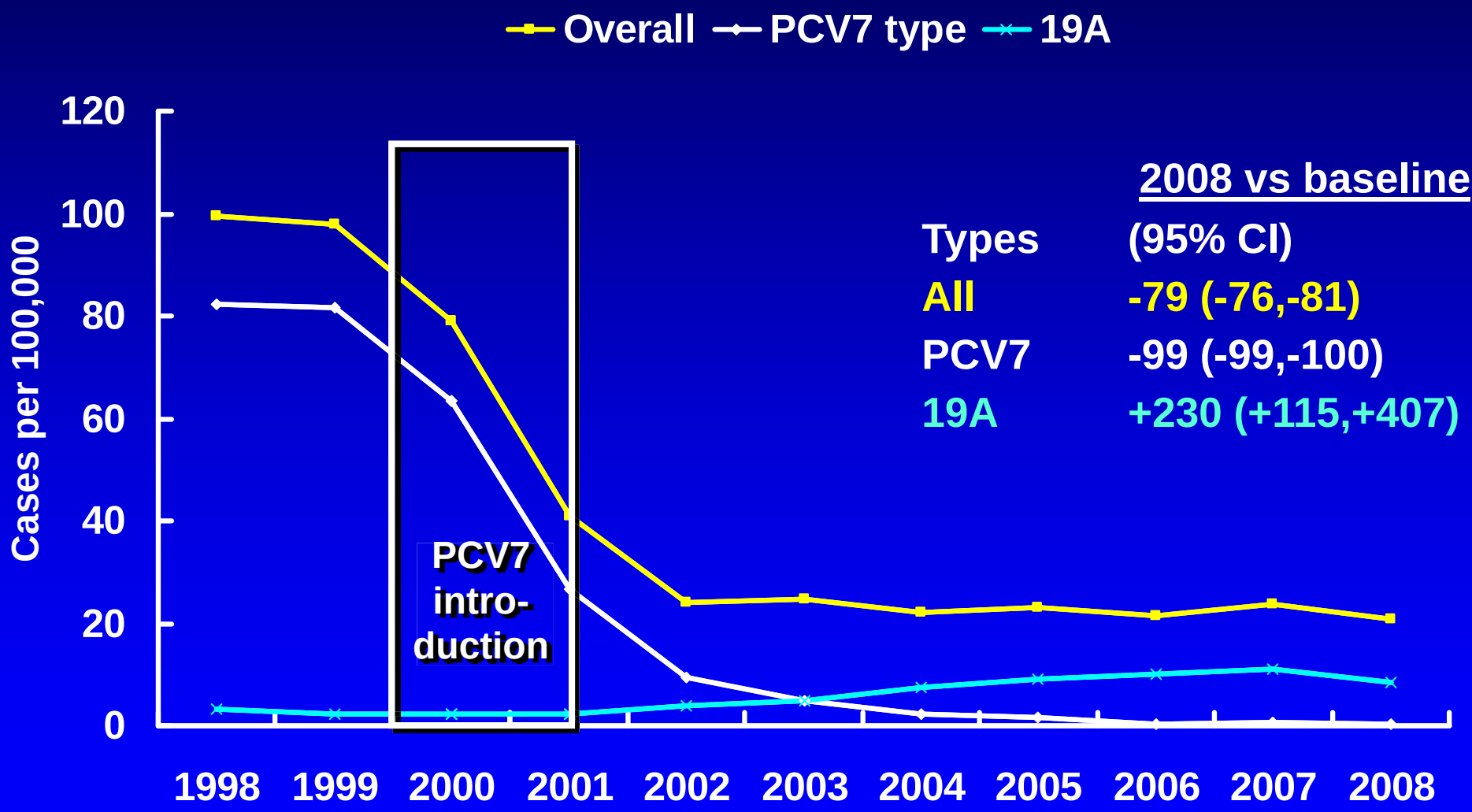
- Approved by FDA on February 19, 2010 for persons 11 through 55 years of age
- Lyophilized serogroup A vaccine reconstituted with liquid containing serogroups C, Y, and W135
- May be used for any person 11 through 55 years of age for whom MCV4 is indicated including revaccination

MMWR 2010;59(No. 9):273

Menveo Vaccine Administration Errors

- Liquid C-Y-W135 component administered without using it to reconstitute the lyophilized A component
- Revaccination may not be needed
  - serogroup A disease is rare in the U.S. so revaccination not needed if the person does not plan to travel outside the U.S.
  - revaccinate (no minimum interval) if international travel anticipated especially to Africa

Rates of Invasive Pneumococcal Disease Among Children <5 years old, 1998-2008



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Pneumococcal Conjugate Vaccine, 13-valent (PCV13)

- Contains the same serotypes of *S. pneumoniae* as PCV7 plus 6 additional serotypes (including 19A)
- Approved by FDA for use among children 6 weeks through 71 months of age
- Same 4-dose schedule as PCV7
- Children who have completed a series of PCV7 should receive 1 dose of PCV13

MMWR 2010;59(No. 6):258-61

ACIP Recommendations for PCV13 Supplemental Dose

- A single supplemental dose of PCV13 is recommended for children who have received a complete age-appropriate series of PCV7
  - healthy children 14 through 59 months
  - children with an underlying medical condition 14 through 71 months (including those who have already received a dose of PPSV)

MMWR 2010;59(No. 9):258-61

TABLE 1. Underlying medical conditions that are indications for pneumococcal vaccination among children, by risk group — Advisory Committee on Immunization Practices (ACIP), United States, 2010

Risk group	Condition
Immunocompetent children	Chronic heart disease*
	Chronic lung disease†
	Diabetes mellitus
	Cerebrospinal fluid leaks
	Cochlear implant
Children with functional or anatomic asplenia	Sickle cell disease and other hemoglobinopathies
	Congenital or acquired asplenia, or splenic dysfunction
Children with immunocompromising conditions	HIV infection
	Chronic renal failure and nephrotic syndrome
	Diseases associated with treatment with immunosuppressive drugs or radiation therapy, including malignant neoplasms, leukemias, lymphomas, and Hodgkin disease; or solid organ transplantation
	Congenital immunodeficiency§

* Particularly cyanotic congenital heart disease and cardiac failure.
† Including asthma if treated with prolonged high-dose oral corticosteroids.
§ Includes B- (humoral) or T-lymphocyte deficiency; complement deficiencies, particularly C1, C2, C3, and C4 deficiency; and phagocytic disorders (excluding chronic granulomatous disease).

MMWR 2010;59(No. 9):258-61

ACIP Recommendations for PCV13 Supplemental Dose

- A single dose of PCV13 may be administered to children 6 through 18 years of age who are at increased risk for invasive pneumococcal disease*
  - functional or anatomic asplenia, including sickle cell disease
  - HIV infection and other immunocompromising conditions
  - cochlear implant
  - CSF leak

*off-label recommendation. *MMWR* 2010;59(No. 9):258-61

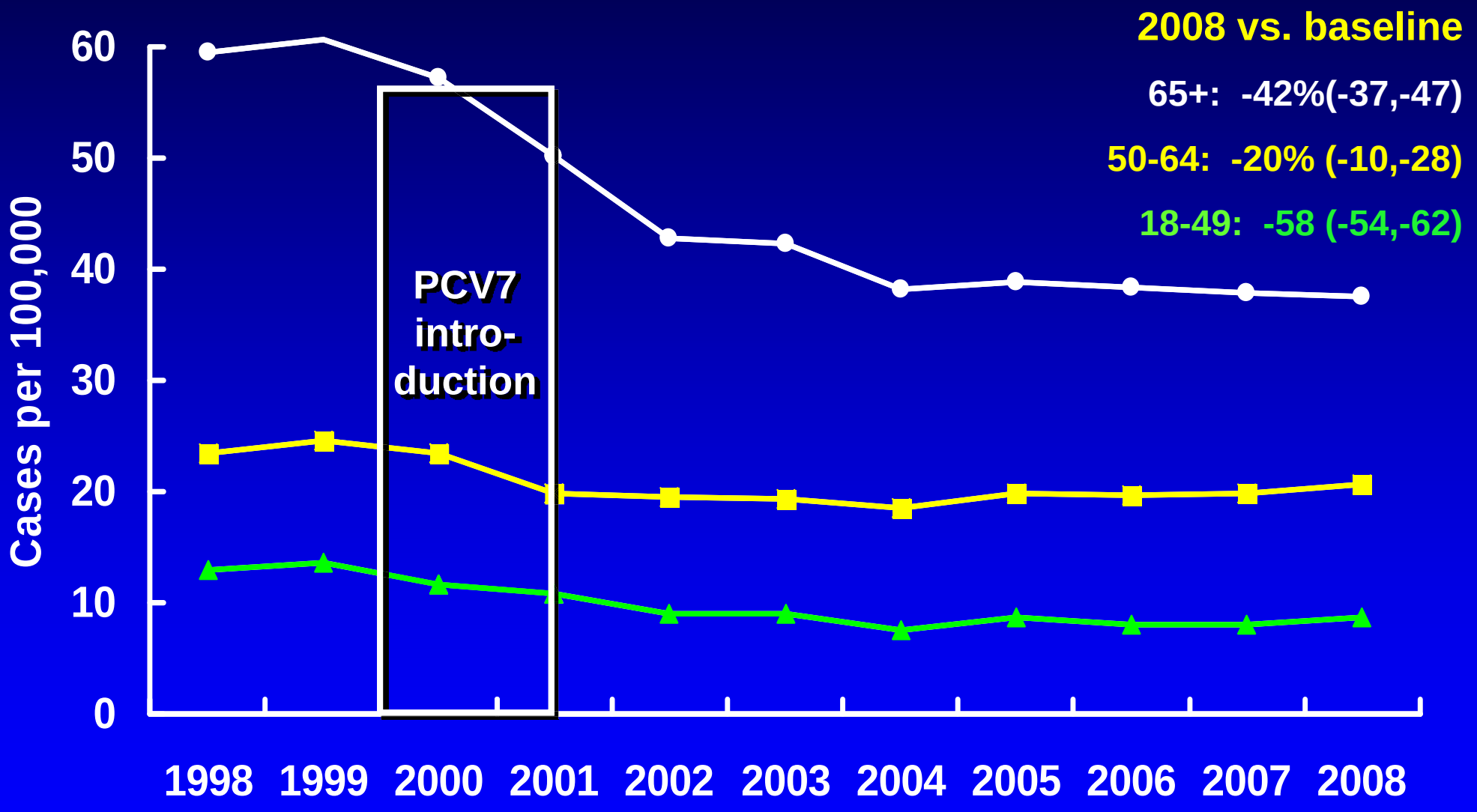
MMWR / March 12, 2010 / Vol. 59 / No. 9

Licensure of a 13-Valent Pneumococcal Conjugate Vaccine (PCV13) and Recommendations for Use Among Children — Advisory Committee on Immunization Practices (ACIP), 2010

On February 24, 2010, a 13-valent pneumococcal conjugate vaccine (PCV13 [Prevnar 13, Wyeth Pharmaceuticals Inc., a subsidiary of Pfizer Inc.]) was licensed by the Food and Drug Administration (FDA) for prevention of invasive pneumococcal disease (IPD) caused by the 13 pneumococcal serotypes covered by the vaccine and for prevention of otitis media caused by serotypes in the 7-valent pneumococcal conjugate vaccine formulation (PCV7 [Prevnar, Wyeth]). PCV13 is approved for use among children aged 6 weeks–71 months and succeeds PCV7, which was licensed by FDA in 2000. The Pneumococcal Vaccines Work Group of the Advisory Committee on Immunization Practices (ACIP) reviewed available data on the immunogenicity, safety, and cost-effectiveness of PCV13, and on estimates of the vaccine-preventable pneumococcal disease burden. PCV13 is administered intramuscularly and is available in single-dose, prefilled syringes that do not contain latex (*2*).

Immunogenicity profile. The immunogenicity of PCV13 was evaluated in a randomized, double-blind, active-controlled trial in which 663 U.S. infants received at least 1 dose of PCV13 or PCV7 (*3*). To compare PCV13 antibody responses with those for PCV7, criteria for noninferior immunogenicity after 3 and 4 doses of PCV13 (pneumococcal immunoglobulin G [IgG] antibody concentrations measured by enzyme immunoassay) were defined for the seven serotypes common to PCV7 and PCV13 (4, 6B, 9V, 14, 18C, 19F, and 23F) and for the six additional serotypes in PCV13 (serotypes 1, 3, 5, 6A, 7F, and 19A). Functional antibody responses were measured by opsonophagocytosis assay (OPA) in a subset of the

Rates of Invasive Pneumococcal Disease (all serotypes) Among Adults ≥18 Years-Old



Moore, IDSA, 2009. ABCs 1998-2008

New Pneumococcal Polysaccharide Vaccine Recommendations

- Routine pneumococcal polysaccharide vaccination is recommended for adults 19 through 64 years of age:
  - with asthma
  - who smoke cigarette
- Data are insufficient to recommend vaccination for persons younger than 19 years with asthma or who smoke

MMWR 2010;59(No. 34):1102-6

Asthma and Invasive Pneumococcal Disease (IPD)

- An estimated 7.3% of U.S. adults have active asthma
- Among adults 18-49 years of age IPD is more common among persons with asthma than persons without asthma (adjusted odds ratio 2.4 [1.8-3.3])
- IPD risk for persons with high-risk asthma was nearly twice that for persons with low-risk asthma

Talbot et al. *N Eng J Med* 2005;352:2082-90

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Early Release / Vol. 59
September 7, 2010

Vital Signs: Current Cigarette Smoking Among Adults Aged ≥18 Years — United States, 2009

ABSTRACT

Background: Cigarette smoking continues to be the leading cause of preventable morbidity and mortality in the United States, causing approximately 443,000 premature deaths annually.

Methods: The 2009 National Health Interview Survey and the 2009 Behavioral Risk Factor Surveillance System were used to estimate national and state adult smoking prevalence, respectively. Cigarette smokers were defined as adults aged ≥18 years who reported having smoked ≥100 cigarettes in their lifetime and now smoke every day or some days.

Results: In 2009, 20.6% of U.S. adults aged ≥18 years were current cigarette smokers. Men (23.5%) were more likely than women (17.8%) to be current smokers. The prevalence of smoking was 31.1% among persons below the federal poverty level for adults aged ≥26 years and the prevalence of smoking was 28.5% among persons with less than a high school diploma compared with 5.6% among those with a graduate degree. Regional differences were observed, with the West having the lowest prevalence (16.4%) and higher prevalences being observed in the South (21.8%) and Midwest (23.1%). From 2005 to 2009, the proportion of U.S. adults who were current cigarette smokers did not change (20.9% in 2005 and 20.6% in 2009).

Conclusions: Previous declines in smoking prevalence in the United States have stalled during the past 5 years; the burden of cigarette smoking continues to be high, especially in persons living below the federal poverty

443,000 premature deaths a year

1,214 deaths per day

~1 death per minute

Smoking and Invasive Pneumococcal Disease (IPD)

- During 2001-2003, 53% of IPD patients 18-64 years of age were current cigarette smokers
- The risk for IPD among immunocompetent cigarette smokers 18-64 years was four times the risk for controls who had never smoked
- Significant dose-response relationships with risk for IPD also were observed for number of cigarettes smoked and pack-years of smoking

CDC unpublished data

Nuorti et al. *N Eng J Med* 2000;342:681-9

Association of Cigarette Smoking and IPD

TABLE 4. INDEPENDENT RISK FACTORS FOR INVASIVE PNEUMOCOCCAL DISEASE AMONG IMMUNOCOMPETENT ADULTS 18 TO 64 YEARS OLD.

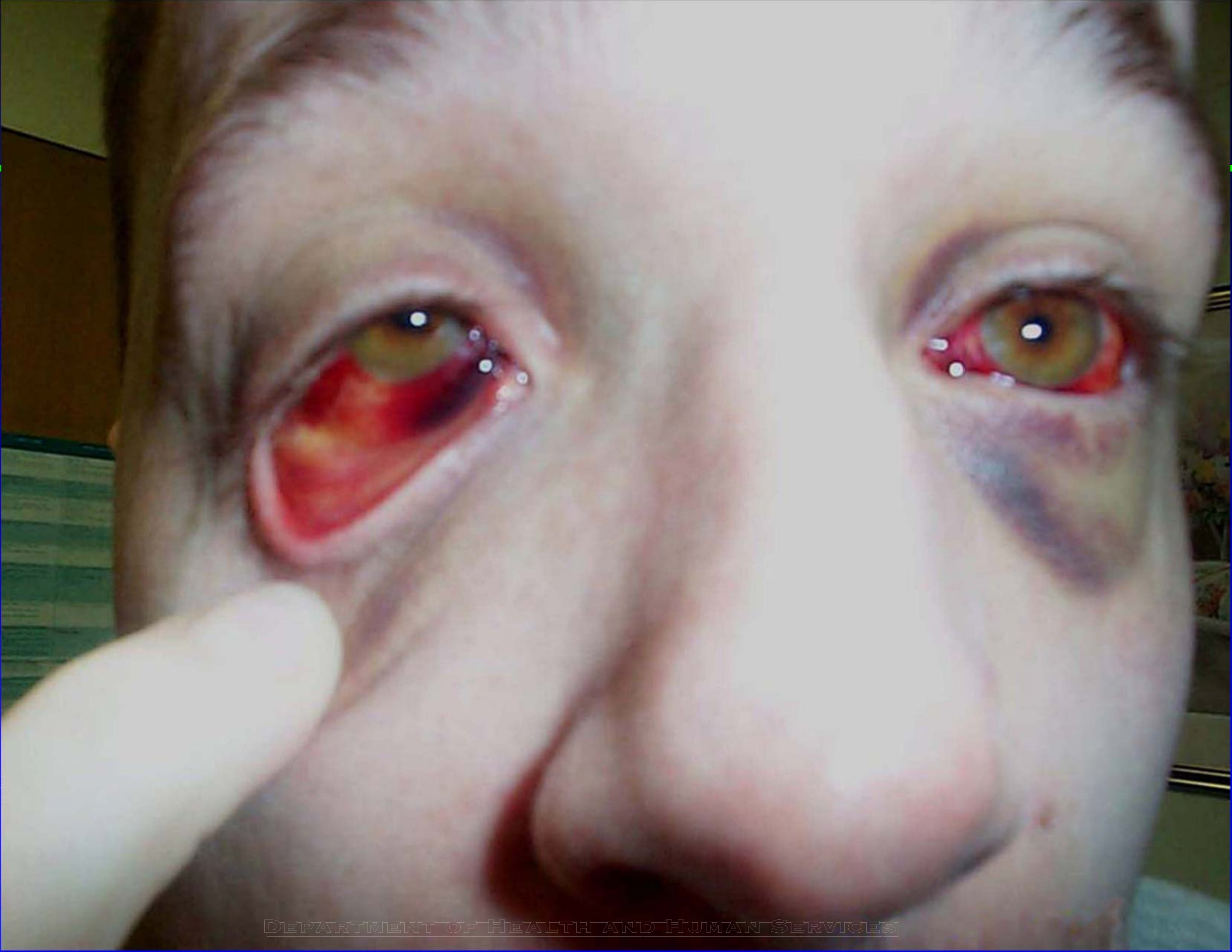
VARIABLE	ODDS RATIO (95% CI)*	P VALUE
Smoking status		
Current smoker	4.1 (2.4–7.3)	<0.001
Former smoker	1.1 (0.5–2.2)	0.91
Passive exposure to smoke	2.5 (1.2–5.1)	0.01
Never smoked and no passive exposure to smoke	1.0	

N Engl J Med 2000;342:681-9

Smoking Cessation and Invasive Pneumococcal Disease

- Quitting smoking reduces the risk for pneumococcal disease
- One study found that the risk for IPD was reduced by approximately 14% each year after quitting smoking and returned to a risk similar to that for persons who had never smoked in approximately 13 years
- Smoking cessation guidance should be part of the therapeutic plan for smokers regardless of immunization status

Nuorti et al. *N Eng J Med* 2000;342:681-9



Pertussis

- 16,858 cases and 14 deaths (12 younger than 3 months of age) reported in 2009
- Increase has continued in 2010
- Outbreaks in several states, particularly California, South Carolina, Michigan, New York and Ohio
- Highest rate among infants
- Many cases among adolescents and young adults

www.cdc.gov/pertussis/

Pertussis-containing Vaccines

- DTaP (pediatric)
  - Approved for children 6 weeks through 6 years (to age 7 years)
  - Contains the same amount of diphtheria and tetanus toxoid as pediatric DT
- Tdap (adolescent and adult)
  - Approved for persons 10 or 11 through 64 years
  - Contains lesser amount of diphtheria toxoid and acellular pertussis antigen than DTaP

Tdap Use in Adolescents and Adults

- Tdap reduces the risk of pertussis by 60% - 80%
- Tdap approved ages
  - 10 through 64 years for Boostrix
  - 11 through 64 years for Adacel
- Tdap not approved by the Food and Drug Administration for children 7 years through 9 years or adults 65 years or older

Wei SC et al. *Clin Infect Dis* 2010;51:315-21

Tdap – Current Recommendations

- Routine vaccination (1 dose) at 11-12 years of age
- All persons 13 through 64 years with emphasis on
  - All healthcare providers
  - All persons with household or other close contact with infants younger than 12 months of age (parents, siblings, babysitters, etc)

MMWR 2006; 55(RR-17)

New Tdap Recommendations*

- Persons aged 7 through 10 years who are not fully immunized against pertussis (including those never vaccinated or with unknown pertussis vaccination status) should receive a **single dose** of Tdap

*These recommendations are provisional until published in Morbidity and Mortality Weekly Report (MMWR). Publication anticipated in December 2010.

New Tdap Recommendations*

- "Not fully immunized"
  - fewer than 4 doses of DTaP
  - 4 doses of DTaP and last dose was prior to age 4 years

*These recommendations are provisional until published in Morbidity and Mortality Weekly Report (MMWR). Publication anticipated in December 2010.

New Tdap Recommendations*

- Adults 65 years and older who have or who anticipate having close contact with an infant younger than 12 months of age and who have not previously received Tdap should receive a single dose of Tdap

*These recommendations are provisional until published in Morbidity and Mortality Weekly Report (MMWR). Publication anticipated in December 2010.

New Tdap Recommendations*

- Tdap can be administered regardless of the interval since the last tetanus and diphtheria containing vaccine

*These recommendations are provisional until published in Morbidity and Mortality Weekly Report (MMWR). Publication anticipated in December 2010.

MERCK

9815611

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use ZOSTAVAX[1] safely and effectively. See full prescribing information for ZOSTAVAX.

ZOSTAVAX®

Zoster Vaccine Live

Suspension for subcutaneous injection

Initial U.S. Approval: 2006

----------INDICATIONS AND USAGE----------
ZOSTAVAX is a live attenuated virus vaccine indicated for prevention of herpes zoster (shingles) in individuals 60 years of age and older (1). ZOSTAVAX is not indicated for the treatment of zoster or postherpetic neuralgia (PHN) (1).

---------- DOSAGE AND ADMINISTRATION----------
Single 0.65 mL subcutaneous injection (2.1)

---------- DOSAGE FORMS AND STRENGTHS ----------
Single dose vials with not less than 19,400 plaque-forming units [PFU] per 0.65 mL dose when reconstituted to a suspension (2.1, 3, 16).

----------CONTRAINDICATIONS----------
- History of anaphylactic/anaphylactoid reaction to gelatin, neomycin, or any other component of the vaccine (4.1).
- History of primary or acquired immunodeficiency states (4.2).
- On immunosuppressive therapy (4.2).
- ZOSTAVAX is not indicated in women of child-bearing age and should not be administered to pregnant females (4.3, 8.1, 17.1).
- ZOSTAVAX is not indicated for prevention of primary varicella infection (Chickenpox) (5.2, 8.4).
- Transmission of vaccine virus may occur rarely between vaccinees and susceptible contacts (5.1).
- Defer vaccination in patients with active untreated tuberculosis (5.5).

---------- ADVERSE REACTIONS----------
The rate of serious adverse events (SAEs) from Days 0 to 42 postvaccination may be increased in recipients of ZOSTAVAX compared to recipients of placebo (Table 1, 6.1.1).

The most frequent vaccine-related adverse events, reported in ≥1% of subjects vaccinated with ZOSTAVAX, were headache and injection site reactions (6.1.1).

----------DRUG INTERACTIONS----------
ZOSTAVAX and PNEUMOVAX®[2] 23 should not be given concurrently because concomitant use resulted in reduced immunogenicity of ZOSTAVAX (7.1, 14).

To report vaccine exposure during pregnancy call 1-800-986-8999.

To report SUSPECTED ADVERSE REACTIONS, contact Merck & Co., Inc. at 1-877-888-4231 or VAERS at 1-800-822-7967 and www.fda.gov/vaers.

See 17 for PATIENT COUNSELING INFORMATION and FDA-Approved Patient Labeling.

Revised: 12/2009

Zoster and Pneumococcal Polysaccharide (PPSV) Vaccines

- Zoster package insert advises that zoster and PPSV should not be administered concurrently
- Based on a study that showed the titer against VZV was lower in persons who received zoster and PPSV at the same visit compared to persons who received these vaccines 4 weeks apart

Zoster and Pneumococcal Polysaccharide (PPSV) Vaccines

- CDC has not changed its recommendation for either vaccine
- Zoster and PPSV should be administered at the same visit if the person is eligible for both vaccines

Pediatrics 2010;126:656-64 (October 2010)

Prenatal and Infant Exposure to Thimerosal From Vaccines and Immunoglobulins and Risk of Autism

WHAT'S KNOWN ON THIS SUBJECT: Most previous research has not revealed an increased risk of autism associated with receipt of thimerosal-containing vaccines. Evidence is limited, however, on the timing of vaccination, especially prenatal exposure, and associations with different subtypes of autism.

WHAT THIS STUDY ADDS: This study revealed no increased risk of ASD associated with receipt of thimerosal-containing vaccines. No increased risk was found for subtypes of ASD, including ASD with regression, and prenatal exposure was not associated with a risk of ASD.

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KEY WORDS
thimerosal, mercury, vaccines, immunoglobulins, autism

ABBREVIATIONS
CDC—Centers for Disease Control and Prevention
MCO—managed care organization
ASD—autism spectrum disorder
TCI—thimerosal-containing injection
AD—autistic disorder
ADI-R—Autism Diagnostic Interview-Revised
ADOS—Autism Diagnostic Observation Schedule
SCQ—Social Communication Questionnaire
OR—odds ratio
Hib—*Haemophilus influenzae* type b

The views in this article are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

abstract

FREE

OBJECTIVE: Exposure to thimerosal, a mercury-containing preservative that is used in vaccines and immunoglobulin preparations, has been hypothesized to be associated with increased risk of autism spectrum disorder (ASD). This study was designed to examine relationships between prenatal and infant ethylmercury exposure from thimerosal-containing vaccines and/or immunoglobulin preparations and ASD and 2 ASD subcategories: autistic disorder (AD) and ASD with regression.

METHODS: A case-control study was conducted in 3 managed care organizations (MCOs) of 256 children with ASD and 752 controls matched by birth year, gender, and MCO. ASD diagnoses were validated through standardized in-person evaluations. Exposure to thimerosal in vaccines and immunoglobulin preparations was determined from electronic immunization registries, medical charts, and parent interviews. Information on potential confounding factors was obtained from the interviews and medical charts. We used conditional logistic regres-

Another Thimerosal Study Showing No Association with Autism

- Case-control study conducted in 3 managed care organizations
- 256 children with autism spectrum disorder (ASD), 752 without ASD
- Case and control children had similar cumulative exposure to ethylmercury
- Exposure to ethylmercury from thimerosal-containing immunizations during pregnancy or in the first 20 months was not associated with an increased risk of any ASD

Pediatrics 2010;126:656-64

What's Next

- Additional combination vaccines
- Meningococcal vaccination of infants
- Expansion of HPV4 recommendations for women older than 26 years
- Revaccination with Tdap
- Expansion of age range for zoster vaccine

CDC Vaccines and Immunization
Contact Information

- **Telephone** 800.CDC.INFO
  (for patients and parents)
- **Email** nipinfo@cdc.gov
  (for providers)
- **Website** www.cdc.gov/vaccines/
- **Vaccine Safety** www.cdc.gov/vaccinesafety/