

Meningococcal Disease Surveillance and Prevention Update

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Outline

- **Background**
- **Meningococcal disease epidemiology**
- **Meningococcal vaccination**
- **Future vaccination prospects**
 - **New recommendations**
 - **New vaccines**
- **Emerging antimicrobial resistance**

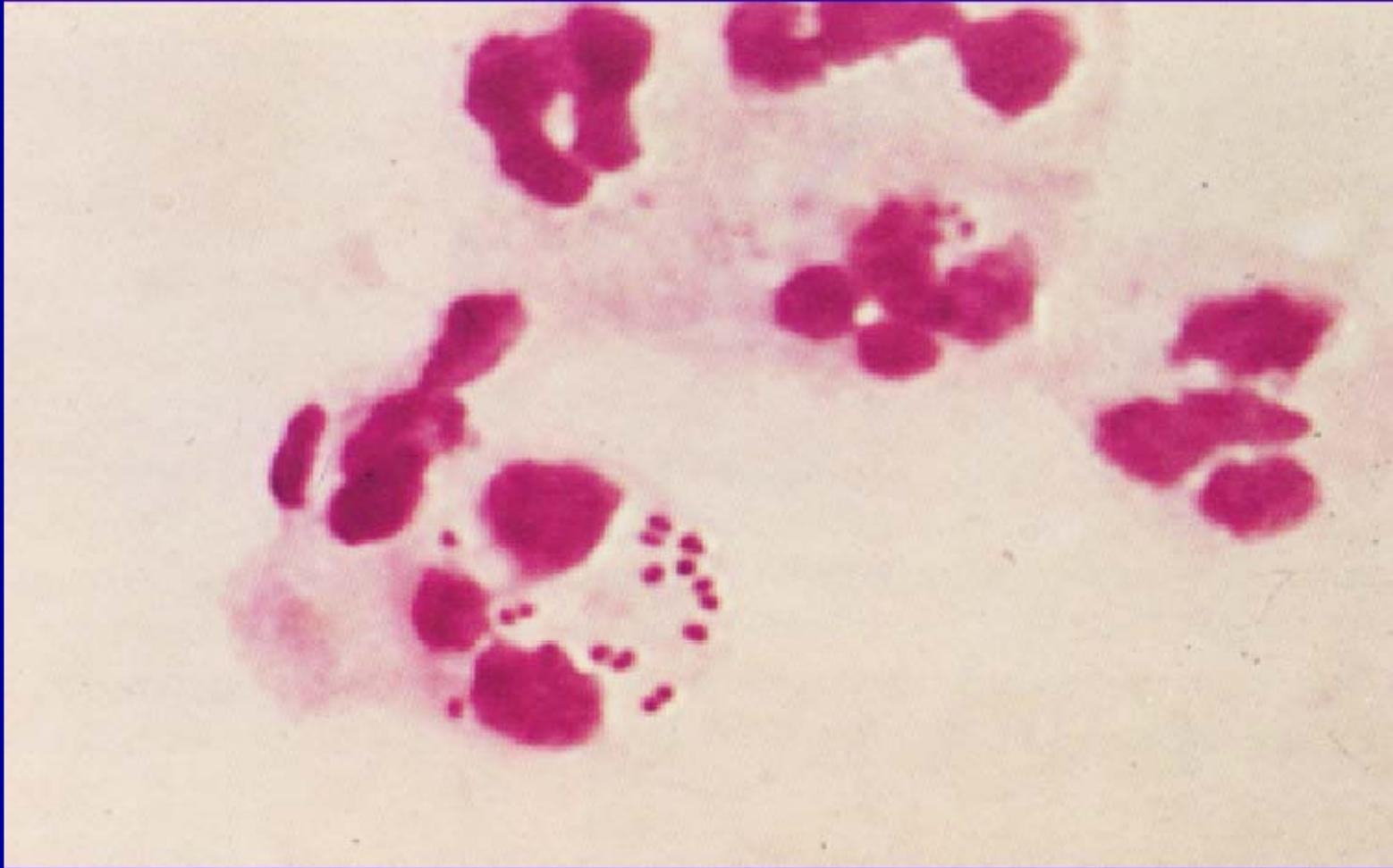
Background

Meningococcal Disease



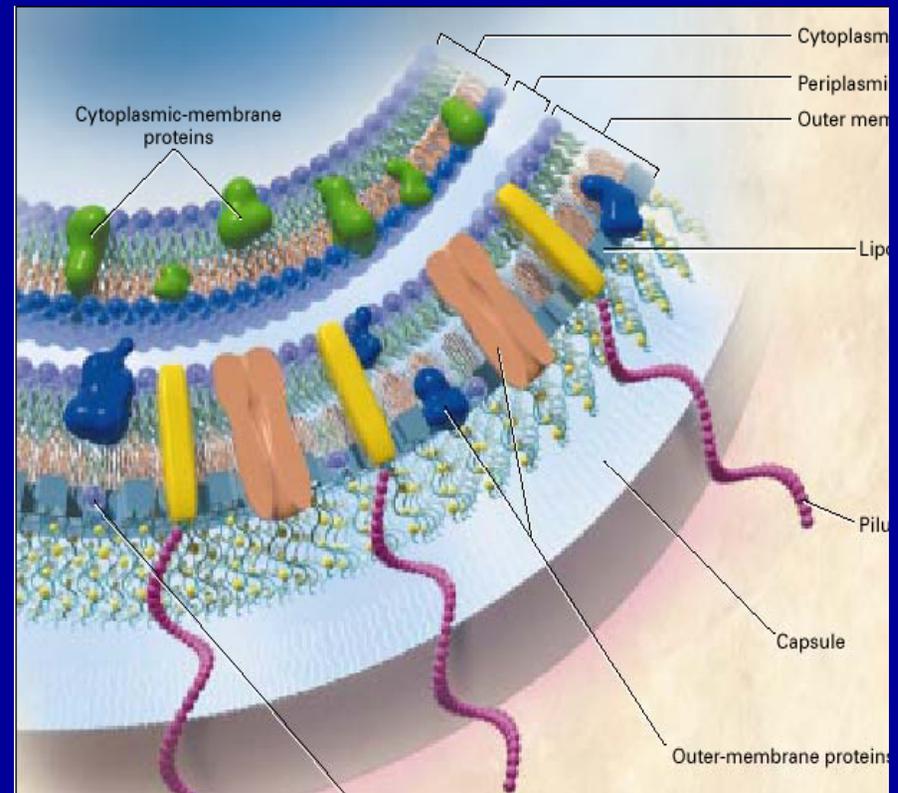
- *Neisseria meningitidis*
- Common cause of meningitis and sepsis
- Death or disability of one in every four patients
- Case fatality rate 9-12%

Gram stain of *N. meningitidis*



Cell membrane cross section

- **Capsular polysaccharide**
 - A, B, C, Y, W-135
 - B, C, Y most common in US
 - B is not covered by vaccine in US



Disease patterns and risk factors

- All pathogenic serogroups can cause meningitis and/or sepsis, but classically:
 - C: sepsis with high CFR
 - B: meningitis with lower CFR
 - Y: often causes pneumonia in elderly
- Associated with increased risk of disease:
 - Terminal complement deficiency
 - Asplenia
 - Antecedent viral infection
 - Household crowding (including freshman dorms and military barracks)
 - Smoking (active and passive)

Case close contacts

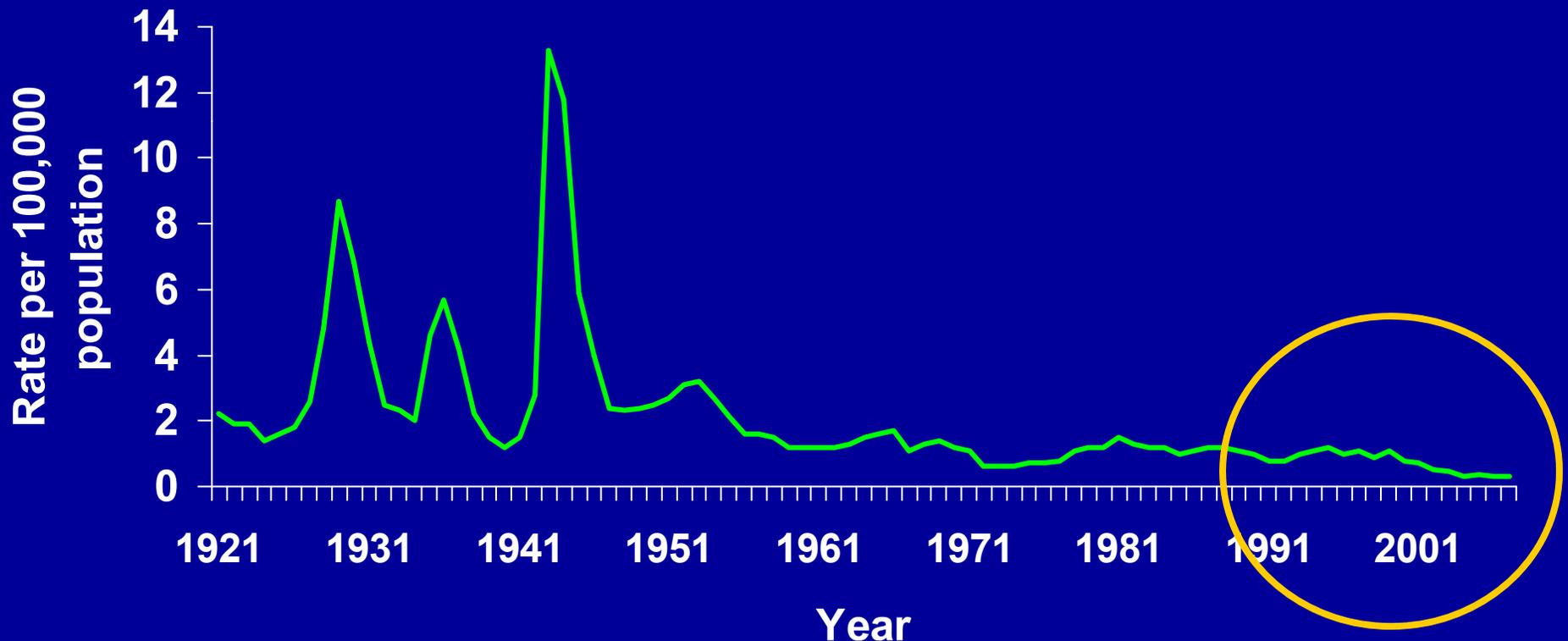
- **Close contacts of case patients are at increased risk for disease (500-800x)**
 - Household members
 - Child-care contacts
 - Direct exposure to oral secretions
 - Kissing
 - Mouth to mouth resuscitation
 - Endotracheal intubation, tube management
- **Chemoprophylaxis urgent, but probably of limited value 14 days after exposure**

Epidemiology

Meningococcal disease surveillance

- **National Notifiable Disease Surveillance System**
- **Active Bacterial Core Surveillance (ABCs)**
- **MeningNet**

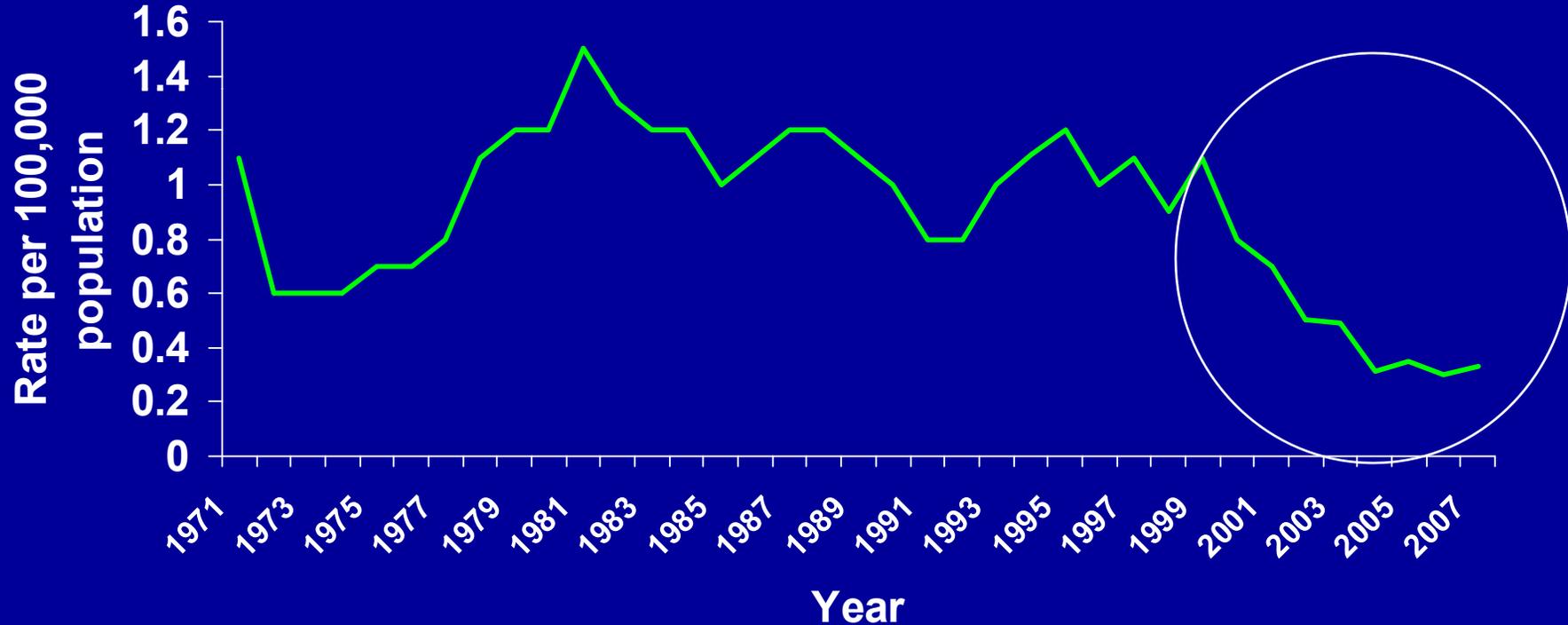
Meningococcal Disease Incidence, US (1921-2007)



1997-2007 uses ABCs data projected to US
population

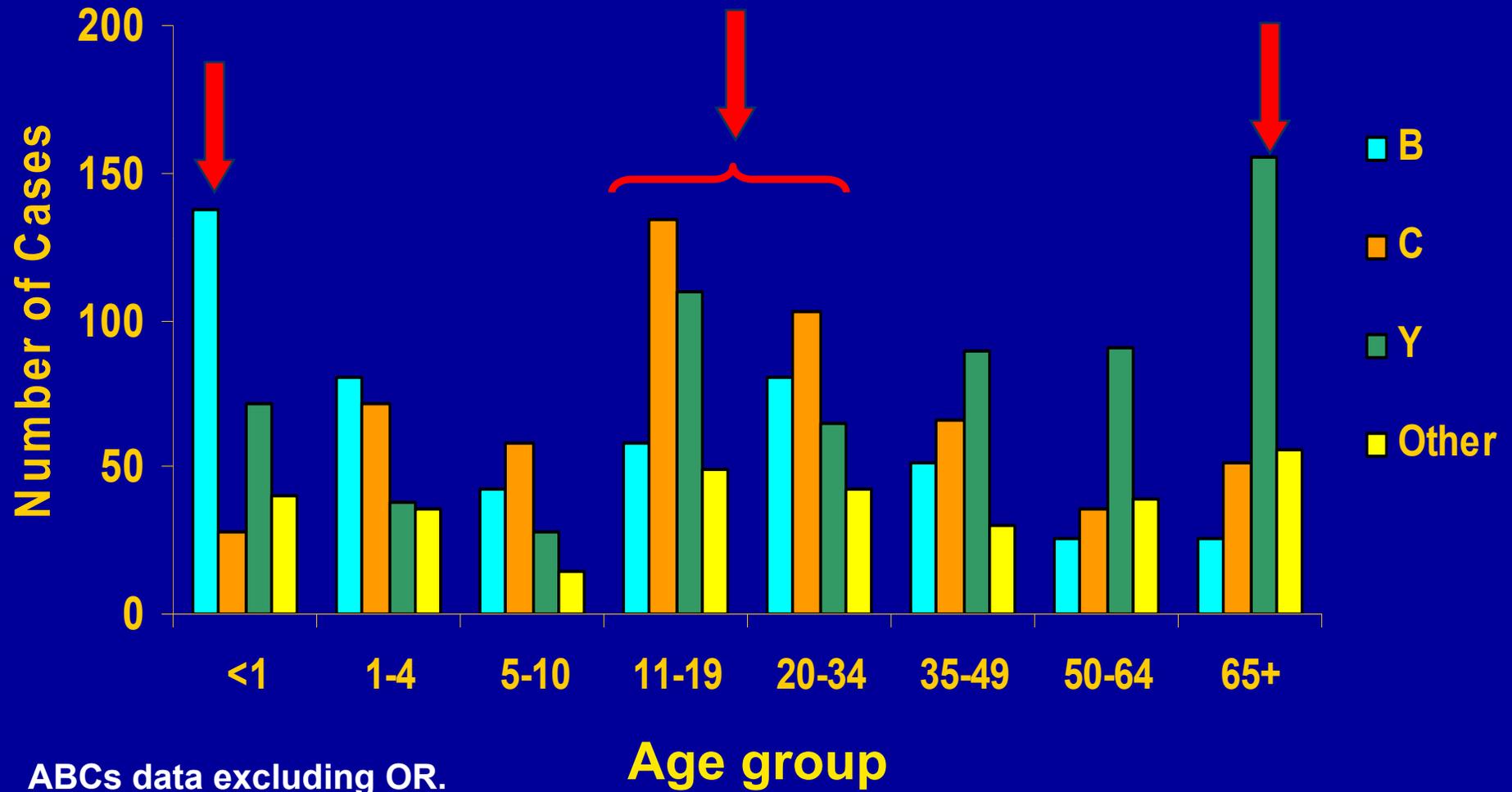
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Meningococcal Disease Incidence, US (1970-2007)



1997-2007 uses ABCs data projected to US population

Cases of Meningococcal Disease by Age and Serogroup, 1996-2005 (n=2003)



Projected Rates of Meningococcal Disease by Serogroup, 1997-2006



ABCs cases from 1997-2006 and projected to the U.S. population

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Meningococcal Vaccines

Tetravalent meningococcal polysaccharide vaccine

- Menomune[®] (MPSV4, Sanofi Pasteur)
- Serogroups A, C, Y, W-135
- Vaccine efficacy
 - VE = 85% (95CI 27%-97%) for serogroup C in 2-29 year-olds

Tetravalent Meningococcal Conjugate Vaccine

- Licensed 2005
- Menactra[®] (MCV4, Sanofi Pasteur)
- Serogroups A,C,Y,W-135
 - 4µg of each capsular polysaccharide
 - conjugated to 48µg diphtheria toxoid
- MCV4 immunogenicity comparable to MPSV4
- Case-control study underway

MCV4 vs. MPSV4: Presumed advantages of conjugate vaccines

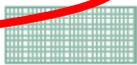
- **T cell-dependent response**
 - Longer duration of protection
 - Primes for immunologic memory
- **Reduction of asymptomatic carriage**

ACIP Recommendations

Recommended Immunization Schedule for Persons Aged 7 Through 18 Years—United States • 2009
For those who fall behind or start late, see the schedule below and the catch-up schedule

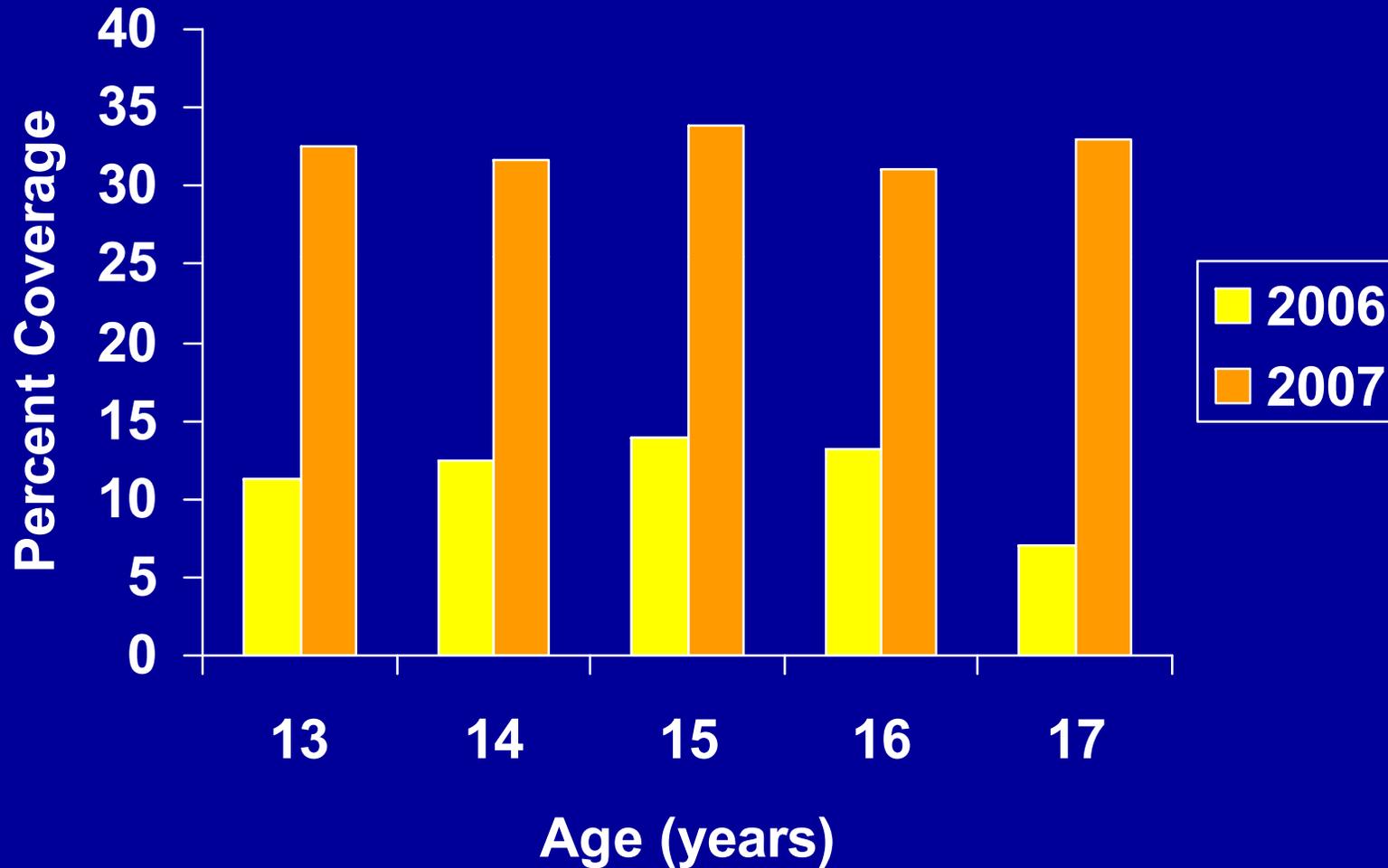
Vaccine ▼	Age ►	7–10 years	11–12 years	13–18 years
Tetanus, Diphtheria, Pertussis ¹		<i>see footnote 1</i>	Tdap	Tdap
Human Papillomavirus ²		<i>see footnote 2</i>	HPV (3 doses)	HPV Series
Meningococcal ³		MCV	MCV	MCV
Influenza ⁴		Influenza (Yearly)		
Pneumococcal ⁵		PPSV		
Hepatitis A ⁶		HepA Series		
Hepatitis B ⁷		HepB Series		
Inactivated Poliovirus ⁸		IPV Series		
Measles, Mumps, Rubella ⁹		MMR Series		
Varicella ¹⁰		Varicella Series		

 Range of recommended ages

 Catch-up immunization

 Certain high-risk groups

NIS-Teen Coverage, 2006-07



What about recent serogroup B disease clusters??

- U PENN, and others
- Serogroup B historically associated with larger community-wide outbreaks
- Factors behind recent clusters unclear
 - Recent increase in incidence?
 - Serogroup replacement?
 - Natural cycles?

Meningococcal disease in MCV4 vaccinated persons

- **14 confirmed cases***
 - 7 (50%) male
 - 7 (50%) attending college
 - 2 (14%) military recruits
 - Median age of vaccination 18.4
 - Median age at time of disease 19.9
- **No common lot of vaccine**
- **Vaccine efficacy vs. waning protection?**

*Cases identified through December 31, 2008

Underlying Medical Conditions

<i>Case</i>	<i>Description</i>
1	Pulmonary embolism and deep vein thrombosis
2	Diabetes and mitral valve prolapse
3	Irritable bowel syndrome, eczema
4	Current smoker
5	Pyelonephritis
6	None reported
7	Seasonal allergies
8	None reported
9	Prior history of bacterial meningitis, recurrent infections
10	None reported
11	None reported
12	None reported
13	Anemia and receiving eculizumab (Soliris)
14	Unknown

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*Cases identified through December 31, 2008

Eculizumab (Soliris®)

- **Approved 2007**
- **Monoclonal antibody targeted against complement protein C5**
- **Indication: Paroxysmal nocturnal hemoglobinuria (PNH)**
- **Increased risk of meningococcal disease***
 - **Meningococcal disease in 2 of 196 PNH patients while receiving eculizumab in a clinical trial**
 - **Black box warning: Vaccination and monitoring recommended**

***Soliris® prescribing information.**

Stay Tuned: Revaccination

- **Duration of protection?**
 - Antibody response known to decrease over time with conjugate vaccines
 - Immunologic memory activation alone is likely too slow to protect against meningococcal disease
- **Revaccination of healthy individuals?**
- **Revaccination of high risk individuals?**

Stay tuned: New Vaccines

- **Expected licensure of Novartis A,C,Y,W-135 vaccine for adolescents and adults**
- **Infant conjugate vaccines about a year away**
- **Serogroup B vaccines 3-5 years?**
 - **Target various outer membrane proteins**
 - **Must be designed to target specific serogroup B strains**

Antimicrobial resistance

Chemoprophylaxis Recommendations (2005)

Drug	Age group	Dosage	Duration and Route
Rifampin*	<1 mo	5 mg/kg q12 hr	2 days PO
	Children ≥1 mo	10 mg/kg q12 hr	2 days PO
	Adults	600 mg q12 hr	2 days PO
Ceftriaxone	Children < 15 yr	125 mg	Single IM dose
	Adults	250 mg	Single IM dose
Ciprofloxacin*	Adults	500 mg	Single PO dose

*Not recommended for pregnant women.

Penicillin resistance

- 1940's therapeutic use
- 1980's reports of intermediate resistance
- Increasing rates of intermediate resistance, especially in Europe
- High level resistance rare

Ceftriaxone resistance

- **India 2006: 8 cases**
 - **Some isolates reportedly multidrug resistant (chloramphenicol, ciprofloxacin)**

Machanda V, Bhada P. JCM 2006, V. 44, pp. 4290-91.

Rifampin resistance

- Chemoprophylaxis use since 1960's
- Reports of resistance developing after chemoprophylaxis (1970's)
- Associated with chemoprophylaxis failure cases
- Primary cases of rifampin-resistant disease is rare

Ciprofloxacin resistance

- Sporadic reports overseas since 1990's
- North Dakota/Minnesota (2007-08)
 - 3 cases and one asymptomatic carrier identified (serogroup B)
 - Ciprofloxacin no longer recommended locally
 - Recommended: ceftriaxone, rifampin, or azithromycin
- California (2008)
 - 1 case identified (serogroup Y)
 - No change in local chemoprophylaxis guidelines

MMWR 2008, 57:173-5.

Wu H, et al. NEJM 2009, 360: 886-892.

Ciprofloxacin resistance: ?s

- Clinical significance?
- Sporadic or emerging?
- Will it follow the same pattern of quinolone-resistant *N. gonorrhoeae*?
- Alternative chemoprophylaxis agents needed
 - Azithromycin resistance
 - Oral 3rd generation cephalosporins

Antimicrobial resistance surveillance

- **Chemoprophylaxis failures**
- **Prospective antimicrobial resistance surveillance**
 - **ABCs**
 - **MeningNet**

Take home messages

- Meningococcal disease incidence decreasing
- Effect of MCV4 on disease epidemiology still unclear
- New vaccines and recommendations are on the horizon
- Antimicrobial resistance is present
- Report
 - Vaccination failures
 - Chemoprophylaxis failures

Thank You!

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Prevention**

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