

# **Recommendations for meningococcal conjugate vaccine in high-risk 2-10 year-olds**

**Advisory Committee on Immunization Practices  
October 24, 2007**

Amanda Cohn, MD

Meningitis and Vaccine Preventable Diseases Branch  
National Center for Immunizations and Respiratory Diseases



# Outline

- Background
- Immunogenicity and Safety
- Proposed recommendations

# Meningococcal Disease

- Causes 1,400-2,800 cases of meningitis or sepsis per year
- Case-fatality ratio 10-15%
- Substantial morbidity: 10-20% survivors have sequelae

# 2-10 year olds at increased risk of meningococcal disease

- Functional or anatomic asplenia
- Terminal complement deficiencies
- Traveling to areas where *N. meningitidis* is hyperendemic or epidemic.
- HIV positive\*
- Meningococcal disease outbreaks

\*Persons with HIV are likely at increased risk for meningococcal disease, although not to the extent that they are at risk for invasive *S. pneumoniae* infection (CDC, May 2005).

# Estimated 2-10 year olds at increased risk

- Total of 70,000 persons with sickle cell anemia in U.S.\*
  - Small portion in 2-10 age group
- Incidence of asplenia unknown
- 2001-2004, 1025 children <13 years with HIV\*\*

\*National Heart, Lung, and Blood Institute. Diseases and conditions index. Sickle cell anemia: who is at risk? Bethesda, MD: US Department of Health and Human Services, National Institutes of Health, National Heart, Lung, and Blood Institute; 2007.

\*\* CDC.MMWR. 55(21);589-592



# Meningococcal Polysaccharide Vaccine (MPSV4), Menomune<sup>®</sup>

- Currently recommended for persons 2-10 years-old and >55 years-old at increased risk of meningococcal disease
- Safe and effective in persons aged  $\geq 2$  years
- Serum bactericidal antibodies (SBA) titers drop in 2-3 years, especially in young children

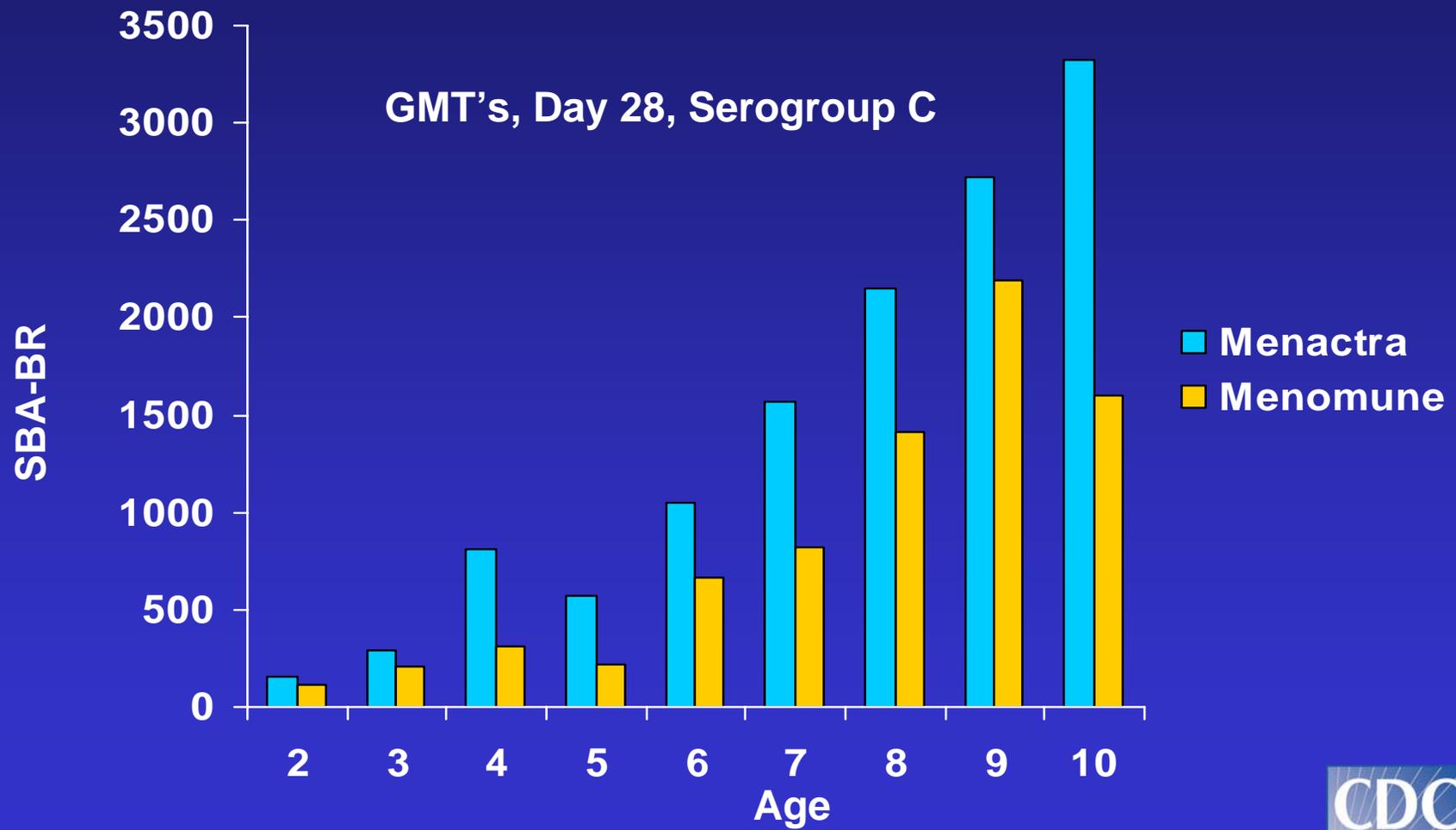
# Meningococcal conjugate vaccine (MCV4), Menactra<sup>®</sup>

- Serogroups A, C, Y, W-135
- Conjugated to 48 µg diphtheria toxoid
- T-cell dependent response
  - Elicits production of memory B-cells
- Should provide longer duration of protection

# Immunogenicity of a single dose of MCV4 in 2-10 yo

- Non-inferiority to MPSV4
  - All subjects received 4 doses of DTaP
  - Mean age 3.7 years (+-2.2), >80% 2-5 years
- For all serogroups, at 28 days and 6 months SBA titer higher in MCV4 group compared to MPSV4 group

# MCV4 vs. MPSV4 in children 2–10 Years of age (GMTs): Serogroup C



Pichichero M et al. *Pediatr Infect Dis J.* 2005;24:57-62.

# Safety of MCV4 in 2-10 year olds

- No serious adverse events in either group
- Majority mild or moderate reactions
  - 91.4% of MCV4 recipients
  - 98.8% of MPSV4 recipients
- All reactions resolved without sequelae
- MCV4 recipients experienced more severe local reactions

# Proportion of study group presenting with reported solicited local reactions within 7 days of immunization

Local Reaction	MCV4 N=692	MPSV4 N=700
Any local reaction	58.8%	58.3%
Redness	29.5%	30.4%
Swelling	20.5%	14.6%
Induration	22.1%	15.6%
Pain	48.1%	46.9%

# Duration of protection

- 173 4-5 year olds
  - Vaccinated with MCV4 23-36 months prior
  - Vaccine naïve
- MPSV4 challenge dose (1/10 of normal dose)
- Immune responses tested either 8 or 28 days after MPSV4 challenge

## Results: SBA GMT at baseline and 8 days after MPSV4 challenge

Serogroup	MCV4-primed		MCV4-naive	
A	256 (112,587)	11,412 (9197,14161)	141 (58,342)	6720 (5205,8676)
C	59 (29,118)	8701 (6168,12239)	17 (8,38)	2448 (1652,3626)
Y	415 (265,649)	7262 (5696,9257)	256 (120,547)	3860 (2751,5415)
W-135	91 (45,181)	11761 (8556,16166)	17 (9,33)	5195 (3849,7011)

- Booster response exhibited 2-3 years after vaccination with MCV4

# Key messages

- Immunogenicity from MCV4 is non-inferior to MPSV4 in 2-10 year-olds
- Safety profiles are similar
  - MCV4 causes more severe local reactions compared to MPSV4
- 2-3 year-olds have a boost response on challenge 2-3 years after vaccination

# Brief Notice to Readers: Proposed Recommendations

- “For children 2-10 years-old with increased risk of meningococcal disease, MCV4 is preferable to MPSV4”
- “For children 2-10 years-old who previously received MPSV4 and remain an increased risk for meningococcal disease, ACIP recommends vaccination with MCV4 3-5 years after receipt of MPSV4.”

# Children with a history of Guillian-Barre Syndrome

- “Persons with a history of GBS may be at increased risk of GBS after MCV4; therefore, a history of GBS is a precaution to receiving MCV4 .”

# VOTE