

Evolving Vaccine Guidance: Influenza, Meningococcal & HPV Vaccines

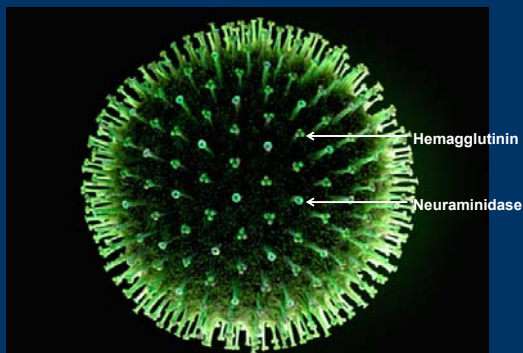
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Disclaimers/Disclosure

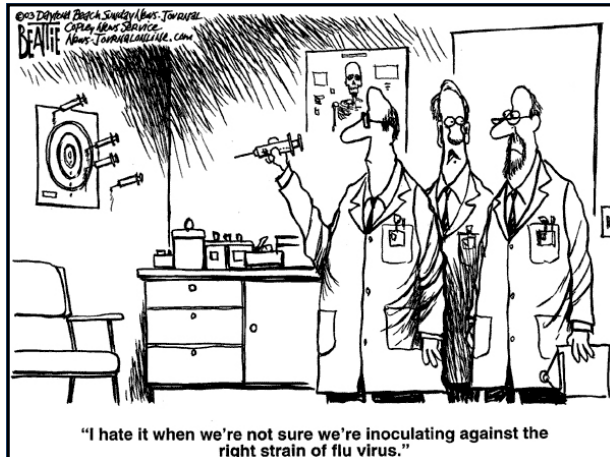
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- I may discuss the use of vaccines in a manner not consistent with the Package Insert, but all recommendations are in accordance with recommendations from the ACIP & AAP

Influenza Virus



AAP Influenza Vaccine Recommendations for 2016-17

- Changes to the strains contained in vaccines
- LAIV should not be used in any setting
- Recommendations for persons with egg allergy have been modified
- New vaccine licensures
 - Flud (aIV3) Seqirus
 - Flucelvax (ccIV4) Seqirus



Will New Influenza Viruses Circulate In 2016-2017?

| <u>2015-16</u> | <u>2016-17</u> |
|---|---|
| - A/California/7/2009 (H1N1)pdm | - A/California/7/2009 (H1N1)pdm |
| - A/Switzerland/9715293/2013 (H3N2) | - A/Hong Kong/4801/2014 (H3N2) |
| - B/Phuket/3073/2013 - Yamagata lineage | - B/Brisbane/60/2008 - Victoria lineage |
| - B/Brisbane/60/2008 - Victoria lineage - For quadrivalent vaccines | - B/Phuket/3073/2013 - Yamagata lineage - For quadrivalent vaccines |

ACIP Voted Down Use of LAIV for 2016-17 Influenza Season

- LAIV VE against any influenza was 3% (-49% to 37%) among children 2 to 17 years
- IIV VE against any influenza was 63% (52% to 72%)
- Other non-CDC studies confirmed LAIV worked less well than IIV
- Data from previous two seasons (2013-14 and 2014-15) showed poor and lower than expected VE for LAIV
- AAP concurred LAIV should not be used

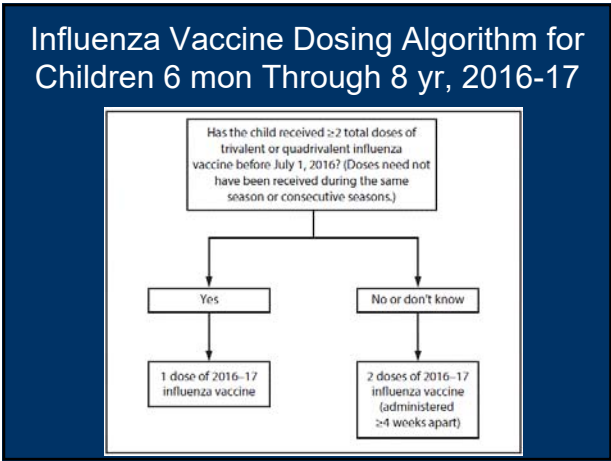
LAIV Effectiveness Against Any Influenza in Children, by Age & Vaccine Type

Adjusted Vaccine Efficacy (95% CI)

| Season (predominant strain) | Age Range (years) | Adjusted Vaccine Efficacy (95% CI) | |
|--------------------------------|----------------------|------------------------------------|-----------------|
| | | LAIV4 | IIV3/IIV4 |
| 2013-14 (H1N1pdm09) | 2-17 | 2% (-53 to 37) | 61% (42 to 74) |
| | 2-8 | -39% (156 to 25) | 60% (32 to 76) |
| | 9-17 | 36% (-31 to 69) | 62% (30 to 80) |
| 2014-15 (H3N2) | 2-17 | 9% (-18 to 29) | 31% (16 to 44) |
| | 2-8 | 9% (-28 to 35) | 26% (2 to 44) |
| | 9-17 | 17% (-27 to 46) | 33% (9 to 51) |
| 2015-16 (H1N1pdm09) | 2-17 | 3% (-49 to 47) | 63% ((52 to 72) |
| | 2-8 | -3% (-76 to 40) | 58% (40 to 70) |
| | 9-17 | 20% (-78 to 64) | 71% (52 to 82) |

From Bernstein H, Kimberlin D. AAP News. August 2016

- ### Inactivated Influenza Vaccines for 2016-17
- Trivalent (IIV3)
 - Fluvirin ≥4 yrs (Seqirus)
 - Afluria ≥9 yrs (Seqirus)
 - Quadrivalent (IIV4)
 - Fluzone ≥6 mon (SP)
 - Fluarix ≥3 yrs (GSK)
 - FluLaval ≥3 yrs (ID Biomedical Corp, GSK)
 - High dose (IIV3)
 - Fluzone (SP) ≥65 yrs
 - Intradermal (IIV4)
 - Fluzone (SP) 18-64 yrs
 - Cell culture derived (ccIIV3)
 - Fluceivax (Seqirus) ≥4 yrs
 - Stratis Jet Injector (IIV3)
 - Afluria (Seqirus) 18-64 yrs
 - Recombinant purified protein (RIV3)
 - Flublok (Protein Sciences Corp) ≥18 yrs
 - Adjuvanted MF59 (aIIV3)
 - Flud (Seqirus) ≥65 yrs



- ### Influenza Vaccine Contraindications & Precautions
- Precautions
 - History of Guillain-Barré syndrome within 6 weeks of previous influenza vaccine
 - Acute illness, moderate to severe
 - Contraindications
 - Severe allergy (anaphylaxis) to vaccine component
 - Age less than 6 months

- ### Influenza Vaccine Other Considerations
- Febrile seizures
 - Deltoid bursitis
 - Guillain-Barré syndrome
 - Thimerosal
 - No risk of getting influenza from IIV
 - Vaccination of Health Care Workers

Egg Allergy is Not a Contraindication for Influenza Vaccine



Warning Signals from the Volatile World of Influenza Viruses

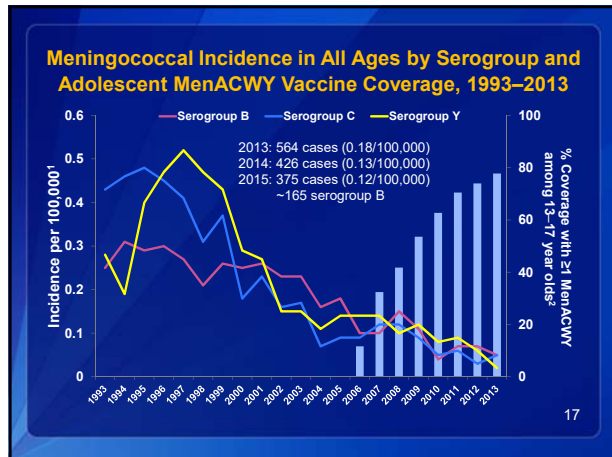


N. meningitidis



Clinically Significant *N. meningitidis* Serogroups

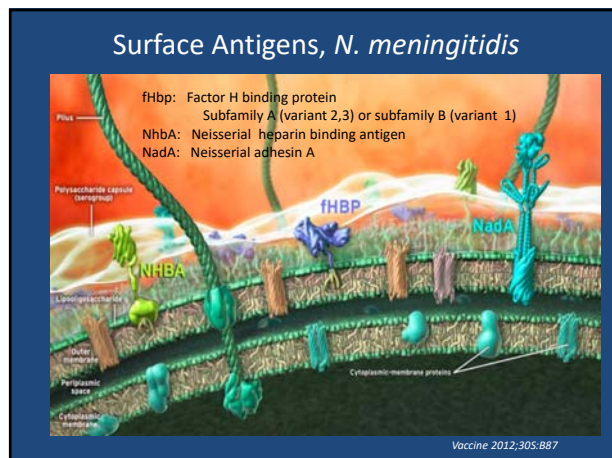
| <u>Serogroup</u> | <u>Characteristics</u> |
|------------------|--|
| A | leading cause of meningitis worldwide most prevalent serogroup in Africa & China rare in Europe and the Americas |
| B | major cause of endemic disease in Europe, the Americas |
| C | major cause of endemic disease in Europe, the Americas |
| Y | associated with pneumonia; increasing problem in U.S. |
| W-135 | small percentage of infections worldwide outbreaks associated with Hajj pilgrims |
| X | rarely encountered |



Six Meningococcal Vaccines

| Trade Name | Vaccine Type | Serogroups | Yr Licensed | Approved Ages |
|----------------------------|--------------------------------------|------------|-------------|-----------------------------|
| Menomune Sanofi Pasteur | polysaccharide | A,C,W,Y | 1981 | ≥2 yrs |
| Menactra Sanofi Pasteur | conjugate MCV4-D | A,C,W,Y | 2005 | 9 mon-55 yrs ^{1,2} |
| Menveo Novartis/GSK | conjugate MCV4-CRM ₁₃₇ | A,C,W,Y | 2010 | 2 mon-55 yrs ² |
| MenHibrix GSK | conjugate HibMenCV-TT | C,Y & Hib | 2012 | 6 wk-18 mon |
| Trumenba Pfizer | protein fHBP | B | 2014 | 10-25 yrs ³ |
| Bexsero GSK | protein MenB-4C | B | 2015 | 10-25 yrs ³ |

¹ Administer at least 4 wks after all PCV doses
² May be given to people 56 years or older
³ May be given to people 26 years or older



Average Annual U.S. Cases By Age Group & Serogroup, 2009-2013

| | Age Group | Cases |
|-----------------|-------------|---------|
| Serogroup B | <5 years | 74-94 |
| | 11-24 years | 54-67 |
| | All ages | 203-260 |
| Serogroup C & Y | <5 years | 34-43 |
| | 11-24 years | 562-77 |
| | All ages | 207-393 |

MCV4 Routinely Recommended

- All children and teens, ages 11 through 18 years
- People <22 years if a first year college student living in residential dorm

Two Meningococcal Serogroup B Vaccines for Persons 10 through 25 Years

- Trumenba (MenB-fHbp, Pfizer)
 - Licensed Oct 2014
 - Schedule: 3 dose (0, 1-2, 6m) or 2 dose (0, 6 mon)
 - Components: 2 highly conserved variants of fHbp
 - Strain coverage estimated >90%
- Bexsero (MenB-4C, Novartis/GSK)
 - Licensed Jan 2015
 - Schedule: 2 dose series (0, 1-6 m)
 - Components: fHbp subfamily B/v1, Nhba, NadA, PorA1.4
 - Strain coverage estimated >90%
 - Licensed in >35 countries starting at 2 months of age

ACIP & AAP Recommendations: Use of Serogroup B Vaccines in Adolescents & Young Adults

May be administered to adolescents and young adults 16 through 23 years of age to provide short term protection against most group B strains (category B)

The preferred age for MenB vaccination is 16 through 18 years of age

Recommended for people ≥10 years at increased risk of MenB (category A)

Groups at Increased Risk for *N. meningitidis*

| MenACWY | MenB |
|------------------------------|------------------------------|
| Complement deficiency | Complement deficiency |
| Anatomic/Functional asplenia | Anatomic/Functional asplenia |
| Outbreak setting | Outbreak setting |
| Microbiologist | Microbiologist |
| Traveler to or reside in | |
| First year college student | |
| Military Recruit | |

People at Increased Risk for Meningococcal Disease

- People >1 month of age
 - functional or anatomic asplenia
 - ~100,000 (11 cases since 1995, 2 serogroup B)
 - persistent complement component deficiency
 - ~80,000 (6 cases since 2005, none B)
 - during an outbreak of caused by vaccine serotype
 - ~60,000 in 5 University outbreaks (all group B)
 - Reside in or travel to country for which meningococcal vaccine is recommended
- Microbiologists who work with meningococcus in a laboratory
 - 100,000 (22 cases 1985-2014, 10 group B)

College Students Have Lower/Equal Risk Of MenB Than Non-College Students

| | |
|--|--------------|
| College Students | 0.09/100,000 |
| 18 through 23 Years Old Non-College Students | 0.14/100,000 |

Immunogenicity of a Meningococcal B Vaccine During Princeton Outbreak

Table 2. Seropositivity and Geometric Mean Titers for the Meningococcal B Outbreak Strain According to Vaccination Status.*

| Characteristic | Two Doses (N = 499) | One Dose (N = 17) | No Vaccination (N = 19) |
|---------------------|---------------------|---------------------|-------------------------|
| hSBA ≥4 | | | |
| No. of participants | 330 | 10 | 4 |
| % (95% CI) | 66.1 (61.8–70.3) | 58.8 (32.9–81.6) | 21.1 (6.1–45.6) |
| GMT (95% CI) | 7.6 (6.7–8.5) | 5.4 (2.5–11.7) | 2.8 (2.3–3.5) |

* Seropositivity is defined as a human serum bactericidal antibody (hSBA) titer of 4 or more. CI denotes confidence interval, and GMT geometric mean titer.

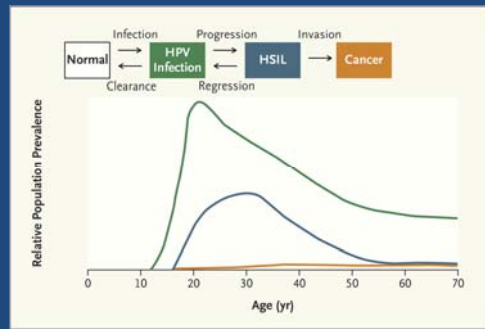
Summary of Different MenB Series Cost-Effectiveness Strategies

| | Cases Prevented | Deaths Prevented | NNV to Prevent 1 Case | NNV to Prevent 1 Death | Cost QALY |
|----------------------|-----------------|------------------|-----------------------|------------------------|-------------|
| At 11 yr | 15 | 2 | 203,000 | 1,512,000 | \$8,700,000 |
| At 16 yr | 28 | 5 | 107,000 | 788,000 | \$4,100,000 |
| At 18 yr | 29 | 5 | 102,000 | 638,000 | \$3,700,000 |
| All college students | 9 | 1 | 368,000 | 2,297,000 | \$9,400,000 |

Unresolved Issues Regarding MenB Vaccines

- Duration of antibody persistence unknown
- Number of vaccine-preventable cases not known
- Impact on carriage not known
- Vaccine pressure on circulating strains not known
- Safety uncertain
 - Theoretical concerns about safety from animal models regarding autoimmune disease
 - FDA aware of concerns at time of licensure
- QALY saved is >20 times higher than any other vaccine

Age at Peak Prevalence for Each Stage in Cervical Carcinogenesis



NEJM 2013;369:2324

Average Annual HPV Associated Cancers, United States 2008-2012

| | Male | Female |
|--------------------|--------------|--------------|
| Cervical Carcinoma | | 11,771 |
| Vaginal SCC | | 802 |
| Vulvar SCC | | 3,554 |
| Penile SCC | 1,168 | |
| Rectal SCC | 237 | 513 |
| Oropharyngeal SCC | 12,638 | 3,100 |
| Anal SCC | 1,750 | 3,260 |
| Total (n=38,793) | 15,793 (41%) | 23,000 (59%) |

SCC = squamous cell carcinoma

MMWR July 8, 2016; 65(26):561

Updated 9vHPV Recommendations

- Vaccinate females and males 9 through 26 years
- If series begun before 15 years of age:
 - 2 dose schedule at 0, 6-12 months
 - If 2 doses 2vHPV, 4vHPV, 9vHPV ≥ 6 mon apart then adequately vaccinated
 - Begin series at 9-11 years
- If begun at 15 years or later:
 - 3 doses recommended at 0, 1-2, 6 months
- For immunocompromised host of any age, 3 doses recommended

Recommendation for HPV Series if 1 or 2 Doses Administered Before 15th Birthday

- For persons initiating series before 15th birthday with 9vHPV, 4vHPV or 2vHPV and
 - Received 2 doses ≥ 6 months apart, are considered adequately vaccinated
 - Received 2 doses < 6 months apart, should receive a 3rd dose ≥ 6 months after 1st dose
 - Received 1 dose, should receive a 2nd ≥ 6 months after 1st dose

Thank You

