Disclosures

• Potential conflicts
  – Safety Review Committee
    • 4vHPV4 in males (Merck)
    • 9vHPV9 (Merck)
  – Data and Safety Monitoring Board
    • Adult and infant PCV15 (Merck)

• No off-label use discussion
Objectives

• Relate the newest recommendations
• Articulate basis for recommendations
• Consider implications for your practice
2016 Topics

• Nasal spray form of flu vaccine is out
• Change for egg allergies and the flu vaccine
• New flu vaccine for those 65 years and older
• New permissive use of MenB vaccines
• The 2-dose HPV vaccine is here!
New ACIP Recommendation

• No LAIV (_________), just IIV
  – 2 years ago
    • Preference for LAIV for children 2 to 8 years old
    • Otherwise IIV3 or IIV4
  – Last year
    • No preference
    • Reason: Lack of consistent relative effectiveness
  – This year
    • No LAIV
    • Persistent failure with effectiveness studies
ACIP

- **Advisory Committee on Immunization Practices**
- Centers for Disease Control and Prevention
- Only federal source of civilian vaccine recs
  - Children
  - Adolescents
  - Adults
- Does *not* create school/daycare mandates
- *Does* decide what *Vaccines for Children* covers
ACIP Membership

- 15 volunteers appointed by Sec’y of HHS
  - 14 medical and public health experts
  - 1 individual consumer representative
- Meets 3 times a year
- Supported by CDC and FDA
- Joined by AAP and AAFP for children
- Joined by AAFP, ACP, and ACOG for adults
Last Year’s Status of LAIV

• Studies in adults
  – Either
    • IIV ≈ LAIV
    • IIV > LAIV

• Studies in children
  – Before 2009 pandemic
    • LAIV > IIV all strains
    • LAIV > IIV drifted H3N2
  – Post 2009 pandemic
    • 2013-2014 LAIV < IIV re H1N1pdm09
    • 2014-2015 Neither effective re drifted H3N2
This Year

- ACIP reviewed preliminary data late May
- US Influenza Vaccine Effectiveness Network
- Children 2-17 years during 2015-2016
  - LAIV vaccine efficacy against any flu virus
    - 3 percent (95% CI of -49 to 37%)
  - IIV vaccine efficacy against any flu virus
    - 63 percent (95% CI of 52 to 72%)
- Other (non-CDC) studies support the conclusion that LAIV worked less well than IIV this season
ACIP Decision

- LAIV should **not be used** during the 2016-2017 flu season
- American Academy of Pediatrics concurs
Vaccine Pain Reduction

• With no LAIV, push for pain reduction
  – AAP, WHO, CDC, ACIP, & AHRQ endorses
• Encourage use of comfort positions
• Offer and encourage pain-reduction methods
  – Topical anesthetics like LMX-4 30 minutes prior
  – Instant topical anesthetics like vibrating ice packs and vapo-coolant sprays
  – Oral sucrose for infants and toddlers
Also New This Year

- ACIP reviewed data for egg allergies
- Risk of withholding vaccine
  - 294,128 hospitalized each yr in US due to flu
    - 21,156 hospitalizations in children <5 years of age
  - 23,607 deaths each year in the US due to flu
    - 124 deaths in children <5 years of age
- Prevalence of egg allergy
  - 0.2 % of adults
  - 1.3 % of children
  - Of 73.7 million children, 1 million egg allergic
Egg and Flu Vaccines

• **In theory** egg protein a problem
  – Most flu vaccine made in egg
  – Most flu vaccine contains ovalbumin
    • Particularly allergenic egg protein
    • RIV is an exception but not LAIV or IIV
Egg and Flu Vaccines

• In practice
  – 27 studies
  – 4100 egg-allergic subjects receiving flu
    • No serious reactions
    • No respiratory distress
    • No hypotension
    • Some hives, wheezing same as non-egg allergic pts
Severe Egg Allergy?

• Most egg-allergy studies included these
  – Histories of severe anaphylaxis
  – N = 513

• These patients also tolerated the vaccine
Growing Consensus

• Major groups
  – U.S. Joint Task Force on Practice Parameters
  – International Consensus (ICON) on Allergic Reactions to Vaccines
  – National Advisory Committee on Immunization
  – Canada (since 2014)

• Any IIV (or LAIV)

• No waiting period

• Don’t limit by severity
ACIP Decision August 26, 2016

- Any flu vax OK for those w/ any egg allergy
- No waiting period recommended for egg
- Consider 15 minutes for all, particularly adolescents, for risk of syncope
- Persons with severe reaction to eggs should be vaccinated in a medical setting with health care provider who is able to recognize and manage severe allergic conditions
A Second IIV for Those ≥65

- Mortality highest in those ≥ 65 years old
- Hospital rates in elderly match infants
- Those ≥65 have lower vaccine response
  - Efficacy in those <65 years 70 to 90%
  - Efficacy in those ≥60 years 58%
  - In subgroup analysis, ≥70 year 57%
  - Rates will vary by season of course
High-Dose Flu Vaccine

- __________ High-Dose (sanofi Pasteur)
  - Usual IIV vaccines contain 15 mcg each strain
  - This vaccine abbrev IIV3-HD 60 mcg each

- Studies demonstrate
  - Higher antibody levels
  - Higher rates of seroprotection
  - Marginally higher rates adverse events

- ACIP: No preference for ≥ 65 years
- Mayo Clinic prefers IIV3-HD over IIV
### High Dose in ≥65 years

<table>
<thead>
<tr>
<th></th>
<th>Percent Antibody Titer ≥ 1:40</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Standard</td>
</tr>
<tr>
<td>A/H1N1</td>
<td>23%</td>
</tr>
<tr>
<td>A/H3N1</td>
<td>51%</td>
</tr>
<tr>
<td>B</td>
<td>30%</td>
</tr>
</tbody>
</table>
Efficacy Data for IIV-HD

- Study just published August 14, 2014 *NEJM*
- Presented to CDC’s ACIP October 2013
- Over 2 seasons in 31,803 people
  - 65 years and older
  - 126 sites in US and Canada
  - 2011-2012 thru 2012-2013
- Relative efficacy 24.2%
New Vaccine for ≥65 Years Old

- _________ (Seqirus) abbreviated aIIV3
- Adjuvanted with MF59
- Licensed by FDA Nov 2015 ≥65 years old
- Delivers higher rates of seroconversion
- Data demonstrating efficacy not available
MenB

- First recs published June 12, 2015 risk-based
- Two vaccines licensed for 10-25 years of age
  - Outbreaks of serogroup B at 2 colleges in 2013
  - Breakthrough Therapy per FDA
    - Based on immunogenicity data alone
    - No efficacy data
  - Accelerated review and approval
- Recommendation
  - ≥10-yrs-old, increased risk for meningococcal dx
Groups at Increased Risk

- Persistent complement component deficiencies
  - C3, C5-9, properdin, factor D, factor H
  - Taking complement blocking eculizumab (______)
- Anatomic or functional asplenia
  - Including sickle cell anemia
- Microbiologists routinely exposed to *N meningitidis*
- Outbreaks of serogroup B meningococcal disease
Two Vaccines

• Wyeth Pharmaceuticals, Inc/Pfizer
  – 3-dose series
  – Licensed October 2014

• Bexsero
  – Novartis Vaccines
  – 2-dose series
  – Licensed January 2015
New Official Permissive Language

• Published October 23, 2015
• MenB vaccine series *may be* administered to adolescents and young adults 16 through 23 years of age for short term protection against meningococcal B disease
• The preferred age for MenB vaccination is 16 through 18 years of age
• ACIP decision means *insurance, VFC covers*
Mayo Clinic Approach

• Offer choice, not recommendation
• Fair and equitable
• Point of care prompt built into EMR
  – 16 through 23 years of age presenting for visit
  – Software scans vaccine hx; if eligible, prompts
• Rooming staff notes prompt
  – Gives one-page letter
  – Gives MenB VIS
Gist of Men B Letter

- We are **offering** the new meningococcal B vaccine, called MenB for short
- Meningococcal B dx is **very rare**, but deadly
- It occurs only 50 to 100 times a year in the U.S., most often in infants
- Demand for MenB vax driven by parents
- Experts advise: choice, **not recommendation**
- Rarity of dx does not justify routine rec
- Most insurance will cover
Two Doses of HPV Vaccine?

• Previous recommendation
  – 3 doses 0, 1-2 months and 6 months
  – Females 11-12 catchup thru 26
  – Males 11-12 catchup thru 21
    • High risk groups through 26
    • Permission to start through 26 for others
  – May start at 9-11

• Uptake major disappointment
  – Only 40% of females 13-17 years old
  – Only 20% of males, 13-17 years old
Why the Problem

• Lack of clinician recommendation
• Concern with timing of vaccine
• Fears with safety
• Pain with injection
• Lack of routine visits to the clinic
• 3 doses doesn’t fit routine preventive care
• Only 40% 13-17 yrs old females completed
• Only 20% 13-17 yrs old males completed
Data Presented at June ACIP

• Multiple studies of 3 dose series
  – Nearly 100% effective 8 to 10 years out
  – No evidence waning at 10 years with 3 doses
  – Seroconversion at 97%, higher than natural

• Two dose versus three doses
  – Phase 3 study: 2 doses 6 months apart vs 3
  – Immunogenicity only, not efficacy
    • 9-14 yrs old w/2 doses same as 15-21 yrs w/3 doses
    • Durability of immune response still under study
  – Other studies: 2 doses slightly less effective
October 19, 2016

• ACIP reviewed data this Oct 19, 2016
• New recs would improve immunity, rates
• Approved
  – Two doses 6 months apart
  – Minimal interval 5 months
  – Only for 9 to 14 years old
  – Mayo Clinic decided October 31 to adopt
Summary

• Don’t use the nasal spray form of flu vaccine
• Vaccinate egg-allergic patients against flu
• Consider new flu option for those ≥65 yrs
• Decide how to approach new MenB option
• CDC encourages clinicians adopt the 2-dose HPV series now for 9-14 years old