IMMUNIZATION UPDATES 2017

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Disclosures

• The speakers have nothing to disclose regarding actual or potential conflicts of interest

• The views expressed in this presentation are those of the speakers and do not reflect the official policy or position of the U.S. Department of Health and Human Services, the Indian Health Services, or the U.S. Government.

Learning Objectives

• Describe recent ACIP changes to the Immunization Schedule

• Review recent immunization related legislative changes in Arizona
Human Papilloma Virus (HPV)

Vaccine Updates

HPV Vaccines

<table>
<thead>
<tr>
<th></th>
<th>4vHPV (Quadrivalent)</th>
<th>2vHPV (Bivalent)</th>
<th>9vHPV (9-Valent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protection from HPV Types:</td>
<td>16,18,11,6</td>
<td>16,18</td>
<td>16,18,11,6,31,33,45,52,58</td>
</tr>
<tr>
<td>Approved Gender:</td>
<td>Females (Males approved 2009)</td>
<td>Females only</td>
<td>Males and Females</td>
</tr>
<tr>
<td>Year Licensed:</td>
<td>2006</td>
<td>2009</td>
<td>2014</td>
</tr>
</tbody>
</table>

The only HPV vaccine now being distributed in the USA is 9vHPV.
HPV Vaccine - Dosing Schedule

- 3-Dose Series
  - Intervals 0, 1 (or 2), 6 months
  - Routine vaccination at age 11 or 12 years old
  - Early as 9 years old for he sexual abuse/assault
  - Females
    - Up to 26 years of age
  - Males
    - Up to 21 years age
    - 22-26 years of age
    - Men who have sex with men, transgender persons
    - Primary or secondary immunocompromising conditions

2-Dose Series vs 3-Dose Series

<table>
<thead>
<tr>
<th></th>
<th>2-Dose Series vs 3-Dose Series</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comparable Immunogenicity</td>
<td>✔️</td>
</tr>
<tr>
<td>Recently approved by FDA</td>
<td>✔️</td>
</tr>
<tr>
<td>Recommended by ACIP</td>
<td>✔️</td>
</tr>
</tbody>
</table>

**Long-lasting immunity**

*HPV clinical trial data has been approved for 3-dose series. Evaluated males and females 9-14 years old and females 15-26 years old. Evaluated long-term outcomes of 3-dose series. No evidence of waning of protection up to 10 years follow up from clinical trials. 2-dose series expected to yield comparable results given similarity in antibody kinetics between the two series and vector.

National Immunization Survey-Teen (NIS-Teen), United States 2015

<table>
<thead>
<tr>
<th></th>
<th>Females n=10,508 (95% CI)</th>
<th>Males n=11,167 (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 dose</td>
<td>62.8% (±1.8)</td>
<td>69.8% (±1.6)</td>
</tr>
<tr>
<td>2 doses</td>
<td>82.2% (±1.8)</td>
<td>90.0% (±1.7)</td>
</tr>
<tr>
<td>3 doses</td>
<td>97.9% (±1.8)</td>
<td>98.1% (±1.8)</td>
</tr>
</tbody>
</table>

- Estimated coverage among males/females 13-17 years of age
HPV 2-Dose Series

- Intervals 0, 6-12 months
- Ages 9-14
- Absent of certain medical conditions that could reduce cell-mediated or humoral immunity
  - HIV
  - Transplantation
  - Malignant neoplasms
  - Immunosuppressive therapies
  - Autoimmune disease
  - T-lymphocyte complete/partial defects
  - B-lymphocyte antibody deficiencies

Patient Case #1

- PT is a 14yo female with PMH exercise-induced asthma and seasonal allergies. Medications include albuterol inhaler (PRN) and loratadine 10mg daily. NKDA and no significant reaction to any vaccine given previously. Mother presents with patient about getting caught up with HPV vaccinations:

- Dates of Vaccines Vaccines given
  - 02/13/2016 4vHPV
  - 12/03/2016 9vHPV

- What would you recommend for PT?
  A. Give 9vHPV now
  B. Give 4vHPV now since originally started with 4vHPV
  C. Restart the series with 9vHPV since started with 4vHPV
  D. Patient does not need HPV vaccination today

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Meningococcal Conjugate Vaccine (MCV)

Vaccine Updates

Timeline of ACIP Recommendations for MCV

2005
- Licensure of first MCV vaccine: MenACWY-D (Menactra®)
- First routine vaccination recommended for adolescents aged 11-12 years, entering high school, and others of increased risk

2006
- Vaccine supply inefficient
- Limited to children entering high school/college, or persons 11-55 years of age at increased risk of meningococcal disease

2007
- Vaccine more available
- Expanded to ALL adolescents aged 11-18 years
- Children 2-10 years at increased risk for disease

2009
- ACIP recommends booster for high risk patients
  - Booster every 5 years (after 3 years if last dose before 7th birthday)

2010
- 2nd licensed product approved: MenACWY-CRM (Menveo®)
  - Routine booster at age 16
  - Patients aged ≥2 years with complement component deficiencies, HIV or asplenia, 2-dose primary series (separated by 2-3 months), then booster every 5 years
Timeline of ACIP Recommendations for MCV

2011
- 2-dose primary series recommended for children 9-23 months at increased risk for meningococcal disease

2012
- Hib-MenCY-TT (MenHibrix®) licensed in USA
- 4-dose series (boosters not recommended for this product)
- Children 2-18 months at increased risk for meningococcal disease

2013
- MenACWY-CRM (Menveo®) also recommended for use starting at age 2 months
- 4-dose series for those increased risk for disease (aplasia, sickle cell, complement deficiencies, high risk areas)

ACIP Updates for Use of MCV 2016
- Increased risk for meningococcal disease in HIV-infected patients
- Majority of disease caused by serogroups A,C,W,Y
- Routine vaccination at 2 months of age for patients with HIV

<table>
<thead>
<tr>
<th>Period (years)</th>
<th>Study Site</th>
<th>Age Group</th>
<th># of cases</th>
<th>Increase in meningococcal disease rate among HIV patients compared with Non-HIV patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000-08</td>
<td>USA</td>
<td>25-64 yrs</td>
<td>491</td>
<td>13-fold</td>
</tr>
<tr>
<td>2003-07</td>
<td>South Africa</td>
<td>All ages</td>
<td>504</td>
<td>11-fold</td>
</tr>
<tr>
<td>2000-11</td>
<td>New York City</td>
<td>15-64 yrs</td>
<td>265</td>
<td>10-fold</td>
</tr>
<tr>
<td>2011-13</td>
<td>United Kingdom</td>
<td>All ages</td>
<td>2133</td>
<td>5-fold</td>
</tr>
</tbody>
</table>

Data from Table 1 in CDC MMWR Weekly/November 4, 65(43);1189-1194

Recommended Schedule for Patients with HIV

- Primary Vaccination

<table>
<thead>
<tr>
<th>Age</th>
<th>Recommended Schedule and Intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2 years</td>
<td>MenACWY-CRM (Menveo®)= 4 doses (2,4,6,12-15 months)</td>
</tr>
<tr>
<td></td>
<td>If started 7-11 months = 2 doses, 2nd dose 12 weeks apart &amp; AFTER 1st Birthday</td>
</tr>
<tr>
<td></td>
<td>MenACWY-D (Menactra®)= 2 doses (9-23 months, 12 weeks apart)</td>
</tr>
<tr>
<td></td>
<td>FDA licensed, but not ACIP recommended to start earlier than two years old</td>
</tr>
<tr>
<td>&gt;2 years</td>
<td>MenACWY (-D or –CRM) = 2 doses (8-12 weeks apart)</td>
</tr>
</tbody>
</table>

- Booster Dose

<table>
<thead>
<tr>
<th>Age</th>
<th>Recommended Schedule and Intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;7 years at</td>
<td>Additional MenACWY (-D or –CRM) after 3 years, then every 5 years</td>
</tr>
<tr>
<td>previous dose</td>
<td></td>
</tr>
<tr>
<td>&gt;2 years at</td>
<td>Additional MenACWY (-D or –CRM) every 5 years</td>
</tr>
<tr>
<td>previous dose</td>
<td></td>
</tr>
</tbody>
</table>

MenACWY-D (Menactra®)
- Give at least 4 weeks upon completion of PCV-13 doses
- Give either before or concomitantly with DTaP
Patient Case #2

EJ is a 9-month old patient that is getting discharged from the Inpatient Ward after being admitted for observation due to a recent LRI. He appears to be up to date in getting his routine vaccinations on schedule. However, the floor nurse consults with you, the inpatient pharmacist on duty, regarding whether EJ requires any additional vaccinations. Upon closer review, you notice he is diagnosed with HIV and has never had a meningococcal vaccine. He appears to have NKDA or contraindications to receiving inactivated vaccines.

What would you recommend for this patient to receive?

A. MenACWY-CRM (Menveo ®)
B. MenACWY-D (Menactra ®)
C. MPSV4 (Menomune ®)
D. Patients with HIV should not receive meningococcal vaccine

Neisseria meningitidis
Seringroup B (MenB)

Recent Updates
MenB Prevalence*

- Recent outbreaks of meningococcal disease for college students (2015)
  - 44 cases/100,000 student (Rhode Island) vs national 0.15 cases/100,000 aged 17-22
  - ~50% of outbreaks in USA caused by serogroup B
- Uncommon in USA, can infect otherwise healthy individuals
- Transmitted via large-droplet respiratory tract secretions
- ~15-29 cases & 2-5 deaths could be prevented annually with routine adolescent MenB vaccination

*Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, CDC, unpublished data, 2013

Men B Vaccines

Oct 2014
- MenB-FHbp (Trumenba®) licensed by FDA
  - 3-dose series (intervals 0,2,6 months)
  - Breakthrough Therapy designation

Feb 2015
- MenB-4C (Bexsero®) licensed by FDA
  - 2-dose series (intervals 0,1 month)
  - Breakthrough Therapy designation

Recommendations for MenB

- Routinely recommended for patients at high-risk (>10 yrs of age)
  - Anatomic/functional asplenia
  - Persistent complement component deficiency
  - Taking eculizumab (Soliris®)
  - Risk of outbreak of serogroup B
  - Laboratory personnel working with meningococcus bacteria
- Recommended per clinical discretion for patients at low-risk
  - 16-23 years of age
    - Preferred range 16-18 yrs
Recommended Schedule and Intervals

<table>
<thead>
<tr>
<th>Low-Risk (16-23 yrs)</th>
<th>High-Risk (&gt;10 yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-doses (6 months apart)</td>
<td>3-doses (0, 2, 6 month schedule)</td>
</tr>
<tr>
<td>2-doses (4 weeks apart)</td>
<td>2-doses (4 weeks apart)</td>
</tr>
</tbody>
</table>

- MenB vaccines are NOT interchangeable
- Administer MenB at different anatomic sites from other vaccines, if possible

*Anatomic/functional asplenia (including sickle cell disease), persistent complement deficiencies (inherited/chronic deficiencies in C3, C5-9, properdin, factor D/H, taking eculizumab)

New Safety Alert
(Canadian Product Information)

- MenB vaccination and eculizumab (Soliris®)
  - Eculizumab treats Paroxysmal Nocturnal Hemoglobinuria (PNH), or atypical Uremic Syndrome (aHUS)
  - Increased risk of anemia or hemolysis after vaccination of MenB-4C
  - Highest risk when patients received dose of eculizumab within 2 weeks of MenB-4C
  - Vaccinate against MenB before starting treatment with eculizumab
  - If already treated with eculizumab, may vaccinate against MenB when disease is controlled and eculizumab concentration in the blood is high

Patient Case #3

- AJ is a 18 yo male with no significant medical history and NKA. The college he will be attending soon requires him to be up to date on all routine vaccinations (including MenB). He has never had a meningococcal vaccine. His vaccination record is shown on the right.

What would you recommend offering for AJ today?

A. Trumenba®, Menveo®, Gardisil-9®
B. Bexsero®
C. Bexsero®, Menactra®
D. Trumenba®, MenHibrix®

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Date Given</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPV</td>
<td>01/16/11</td>
</tr>
<tr>
<td>Tdap</td>
<td>01/16/11</td>
</tr>
<tr>
<td>IV4 (Flu)</td>
<td>10/31/16</td>
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<tr>
<th>Vaccine</th>
<th>Date Given</th>
</tr>
</thead>
<tbody>
<tr>
<td>4vHPV</td>
<td>01/16/11</td>
</tr>
<tr>
<td>Tdap</td>
<td>01/16/11</td>
</tr>
<tr>
<td>IIV4 (Hib)</td>
<td>10/31/16</td>
</tr>
</tbody>
</table>

SIRVA
Shoulder Injury Related to Vaccine Administration

SIRVA: Shoulder Injury Related to Vaccine Administration

Article Excerpt: Are Vaccines Causing Shoulder Injuries?

Attorney Paul Brazil has represented scores of clients with shoulder problems who have received cash awards.

"Most cases fall somewhere in the $20,000 to $100,000 range," he said.

While any injectable vaccine can cause this damage, Brazil says most of his cases involved the flu shot.

"In my personal experience, it seems that a lot of vaccine patients got the vaccine at a pharmacy," he said.

Debbie got her shot from a pharmacy and was awarded $160,000.

"Tell everyone. Do not get a shot at any kind of a pharmacy," she said.

Description of SIRVA

WHAT
- Severe, persistent shoulder pain and limited ROM after the administration of an injected vaccine
- Prolonged restriction of function that can include:
  - Deltoid or shoulder bursitis  - Rotator cuff tear  - Tendonitis  - Adhesive capsulitis  - Frozen shoulder  - Impingement

WHY
- Injury to the musculoskeletal structures - unintended injection of vaccine antigen or needle trauma into or around the shoulder bursa, tendons, or ligaments

WHEN
- Within 24-48 hours of injection
Location, Location, Location…

SIRVA is not related to the vaccine itself, but rather the site of injection.
- When properly administered, IM injections produce a systemic immune response
- Transient pain is common at the injection site, or mild soreness for 1-2 days
- With SIRVA, the vaccine is produces an immune response, but it provokes a LOCAL immune-mediated inflammatory response in the bursa.

**SIRVA is the first recognized side effect based on HOW a vaccine is given.**

Shoulder Anatomy

The Subacromial bursa may extend 3 to 6 cm below the acromion border.

Injection Technique - Considerations

New guidance for injections supported by research and published case reviews

1. Ensure the patient is sitting
2. Get eye level with the patient (i.e. kneel or sit) to ensure a 90 degree angle is achieved for the IM injection

**NEVER STAND WHILE THE PATIENT IS SITTING. A 90 DEGREE ANGLE CANNOT BE ACHIEVED.** (exception is if pt is on an elevated exam table or similar)
Injection Technique - Considerations

3. Ensure the patient rests their hand in their lap or dangles the arm downward. Avoid having the patient rest the arm on a desk or table, since this changes the visibility of the landmarks.

4. Aim for the lower 2/3 of the in the thickest part of the deltoid.

5. Spacing should be above the armpit, approximately 2-3 fingerbreadths (2 inches) below the acromion.

6. Some experts are suggesting using a smaller needle length in females 70kg or less, to avoid over penetrating the deltoid.

7. Some experts recommend a few degrees of abduction laterally so the bursa is mostly covered by the acromion.

Zoster

- Lifetime risk of shingles = 30%

- One episode of shingles does not predispose an individual to a subsequent one
  - Estimates of recurrence range from 1-5%

- ACIP: Vaccinate immunocompetent adults ≥ 60yrs
  - Regardless of prior chickenpox exposure
  - Regardless of prior shingles episode

- FDA: Vaccinate immunocompetent adults ≥ 50yrs

The greatest burden of disease in Zoster and PHN lies in the latter decades of life.
Zoster

<table>
<thead>
<tr>
<th>Age group</th>
<th>Vaccine Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>50-59</td>
<td>70%</td>
</tr>
<tr>
<td>60-69</td>
<td>64%</td>
</tr>
<tr>
<td>70-79</td>
<td>41%</td>
</tr>
<tr>
<td>≥ 80</td>
<td>18%</td>
</tr>
</tbody>
</table>

- Overall (average) efficacy = 51%
- Weigh the benefit of administering at a time with good efficacy, but unknown duration of immune response from vaccination

Zoster

- Efficacy - prevention of shingles
  - About 51% effective overall, varies by age group

- Efficacy - prevention of Post Herpetic Neuralgia (PHN)
  - About 66% across all age groups

- Even if zoster or PHN occurs, vaccination reduces burden of illness (severity & duration) by 61%

Zoster 50 vs. 60 years

ACIP reviewed data for 50-59 year olds

- Rationale for ACIP not changing the current recommendations:
  - Zoster administration should be timed to achieve the greatest reduction in burden of shingles and its complications
  - There is insufficient evidence for long term protection offered by the zoster vaccine
  - Persons vaccinated under 60 years of age may not be protected when the incidence of HZ and its complications are highest

2013 IDSA “Clinical Guideline for Vaccination of the Immunocompromised Host”

- Zoster should be considered in pts who will undergo immunosuppressive therapy and are aged 50-59 years.
Zoster vaccine after shingles

• When can zoster vaccine be given for a patient with active shingles that is over the age of 60?

From “Ask the Experts”:
The general guideline for any vaccine is to wait until the acute stage of the illness is over and symptoms abate. However, a recent case of shingles is expected to boost the person’s immunity to varicella. Zoster vaccine is also intended to boost immunity to varicella. Administering zoster vaccine to a person whose immunity was recently boosted by a case of shingles might reduce the effectiveness of the vaccine. ACIP does not have a specific recommendation on this issue. But it may be prudent to defer zoster vaccination for 6 to 12 months after the shingles has resolved so that the vaccine can produce a more effective boost to immunity.

www.immunize.org
An excellent reference for all vaccine questions or tricky scenarios

Summary of Changes
ACIP Immunization Schedule 2017
2017 Immunization Schedule Changes

**HIV**
- MCV4 is now routinely recommended
  - Initial series: 2 doses 2 months apart
  - Boosters: 1 dose every 5 years

**HPV**
- Anyone who started HPV series before age 15 years and received 2 doses at least 5 months apart are considered adequately vaccinated and do NOT need an additional dose of HPV vaccine.

**2017 Immunization Schedule Changes**

**Hep B**
- Chronic Liver Disease now clarified including, but not limited to, hepatitis C infection, cirrhosis, fatty liver disease, alcoholic liver disease, autoimmune hepatitis, and ALT/AST level > 2 times upper limit of normal

**Tdap**
- 1 dose in each pregnancy, but now preference for earlier in the 27-36 week gestational period, which will maximize passive antibody transfer to the infant
References


References

- online at http://japha.org/