Immunization Updates

New Shingles Vaccine
Perinatal Tdap
Influenza
Hepatitis Vaccines
CDPH Resources
Disclosures

• I have no financial interests in immunizations discussed here

• I may discuss off-label use of licensed vaccines
Herpes Zoster (HZ) and Postherpetic Neuralgia (PHN) 
Epidemiology, United States

- ~1 million cases annually\(^1,2\)
- Incidence of HZ and PHN increase with age\(^2,3,4\)
- HZ (cases per 1,000 population)
  - Children: <1
  - 80 years and older: >15
- PHN
  - 50 years and older: 10-18% of HZ cases develop PHN
- Zoster Vaccine Live (ZVL, Zostavax) licensed in U.S. since 2006
  - 33% of individuals 60 years and older report receipt.\(^5\)

4. Harpaz et al, IDWeek 2015
5. CDC, provisional unpublished data from NHIS
Vaccination Coverage of Zoster Vaccine Live, among Adults ≥60 yrs, United States, 2007-2016

What’s new?
Recombinant Zoster Vaccine (RZV) - Shingrix

- 2 components
  - Glycoprotein E – recombinant protein
  - Adjuvant ASO1B

- Efficacy & safety evaluated in 2-part, phase III RCT
  - >30,000 subjects

- FDA licensure on Oct 20, 2017
  - https://www.fda.gov/biologicsbloodvaccines/vaccines/approvedproducts/ucm581491.htm
Zoster vaccines – Important Differences!

<table>
<thead>
<tr>
<th>Zoster vaccine</th>
<th>Storage</th>
<th>Route of injection</th>
<th>Doses in Series</th>
</tr>
</thead>
<tbody>
<tr>
<td>RZV (Shingrix)</td>
<td>Refrigerator</td>
<td>IM</td>
<td>2</td>
</tr>
<tr>
<td>ZVL (Zostavax)</td>
<td>Freezer</td>
<td>SQ</td>
<td>1</td>
</tr>
</tbody>
</table>

Improperly stored vaccine is useless!
Herpes Zoster - Vaccine efficacy and effectiveness for RZV and ZVL, by age group, during the first $4^\dagger$ years following vaccination

<table>
<thead>
<tr>
<th>Age Group</th>
<th>RZV (ZOE 50/70)^</th>
<th>ZVL (RCTs*)</th>
<th>ZVL (Baxter 2017)</th>
<th>ZVL (Izurieta 2017)</th>
</tr>
</thead>
<tbody>
<tr>
<td>50-59 yrs</td>
<td>62</td>
<td>64</td>
<td>36</td>
<td>55</td>
</tr>
<tr>
<td>60-69 yrs</td>
<td>70</td>
<td>55</td>
<td>38</td>
<td>48</td>
</tr>
<tr>
<td>70+ yrs</td>
<td>64</td>
<td>48</td>
<td>48</td>
<td>32</td>
</tr>
</tbody>
</table>

$^\dagger$ Median follow up may be less than 3 yrs: Schmader 2012= 1.3 yrs

^ ZOE 50/70= 50-59 & 60-69yr: Lal 2015, 70+yrs: Cunningham 2016

* RCTs= 50-59 yrs: Schmader 2012, 60-69 and 70+ yrs: Oxman 2005,
Herpes Zoster - Vaccine efficacy for ZVL and RZV, by year following vaccination

Note: The Shingles Prevention Study, Short-term Persistence Study, and Long-term Persistence Study followed the same study population over time.
ACIP Recommendations
Zoster Vaccines – Recap

Age 50 years and older
- Administer 2 doses of RZV 2–6 months apart regardless of
  - past episode of herpes zoster, or
  - receipt of past doses of ZVL
    - wait at least 2 months after ZVL before dose of RZV.

Age 60 years or older
- Administer either RZV (preferred) or ZVL
  - wait at least 2 months after ZVL before dose of RZV
ACIP Recommendations
Zoster Vaccines – Co-morbidity

- Persons with **chronic medical conditions** (e.g., chronic renal failure, diabetes mellitus, rheumatoid arthritis, and chronic pulmonary disease) should receive RZV.

- **Immunocompromised persons**. No recommendations yet.
  - To be discussed as additional data become available.
RZV (Shingrix) Reactogenicity

- Before vaccination, counsel about expected reactogenicity
  - pain (78%)
  - myalgia (45%)
  - fatigue (45%)

- Reactions to 1st dose did not predict reactions to 2nd dose

- Vaccine recipients should be encouraged to complete the series even if they experienced a grade 1–3 reaction to the first dose
RZV (Shingrix) Clinical Guidance

- RZV may be co-administered with other vaccines
  - RZV+ QIV (Fluarix) – no interference or safety problems
  - RZV+ PPSV23 (Pneumovax23) or Tdap (Boostrix) – studies ongoing
  - RZV+ Fluad – have not been studied

https://www.fda.gov/biologicsbloodvaccines/vaccines/approvedproducts/ucm581491.htm
Pertussis Cases by Onset Date, CA, 2008-2018

Cyclical peaks occur every 3-5 years: immunity wanes after infection or immunization

Next peak likely in 2018 or 2019!

*2018 case numbers will increase due to reporting delays

*Reported to CDPH as of 4/2/2018
Pertussis in Infants <4 months of Age

• Most severe disease and deaths occur in infants <4 months of age
  ▪ 2017: 119 cases (1/1000 births)
  ▪ Infants born to mothers with Medi-Cal coverage had >2 times the risk of pertussis compared to privately insured*

• Prenatal Tdap is the focus of pertussis control
  ▪ Tdap at earliest opportunity between 27-36 weeks gestation of every pregnancy

• Administer first dose of DTaP vaccine to infants promptly at 6-8 weeks of age
  ▪ A dose as early as 6 weeks will help protect infants sooner if their mothers did not receive Tdap during pregnancy

Figure 1. Receipt of Tdap vaccine during pregnancy among women with a live birth in 2016, in California, by maternal characteristics, MIHA 2016*

![Bar chart showing receipt of Tdap vaccine by insurance status.]

Figure 4. Receipt of influenza vaccine during pregnancy among women with a live birth in 2016, in California, by maternal characteristics, MIHA 2016†

![Bar chart showing receipt of Flu vaccine by insurance status.]

* MIHA: Maternal-Infant Health Assessment
† MIHA: Maternal-Infant Health Assessment
Figure 2. Receipt of Tdap vaccine during pregnancy among women with a live birth in 2016, by MIHA region\textsuperscript{10}, 2016\textsuperscript{+}
Influenza – 2/18 ACIP Meeting

- Live attenuated influenza vaccine returns as one of many vaccine options for 2018-2019 influenza season
- 2017-18 (A/Slovenia) vs. 2015-16 (A/Bolivia) H1N1 strains
  - Increased reproduction in human cells, more immunogenic
  - No effectiveness data yet
- License indication unchanged: healthy, 2-49 years of age
Influenza vaccine 2018-2019 season

- WHO recommends that vaccines for use in the 2018-2019 northern hemisphere influenza season contain:

  **Trivalent**
  - A/Michigan/45/2015 (**H1N1**) pdm09-like virus;
  - A/Singapore/INFIMH-16-0019/2016 (**H3N2**) -like virus – CHANGE
  - B/Colorado/06/2017-like virus (**B/Victoria/2/87** lineage) – CHANGE

  **Quadrivalent** – above +
  - B/Phuket/3073/2013-like virus (**B/Yamagata/16/88** lineage)

Hepatitis A Outbreak, California, 2016-2018

N = 704 cases of 4/11/18
Hepatitis A Outbreak Cases as of 11/10/17
Hospitalization or Death for Persons with CLD

<table>
<thead>
<tr>
<th></th>
<th>San Diego</th>
<th>Santa Cruz</th>
<th>Los Angeles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Start of outbreak</td>
<td>11/2016</td>
<td>4/2017</td>
<td>9/2017</td>
</tr>
<tr>
<td>Cases</td>
<td>546</td>
<td>76</td>
<td>11</td>
</tr>
<tr>
<td>Deaths</td>
<td>20</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Homeless or illicit drug use (%)</td>
<td>69%</td>
<td>81%</td>
<td>55%</td>
</tr>
<tr>
<td>Hospitalized (%)</td>
<td>68%</td>
<td>43%</td>
<td>73%</td>
</tr>
<tr>
<td>HCV or HBV coinfection (%)</td>
<td>19%</td>
<td>39%</td>
<td>-</td>
</tr>
<tr>
<td>Male (%)</td>
<td>68%</td>
<td>63%</td>
<td>91%</td>
</tr>
<tr>
<td>Median age (years)</td>
<td>43</td>
<td>37</td>
<td>40</td>
</tr>
</tbody>
</table>
Low coverage rates, HAV + HBV vaccines

2014 and 2015 National Health Interview Surveys
Adults aged ≥ 18 years self-reporting receipt of vaccines

HAV
- 19% ≥1 dose  12% ≥2 doses  Chronic Liver Disease (CLD)
- 15% ≥1 dose  9% ≥2 doses  No CLD

HBV
- 36% ≥1 dose  29% ≥3 doses  CLD
- 30% ≥1 dose  25% ≥3 doses  No CLD

Yue X et al., Vaccine 2018;36:1183  [https://doi.org/10.1016/j.vaccine.2018.01.033](https://doi.org/10.1016/j.vaccine.2018.01.033)

* Rate per 100,000 population.

CDC, 2016: https://www.cdc.gov/mmwr/volumes/65/su/su6501a6.htm
FIGURE 3—Anti-HAV Prevalence by Age Group, Pine Ridge and Rosebud Reservations, South Dakota, June 1985

ACIP Updates – Adult Hepatitis B Prevention

- Reminder to vaccinate persons with chronic liver disease
  - Hepatitis C virus [HCV] infection
  - Cirrhosis
  - Fatty liver disease
  - Alcoholic liver disease
  - Autoimmune hepatitis
  - ALT or AST level greater than twice the upper limit of normal

New Hepatitis B Vaccine for Adults

- Single-antigen HepB (HEPLISAV-B, Dynavax Technologies Corp.)
- 11/2017: Licensed by FDA for persons ≥ 18y years of age
- 2/2018: ACIP voted to recommend – published recommendations to follow
- Joins other inactivated HBV vaccines in U.S
  - Engerix-B, Recombivax HB, Pediarix, Twinrix

- Yeast-derived recombinant HBsAg
- 1018 adjuvant
  - 22-mer oligonucleotide sequence containing CpG that binds Toll-like receptor 9 to stimulate directed immune response
- 2 doses given at least 1 month apart
Heplisav-B – Seroprotection and Safety

### Immunogenicity
- Healthy: 90%–100% vs. 71%–90% (3 doses Engerix-B)
- Diabetes Type II: 90% vs. 65% (3 doses Engerix-B)
- Chronic kidney disease: 90% (3 doses) vs. 81% (4 double doses Engerix-B)

### Safety and reactogenicity
- Mild adverse events: 46% vs. 46% (Engerix-B)
- Serious adverse events: 5% vs. 6% (Engerix-B)
- Cardiovascular events: 0.27% vs. 0.14% (Engerix-B)
- Potentially immune-mediated events (e.g., granulomatosis + polyangiitis, Graves’ disease): 0.1%–0.2% vs. 0%–0.7% (Engerix-B)


# Meningococcal Vaccines—High-risk Populations

Different vaccines protect against different serogroups.

## Risk groups:
- **Exp. Increased Exposure** to meningococcal serogroups
- **CD. Persistent Complement component Deficiencies** (including those persons taking eculizumab [Soliris®])
- **Asp. Functional or Anatomic Asplenia** (including sickle cell disease)
- **HIV. HIV Infection**

## Age at first dose

<table>
<thead>
<tr>
<th>Age at first dose</th>
<th>Exp.</th>
<th>CD</th>
<th>Asp.</th>
<th>HIV</th>
<th>1) MenACWY vaccines $^2$</th>
<th>Boosters for those who remain at increased risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>2–6 months</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>2 months ACWY-CRM Menevo$^<em>$ 4 months ACWY-CRM Menevo$^</em>$ 6 months ACWY-CRM Menevo$^<em>$ 12-15 months ACWY-CRM$^</em>$ Menevo$^*$</td>
<td>If primary dose(s) given when younger than 7 years: 3 years ACWY-CRM or -D$^4$ Menevo$^<em>$ or Menactra$^</em>$ Every 5 years ACWY-CRM or -D$^4$ Menevo$^<em>$ or Menactra$^</em>$</td>
</tr>
<tr>
<td>7–23 months</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>4 months ACWY-CRM Menevo$^<em>$ 6 months ACWY-CRM Menevo$^</em>$ 12-15 months ACWY-CRM$^<em>$ Menevo$^</em>$</td>
<td>If primary dose(s) given at age 7 years or older: Every 5 years ACWY-CRM or -D$^4$ Menevo$^<em>$ or Menactra$^</em>$</td>
</tr>
<tr>
<td>9–23 months</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>2 months ACWY-D$^{4,6}$ Menevo$^<em>$ or Menactra$^</em>$ 6 months ACWY-D$^{4,6}$ Menevo$^<em>$ or Menactra$^</em>$</td>
<td></td>
</tr>
<tr>
<td>2 years and older</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>2 months ACWY-CRM or -D$^{4,6}$ Menevo$^<em>$ or Menactra$^</em>$ 6 months ACWY-CRM or -D$^{4,6}$ Menevo$^<em>$ or Menactra$^</em>$</td>
<td></td>
</tr>
</tbody>
</table>

## 2) Also give MenB vaccine—may be given at same time as MenACWY vaccine. Use the same brand for each dose in the series.

<table>
<thead>
<tr>
<th>Age at first dose</th>
<th>Exp.</th>
<th>CD</th>
<th>Asp.</th>
<th>HIV</th>
<th>1st dose</th>
<th>2nd dose</th>
<th>3rd dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 years and older</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>MenB-4C Boxero$^<em>$ 1 month MenB-4C Boxero$^</em>$ 1-2 months MenB-FHbp Trumenba$^*$ 6 months between 1st and 3rd dose</td>
<td>OR 1 month MenB-FHbp Trumenba$^<em>$ 2nd dose MenB-FHbp Trumenba$^</em>$</td>
<td>3rd dose MenB-FHbp Trumenba$^*$</td>
</tr>
</tbody>
</table>

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[http://eziz.org/assets/docs/IMM-1218.pdf](http://eziz.org/assets/docs/IMM-1218.pdf)
Pneumococcal Vaccine Timing—For Children

A. Chronic conditions:
- Diabetes
- Heart Disease (particularly failure or cyanotic disease)
- Lung disease (excluding asthma, unless immunocompromised by prolonged high-dose oral corticosteroids – see below)

Children younger than 6 years of age should have received the standard or catch-up doses of PCV13 described above before receiving PPSV23.

B. Immunocompromised (including HIV infection or immunosuppressive treatments),
- Hemoglobinopathy (including sickle cell disease),
- Asplenia,
- Chronic renal failure, or
- Nephrotic syndrome

PCV 13 ➔ 8 weeks ➔ PPSV 23 ➔ 5 years ➔ PPSV 23

C. CSF leaks or Cochlear implants

PCV 13 ➔ 8 weeks ➔ PPSV 23
HPV Vaccine – 2 or 3 Doses?

9-14 YEARS¹

2 DOSES

Routine: 11-12 years
As early as 9 years
Catch-up at 13-14 years

HPV9
Gardasil-9®

6-12 months²

HPV9
Gardasil-9®

15+ YEARS⁴ OR COMPROMISED IMMUNE SYSTEM³

3 DOSES

15–26 years⁴
OR
9–14 years with a compromised immune system³

HPV9
Gardasil-9®

1–2 months⁵

HPV9
Gardasil-9®

6 months between 1st and 3rd dose

HPV9
Gardasil-9®

http://eziz.org/assets/docs/IMM-1254.pdf
Thank you - Questions?

Many thanks to following CDC staff for sharing their slides:

• Kathleen Dooling, MD MPH – Zoster
• David Kim, MD – Hepatitis B