Immunization Update: What’s New?

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Red Stick Potpourri
LA Chapter-American Academy of Pediatrics
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Disclosure

I have no relevant financial relationships to disclose
Objectives

- Discuss epidemiology of selected vaccine preventable diseases
- Discuss recent ACIP and AAP recommendations for use of vaccines
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Influenza

- Annual epidemics
- Substantial morbidity and mortality
  - Pregnant women
  - Healthy infants < 6 months old
  - Children < 2 y/o
  - Persons with chronic conditions
  - > 65 y/o
- The severity of each influenza season is unpredictable
- #1 vaccine-preventable cause of death in children in US
2017-18 influenza season

- High-severity season
  - Widespread activity across US for an extended period
  - High levels of outpatient and emergency department visits, hospitalization rates
Pediatric deaths associated with influenza

- 179 laboratory-confirmed deaths in 2017-18 season
- Deaths 2010-16\(^1\)
  - 675 reported to CDC
  - 50% with no preexisting medical condition
  - 73% unimmunized
- Mortality rates
  - All: (0.15)
  - < 6 mos (0.66)
  - 6-23 mos (0.33)

\(^1\)Pediatrics 2018;141(4):e20172918
Key Strategies to Reduce the Burden of Influenza in Pregnant Women and Infants < 6 Months Old

- Maternal immunization
- Immunization of infant contacts
- Prompt recognition of infant influenza-like illness and treatment with antiviral
- Prompt management of influenza-like illness in contacts
Use of LAIV4 for 2018-19 influenza season

**ACIP**
- Updated LAIV4 formulation
  - Favorable H1N1 immunogenicity studies
- Reintroduced LAIV4 as an option
- “Providers may choose any licensed, age-appropriate vaccine (IIV, RIV4, or LAIV4)”

**AAP**
- Recommends inactivated vaccine (IIV3/IIV4) as primary choice for all children
  - LAIV4 effectiveness
    - Consistently inferior to IIV against H1N1 in past seasons
    - H1N1 effectiveness unknown for upcoming season
- “LAIV4 may be offered for appropriately aged children who would not otherwise receive an influenza vaccine”

ACIP Meeting, 6/20/18
AAP News, 6/7/18
Influenza prevention and treatment: Key points

- Immunize all 6 mos and older
- New A (H3N2) and B (Victoria lineage) components
- Complete immunization by end of Oct
- Algorithm for # of doses for 6 mos – 8 yrs unchanged
- Egg allergy is not a contraindication
- Encourage immunization of pregnant women
- Prompt identification and timely antiviral treatment
Pertussis
Reported NNDSS pertussis cases: 1922-2016

SOURCE: CDC, National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System and 1922-1949, passive reports to the Public Health Service
Pertussis

- High mortality in infants <3 months of age
  - Pertussis related deaths, US, 2000-2016
    - Average – 16 (range: 6-35)

- Current ACIP/AAP strategy: protect the young infant
  - Maternal Tdap, every pregnancy
  - Infant DTaP doses on schedule
  - Cocooning
- **2011-2014**

- 6 US Emerging Infection Program Network states

- Maternal vaccination: ≥ 14 days before delivery

- 240 cases, 535 controls
  - 7.1% of case mothers and 16.8% control received Tdap in 3rd trimester

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**Table 3. Effectiveness of Maternal Tdap Vaccination at Preventing Infant Pertussis, by Timing of Vaccination**

<table>
<thead>
<tr>
<th>Vaccination Status</th>
<th>Cases, No. (%)</th>
<th>Controls, No. (%)</th>
<th>Multivariable VE, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>240 (96)</td>
<td>535 (97)</td>
<td></td>
</tr>
<tr>
<td>Unvaccinated</td>
<td>104 (43.3)</td>
<td>177 (33.1)</td>
<td>Reference</td>
</tr>
<tr>
<td>Before pregnancy</td>
<td>24 (10.0)</td>
<td>67 (12.5)</td>
<td>50.8 (2.1-75.2)</td>
</tr>
<tr>
<td>First or second trimester</td>
<td>5 (2.1)</td>
<td>27 (5.1)</td>
<td>64.3 (-13.0 to 88.8)</td>
</tr>
<tr>
<td>Third trimester</td>
<td>17 (7.1)</td>
<td>90 (16.2)</td>
<td>77.7 (48.3-99.0)</td>
</tr>
<tr>
<td>After pregnancy</td>
<td>90 (37.5)</td>
<td>174 (32.5)</td>
<td>4.9 (-49.3 to 39.5)</td>
</tr>
</tbody>
</table>

**Table 4. Effectiveness of Maternal Tdap Vaccination at Preventing Infant Pertussis Hospitalizations, by Timing of Vaccination**

<table>
<thead>
<tr>
<th>Vaccination Status</th>
<th>Cases, No. (%)</th>
<th>Controls, No. (%)</th>
<th>Multivariable VE, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>157 (96.5)</td>
<td>336 (97)</td>
<td></td>
</tr>
<tr>
<td>Unvaccinated</td>
<td>76 (48.4)</td>
<td>109 (32.4)</td>
<td>Reference</td>
</tr>
<tr>
<td>Before pregnancy</td>
<td>18 (10.2)</td>
<td>48 (13.7)</td>
<td>76.2 (37.2-91.0)</td>
</tr>
<tr>
<td>First or second trimester</td>
<td>2 (1.3)</td>
<td>20 (6.0)</td>
<td>91.4 (24.8-89.0)</td>
</tr>
<tr>
<td>Third trimester</td>
<td>6 (3.8)</td>
<td>47 (14.0)</td>
<td>90.5 (65.2-97.4)</td>
</tr>
<tr>
<td>After pregnancy</td>
<td>57 (36.3)</td>
<td>114 (33.9)</td>
<td>32.5 (-23.5 to 63.1)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; VE, vaccine effectiveness.
*The following variables were included in the final model: household size >2 persons, maternal education, household member with pertussis diagnosis, and infant age (weeks).
Elimination of Perinatal Hepatitis B: Providing the First Vaccine Dose Within 24 Hours of Birth

COMMITTEE ON INFECTIOUS DISEASES, COMMITTEE ON FETUS AND NEWBORN
Hepatitis B

- Rate of acute HBV infections has declined by 90.6% since 1982
- 952 perinatal cases annually (CDC estimate)
  - 90% will develop chronic HBV infection
  - Prophylaxis (HBIG and vaccine) reduces transmission by 94%
Continued failure to eliminate maternal-infant transmission of Hep B

- Failure to provide appropriate prophylaxis
- At-risk infants not identified
  - Errors in:
    - Maternal testing
    - Reporting test results
    - Transcription of maternal HBsAg test results
    - Interpreting test results

- Maternal factors
  - High viral load, HBeAg status, ALT levels, etc.
    - Maternal antiviral therapy [tenofovir] may decrease risk \((NEJM 2016;374(24):2324-34)\)
Birth dose of hepatitis B vaccine by maternal HBsAg status

**Mother HBsAg positive**
- All newborns at all birth weights
- Hepatitis B vaccine and HBIG within 12 hours of birth

**Mother HBsAg negative**
- Birth weight ≥2000 g
  - Hepatitis B vaccine within 24 hours of birth

- Birth weight <2000 g
  - Hepatitis B vaccine at 1 month of age or at hospital discharge (whichever is first)

**Mother HBsAg unknown**
- All newborns at all birth weights
  - Hepatitis B vaccine within 12 hours of birth
    - Birth weight ≥2000 g
      - HBIG within 7 days of birth if maternal status is confirmed positive, or by 7 days of life or at hospital discharge (whichever is first) if status remains unknown
    - Birth weight <2000 g
      - HBIG within 12 hours of birth unless maternal status is confirmed negative by that time

**FIGURE 1**
Administration of the birth dose of hepatitis B vaccine by maternal HBsAg status.
HepB vaccine for infants born to HBsAg-negative mothers

- **Rationale**
  - Creates a safety net
  - Infants receiving first dose by 3 days of age
    (National Immunization Survey, 2010-2015)
    - 2010 = 65%
    - 2015 = 71%
  - Delay of first dose for 1-2 months was associated with 4 fold increase in infection rate
    (British Columbia, 1984-89)
HepB vaccine for infants born to HBsAg-negative mothers

- **Action**

  Assure your hospital policies include giving birth dose of HepB vaccine to all infants > 2000 grams born to HBsAg negative mothers within 24 hours of birth
Infants Born to Mothers Receiving Biologic Response Modifiers

- **Anakinra** – interleukin 1 receptor antagonist – Rheumatoid arthritis
- **Etanercept** – TNF receptor – Rheumatoid arthritis, psoriasis, ankylosing spondylitis
- **Infliximab** – monoclonal antibody to TNF – Crohn’s, rheumatoid arthritis, ankylosing spondylitis
- **Rituximab** – antibody to CD20 surface immunoglobulin – variety of autoimmune diseases
Biologic response modifiers: Clearance in infants born to mothers receiving infliximab

- 44 pregnant women treated for IBD
  - All infants had detectable infliximab in cord blood at birth
    - The mean time to clearance was 7.3 mos (95% CI, 6.2–8.3 mo)
    - Five (11%) infliximab-exposed infants had a detectable concentration at 9 months
      - 1 had a detectable level at 12 months
Interim recommendations for live vaccines for infants born to mothers receiving biologic response modifiers

- Until further data are available, no live vaccines should be given to an infant in the first 12 months after the last maternal exposure to biologic response modifiers *in utero*
  - No rotavirus vaccine
  - 6-12 m/o exposed to measles or traveling internationally – No MMR, use IGIV

2018 Red Book, pgs 86-87
Mumps
Reported Mumps Cases, United States, Vaccine Era, 1968-2016

Source: National Notifiable Diseases Surveillance System (passive surveillance); 2016 data is preliminary (May 31, 2017) and subject to change.
Mumps outbreak data: January 2016 – June 2017

- 150 outbreaks (9,200 cases)
  - Median number of cases per outbreak: 10
  - Median age of case-patients: 21 yrs

- Setting
  - University - 75 outbreaks, 40% of cases
  - Community – 48 outbreaks, 57% of cases
  - Schools other than university – 19 outbreaks, 3% of cases

- Vaccine status: 6.5% - 1 dose; 54.5% - 2 doses; 21.9% - unknown
Mumps outbreak data: January 2016 – June 2017

- 2 dose effectiveness – 88%
  - Increased risk with longer time since MMR2

- Complication rate – lower for vaccinated
  - Orchitis – 4.3%

- 3rd dose of MMR vaccine used in 35 outbreaks
  - Limited data on effectiveness
  - Attack rate: 350 recipients – 3.8%

Marin, ACIP Presentation. October 25, 2017
MMR vaccine during mumps outbreak

- Persons previously vaccinated with two doses of a mumps-containing vaccine who are identified by public health as at increased risk for mumps because of an outbreak should receive a third dose of a mumps-containing vaccine to improve protection against mumps disease and its complications.
Mumps: Key Points

- Consider mumps in differential diagnosis of acute parotitis
  - If another etiology is not apparent
    - RT-PCR on Stenson duct exudate, throat washings, saliva, CSF
    - IgM
    - Tissue culture
  - Contact Public Health
Hepatitis A

Outbreak of Hepatitis A Virus (HAV) Infections among Persons Who Use Drugs and Persons Experiencing Homelessness

Summary

The Centers for Disease Control and Prevention (CDC) and the Health Alert Network (HAN) have issued new guidelines for the prevention of hepatitis A among persons who use drugs and persons experiencing homelessness.

CDC

Viral Hepatitis

Outbreaks

Hepatitis A Outbreaks

- Outbreaks of hepatitis A in multiple states among people who use drugs, and for people who are homeless – 2017
- Multistate outbreak of hepatitis A linked to frozen strawberries – 2016
- Hawaii outbreak of hepatitis A – 2016
- Multistate outbreak of hepatitis A virus infections – 2013

Highlights

- Read the Advice to Retailers, Public Health Officials, and Consumers
- Several states, CDC, and the U.S. Food and Drug Administration completed investigation of a multistate outbreak of foodborne hepatitis A, caused by contaminated strawberries.

Northeastern Arkansas hepatitis A outbreak unusually severe

LITTLE ROCK, Ark. — An atypical and unusually severe hepatitis A outbreak in northeastern Arkansas has infected at least 85 people and caused at least one death since February, health officials said Tuesday.
Hepatitis A: Issues

- Changing epidemiology
  - Increased rate in older age groups
  - Increase in outbreaks
    - Homeless, drug abuse, food related
- ISG in short supply
  - Anti-HepA antibody titers are lower
- Vaccine is preferred for post-exposure prophylaxis
Hepatitis A vaccine

- Lowest uptake for routine vaccinations of young children
    - 1 dose 86%
    - 2 doses 61%
  - 13-17 y/o:
    - 1 dose 74%
    - 2 doses 64%

- Goal: Improve immunization rates in childhood

MMWR 2017;66(43):1171-1177
Human papillomavirus
Rate (cases per 100,000 persons) of all HPV-associated cancers combined (cervical carcinoma and squamous cell carcinomas of the vagina, vulva, penis, anus,* and oropharynx) by state, 2010–2014

Incidence rates are per 100,000 persons and were age-adjusted to the 2000 U.S. standard population.

U.S. HPV vaccine program: Highlights

- Initiated twelve years ago
  - Girls – 2006; Boys – 2011
- 9-valent HPV vaccine was licensed 2014
  - Only HPV vaccine used in US since 2016
  - 2 dose schedule recommended in 2016 for <15 y/o
- Over 270 million doses of HPV vaccines worldwide
  - Strong safety record
HPV vaccine: Evidence of population impact

- HPV vaccine type prevalence
  - Australia, Norway, Denmark, Sweden, UK, US

- Genital warts
  - Australia, New Zealand, Denmark, Sweden, Germany, Quebec, US

- Cervical lesions (intraepithelial neoplasia)
  - Australia, British Columbia, Denmark, Sweden, US

- Juvenile Recurrent Respiratory Papillomatosis
  - Australia
Prevalence of HPV vaccine types before and after introduction of 4vHPV in females

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<tr>
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<tbody>
<tr>
<td>HPV 6/11/16/18</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>14-19 y/o</td>
<td>11.5%</td>
<td>4.3%</td>
<td>3.3%</td>
<td>↓ 71%</td>
</tr>
<tr>
<td>20-24 y/o</td>
<td>18.5%</td>
<td>12.1%</td>
<td>7.2%</td>
<td>↓ 61%</td>
</tr>
<tr>
<td>25-29 y/o</td>
<td>11.8%</td>
<td>11.7%</td>
<td>8.8%</td>
<td>↓ 25%</td>
</tr>
<tr>
<td>HPV16/18</td>
<td>7.1%</td>
<td>2.8%</td>
<td>-----</td>
<td>↓ 60%</td>
</tr>
</tbody>
</table>

4vHPV types in sexually active, unvaccinated vs vaccinated with ≥1 dose (14-24 y/o) 12.2% vs 2.0%\(^3\) VE = 83%

Rates of non-4vHPV and non-4vHPV-HR types were unchanged

National Health and Nutrition Examination Survey (NHANES), US, 2003-2014; Nationally representative cross-sectional survey; self collected cervicovaginal swab, pre- and post-vaccine introduction

\(^1\)Pediatrics 2016;137(3):e20151968  \(^2\)J Infect Dis 2017;0000:1–10  
\(^3\)89% decrease in immunized, 34% decrease in unimmunized
Cervical cancer rates

- National Program for Cancer Registries and Surveillance, Epidemiology and End Results Incidence

- 2003-06 vs 2011-14

- 4-yr average incidence
  - 29% decrease in annual incidence in 15-24 y/o
  - No significant decrease in 25-34 y/o after 2006

Estimated vaccination coverage among adolescents aged 13–17 years, NIS-Teen, United States, 2006–2016

Walker T, et al. MMWR 2017; 66  NIS-Teen, National Immunization Survey-Teen;  Note: revised definition of adequate provider data in 2013
Estimated vaccination coverage, 13-17 year olds, National Immunization Survey-Teen, US and LA, 2015 and 2016

<table>
<thead>
<tr>
<th></th>
<th>≥1 Tdap</th>
<th>≥1 MenACWY</th>
<th>≥1 HPV, girls</th>
<th>UTD, girls</th>
<th>≥1 HPV, boys</th>
<th>UTD, boys</th>
</tr>
</thead>
<tbody>
<tr>
<td>US 2015</td>
<td>86.4%</td>
<td>81.3%</td>
<td>62.8%</td>
<td>41.9%</td>
<td>49.8%</td>
<td>28.1%</td>
</tr>
<tr>
<td>US 2016</td>
<td>88.0%</td>
<td>82.2%</td>
<td>65.1%</td>
<td>49.5%</td>
<td>56.0%</td>
<td>37.5%</td>
</tr>
<tr>
<td>LA 2015</td>
<td>91.0%</td>
<td>90.9%</td>
<td>60.0%</td>
<td>39.5%</td>
<td>49.5%</td>
<td>30.5%</td>
</tr>
<tr>
<td>LA 2016</td>
<td>93.7%</td>
<td>90.9%</td>
<td>69.9%</td>
<td>50.8%</td>
<td>51.5%</td>
<td>33.2%</td>
</tr>
</tbody>
</table>

HPV UTD includes persons receiving ≥3 doses and 2 doses when first dose before 15th birthday and time between 1st and 2nd dose was at least 5 months minus 4 days

MMWR 2016;65(33):850-858; MMWR 2017;66(33):874-882
Resources

- Advisory Committee on Immunization Practices
  - http://www.cdc.gov/vaccines/hcp/acip-recs/index.html

- AAP Committee on Infectious Diseases
  - Pediatrics
  - Red Book
  - Red Book Online