Immunization Safety Office Updates

Centers for Disease Control and Prevention

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Advisory Commission on Childhood Vaccines (ACCV)
December 2, 2016

Topics

- Update on selected sessions from the October 2016 Advisory Committee on Immunization Practices (ACIP) meeting including ISO's safety summary on Tdap in pregnant women
- Selected vaccine safety publications

October 2016 ACIP meeting summary

- **Hepatitis B Vaccine (HepB)**
  - **American Association for the Study of Liver Disease (AASLD) recommendation**
    - **Antiviral therapy to reduce the risk of perinatal transmission of hepatitis B in HBsAg+ pregnant women with HPV DNA level >200,000IU/ml**
  - **Removal of permissive language for delaying birth dose**
    - **For all medically stable infants weighing ≥2000 grams at birth and born to HBsAg(-) mothers, HepB dose #1 should be administered within 24 hours of life**
  - **Recommendation for HepB vaccine for persons with hepatitis C infections**
- **Vote* Hepatitis Vaccine**
  - **Yes to accept updated HepB recommendations and Vaccine for Children (VFC) resolution**

*Language regarding votes is provisional until published in the MMWR

http://www.cdc.gov/vaccines/acip/meetings/meetings-info.html

October 2016 ACIP meeting summary (cont.)

- **Vote* Pertussis Vaccine**
  - Yes to accept updated statement in Prevention of Pertussis, Tetanus, and Diphtheria with Vaccines in the United States: Recommendations of the Advisory Committee on Immunization Practices (ACIP)
    - No new vaccine recommendations
    - To be updated/included "Guidance for use" of Tdap for pregnant women and summary of supporting data
      - Tdap should be administered between 27 and 36 weeks gestation, although it may be administered at any time during pregnancy
      - Currently available data suggest that vaccinating earlier in the 27 through 36 week window will maximize passive antibody transfer to the infant
    - Summary of Tdap safety studies in pregnant women their infants

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October 2016 ACIP meeting summary (cont.)

CDC Immunization Safety Office - monitoring activities for maternal Tdap safety

- Vaccine Adverse Event Reporting System (VAERS)
  - Ongoing monitoring
- Vaccine Safety Datalink (VSD)
  - Surveillance and research outcomes include
    - Preterm delivery and small for gestational age (SGA); acute vaccine-related adverse events; obstetric events; birth defects
  - Has access to EMR and medical records to validate cases and denominator(s) for rates
- Clinical Immunization Safety Assessment (CISA) Project*
  - Tdap safety in pregnant women (NCT02209623)
  - Safety of simultaneous Tdap and Inactivated Influenza Vaccine (IIV) in pregnant women (NCT02783170)

October 2016 ACIP meeting summary (cont.)

CDC Immunization Safety Office: Maternal pertussis vaccination – safety data collected in the United States continue to be reassuring

- Pattern of adverse events observed in VAERS in pregnant women receiving Tdap and their infants is consistent with expectations
- Studies of >50,000 women receiving Tdap during pregnancy in the VSD show no increased risk for adverse maternal or infant health outcomes*
- Clinical study in the CISA Project shows Tdap was well tolerated in both pregnant and non-pregnant women, including pregnant women receiving a repeated Tdap dose

*Kharbanda EO et al. JAMA. 2014;312(18):1897-904.; Sukumaran L, et al. JAMA. 2015 314(15):1581-7, Sukumaran L, et al. ObGyn. 2015;126(5): 1069–1074; Kharbanda EO et al. Vaccine 2016; 34: 968-73.

October 2016 ACIP meeting summary (cont.)

- Human papillomavirus vaccines:
- Workgroup proposed a recommendation for a 2-dose schedule for persons initiating the series at age 9-14 years
  - FDA approved a 2-dose series of 9vHPV for persons aged 9-14 years in October 2016
  - Trials of all HPV vaccines found antibody response after 2 doses in 9-14 year olds is non-inferior to 3 doses in the group in which efficacy demonstrated
  - For persons initiating vaccination on or after the 15th birthday, the recommended schedule is 3 doses of HPV vaccines
- Merck will distribute only 9vHPV in the US after Oct. 2016
- 2vHPV and 4vHPV will continue to be available outside the United States

http://www.cdc.gov/vaccines/acip/meetings/meetings-info.html

October 2016 ACIP meeting summary (cont.)

- **Vote* HPV Vaccine**
  - For persons initiating vaccination before the 15th birthday, the recommended immunization schedule is 2 doses of HPV vaccine. The second dose should be administered 6-12 months after the first dose
  - For persons initiating vaccination on or after the 15th birthday, the recommendation is 3 doses at 0, 1-2, and 6 months
- Yes to accept updated recommendations and the Vaccine for Children (VFC) resolution

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October 2016 ACIP meeting summary (cont.)

- Trumenba (licensed for use as 2-dose or 3-dose series) - changed recommendation to
  - For persons at increased risk for meningococcal B disease and during outbreaks a 3-dose series is recommended (0, 1-2, 6 mos.)
  - Healthy adolescents not at increased risk for meningococcal B disease should receive 2 doses (0 and 6 mos.)
- Vote* Meningococcal Vaccine
  - Yes to accept updated recommendations and Vaccine for Children (VFC) resolution

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October 2016 ACIP meeting summary (cont.)

- Herpes zoster vaccine:
- GSK developed an ($AS01_B$) adjuvanted, inactivated subunit zoster vaccine (HZ/su) with a 2-dose schedule (0 and 2 months) for persons ≥50 yrs. old
  - Will submit biologics license application (BLA) to FDA by end of 2016
  - Efficacy for prevention of herpes zoster
    - 97% for 50-59 yrs. old
    - 91% for 80 yrs. or older
    - Vaccine efficacy ≥85% maintained after 4 years for all age groups
  - Reactogenicity
    - 79% report reaction to the vaccine (placebo=30%)
    - 12% report grade 3 reactions (interfere with daily life) (placebo=2%)

http://www.cdc.gov/vaccines/acip/meetings/meetings-info.html

October 2016 ACIP meeting summary (cont.)

- Zika virus update:
- US government interagency working group
  - Evaluate candidate vaccines for safety, immunogenicity, and efficacy
  - Have one or more candidate vaccines available in 2018 for emergency use in US population with high risk
  - Many vaccine candidates in preclinical development or phase 1 clinical trials by end of 2016
  - Phase 2 studies scheduled to begin in 2017
  - Session on Zika vaccine planned for February 2017 ACIP meeting

October 2016 ACIP meeting summary (cont.)

- **Pneumococcal vaccine:**
- **In August 2014, approved universal recommendation for PCV13 in adults ≥65 years with a note to re-evaluate in 2018 and revised as needed**
- **Impact of PCV13**
  - **PCV13 introduction among children in the United States reduced invasive pneumococcal disease (IPD) incidence among healthy adults and those with underlying conditions**
  - **Similar reductions among those with and without PCV13 indications suggest that benefits observed to date are largely due to indirect PCV13 effects**
  - **Adults with PCV13 and PPV23 indications continue to experience higher IPD rates compared with healthy adults in the post PCV13 period**
  - **Most of the remaining burden of IPD in adults is due to non-PCV13 serotypes**

October 2016 ACIP meeting summary (cont.)

- **Influenza surveillance update**
  - **Low level of influenza activity in US and Northern hemisphere countries; 90% H3N2 strains in US**
  - **Influenza A(H1N1)pdm09, A(H3N2) and both B lineages continue to circulate worldwide**
  - **Recommended components of 2017 Southern Hemisphere vaccine include an updated H1N1 strain (first change in H1 component since 2009 pandemic)**
  - **Global laboratory data continue to indicate that most currently circulating virus are antigenically similar to the vaccine viruses included in the 2016-17 US vaccines**
- **Two newly licensed influenza vaccines**
  - **Afluria Quadrivalent, August 2016 (Seqirus)**
  - **Flublok Quadrivalent, October 2016 (Protein Sciences)**

October 2016 ACIP meeting summary (cont.)

- Respiratory syncytial virus epidemiology update in older adults
  - RSV is an important cause of community acquired lower respiratory tract infection in hospitalized adults
- Novavax RSV F-protein recombinant nanoparticle vaccine candidate
  - Phase 2 trials in older adults showed efficacy at 41% against RSV
  - Phase 3 trial in older adults failed to show efficacy (attack rate lower than expected and lower than phase 2 study)
  - Phase 2 and 3 trials in older adults showed acceptable safety profile
- Different RSV formulation with aluminum adjuvant being tested in pregnant women with Data Safety Monitoring Board in place
- Historical note: 1966 formalin inactivated RSV vaccine – infants vaccinated had worse clinical course after RSV, may have been due to deficiency in vaccine stimulation of functional antibodies

Selected publications

- Grohskopf et al. Prevention and Control of Seasonal Influenza with Vaccines Recommendations of the Advisory Committee on Immunization Practices–United States, 2016–17 Influenza Season. MMWR Recomm Rep. 2016;65(5):1-54.
  - http://www.cdc.gov/mmwr/volumes/65/rr/rr6505a1.htm

- Bardenheier et al. Anthrax Vaccine and the Risk of Rheumatoid Arthritis and Systemic Lupus Erythematosus in the U.S. Military: A Case-Control Study. Mil Med. 2016;181(10):1348-1356.
  - Anthrax Vaccine Adsorbed (AVA) given to U.S. military personnel was associated with recent onset rheumatoid arthritis, but did not increase the risk of developing RA in the long term. AVA was not associated with systemic lupus erythematosus.

Selected publications

- Lauren et al. Case Report of Subcutaneous Nodules and Sterile Abscesses Due to Delayed Type Hypersensitivity to Aluminum-Containing Vaccines. Pediatrics. 2016. pii: e20141690. [Epub ahead of print]
  - Although anaphylaxis, or type I hypersensitivity, is recognized as a potential reaction after vaccination, delayed type hypersensitivity or type IV reactions are less so.
  - Authors presented a case of persistent subcutaneous nodules and sterile abscesses in the setting of delayed type hypersensitivity to aluminum, confirmed by patch testing and recurrence on re-exposure.
  - Authors reviewed sources of aluminum in common immunizations, principles for treatment, and strategies for management of future vaccinations for this patient.

Selected publications

- **Baxter et al. Acute Demyelinating Events Following Vaccines: A Case-Centered Analysis. Clin Infect Dis. 2016. pii: ciw607. [Epub ahead of print]**
  - **Authors found no association between transverse myelitis and prior immunization.**
  - **There was a possible association of acute disseminated encephalomyelitis with Tdap vaccine, but the excess risk is not likely to be more than 1.16 cases of acute disseminated encephalomyelitis per million vaccines administered.**

Selected publications

- DeSilva et al. Tdap Vaccination During Pregnancy and Microcephaly and Other Structural Birth Defects in Offspring. JAMA. 2016;316(17):1823-1825.
  - Maternal Tdap was not significantly associated with increased risk for microcephaly for vaccinations occurring at less than 14 weeks' gestation.
  - Adjusted analyses were similar for any structural defect and selected structural defects.

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Thank You

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