Immunization Update and ACIP Highlights – October 2022
November 2, 2022

The Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control (CDC) met virtually on October 19 and 20 for its regular triennial vaccine meeting. For archives of minutes and slides, go to the ACIP meeting website and click on "Meeting Materials." COVID vaccine recommendations are available on the CDC's Clinical Considerations website. Below are the key highlights:

- **Pneumococcal Vaccines**
  - **VOTE**: Adults 19 and older who have only received a Pneumococcal Conjugate vaccine 13-valent (PCV13), namely those 19–64 immunocompromised or 65 and older should complete their series with either a Pneumococcal Conjugate Vaccine 20-valent (PCV20) at least one year after the PCV13 or one to three doses of Pneumococcal Polysaccharide Vaccine 23-valent (PPSV23) as previously recommended.
  - **VOTE:** Immunocompromised adults 19–64 who have received a PCV13 and a PPSV23 dose should complete their series with either a dose of PCV20 or one dose of PPSV23 at least 5 years after last pneumococcal vaccine.
  - **VOTE:** Adults aged 65 and older who have completed their pneumococcal series of PCV 13 and PPSV23 have the option to receive a dose of PCV20 in shared clinical decision making. Clinicians should wait for Centers for Medicare & Medicaid Services (CMS) and other insurers to update their coverage to three doses of pneumococcal vaccine prior to administering this third dose.
  - Recommendations for administering PCV20 to hemopoietic stem cell transplant (HSCT) recipients were discussed.
- **COVID-19 Vaccines**
  - **VOTE**: Vaccines for Children (VFC) – Children aged 0 through 18 years can access COVID-19 vaccines through the VFC program when those vaccines are commercialized.
  - Novavax COVID-19 monovalent booster is authorized 6 months after completion of a primary series for adults aged 18 years and older if an mRNA bivalent booster dose is not medically or accessibly available **or** if a booster vaccine would otherwise not be received.
  - Pregnancy: Vaccination before or during pregnancy protects the mother from severe disease and hospitalization with no higher rate of adverse pregnancy outcomes, and vaccination during pregnancy protects the aged 0–5 month infant from severe disease and hospitalization.

- **Immunization Schedules**

  VOTE: The 2023 Child/Adolescent and Adult Immunization schedules were approved and will be published in February 2023.

- **RSV Vaccines**
  - **Adult:** Clinical trials of an adjuvanted, 1-dose RSV vaccine and a non-adjuvanted, 2-dose RSV vaccine for adults aged 60 and older were reviewed.

- **Maternal/Pediatric:** Although not a vaccine, antibody prophylaxis therapy Nirsemivab is currently being discussed for use in infants.

- **Meningococcal Vaccine**
  - Menveo 1-vial solution has been approved for use in persons aged 10 to 55 years. The original 2-vial solution needing reconstitution continues to be available for persons aged 2 months to 55 years. The new formulation is not anticipated to be available until mid-2023.
  - Pentavalent (A, B, C, W, Y) vaccines are being evaluated by the work group for a possible recommendation in October 2023.

- **Influenza**

  Final vaccine effectiveness results for the 2021–2022 season and recombinant influenza vaccine (RIV) in pregnant women were reviewed.

- **Other Topics**

  The ACIP discussed the recent vaccine-derived **poliovirus,** type 2 (VDPV2) outbreak in New York State. ACIP polio workgroup is examining whether adult boosters should be recommended and is reviewing WHO strategies of fractional doses of inactivated polio vaccine (fIPV) and novel oral polio vaccine. **Monkeypoxvirus** vaccine, **Dengue** vaccine**,** and **Chikungunya** vaccine were also discussed.

Pneumococcal Vaccine

Recommendations for adult pneumococcal vaccines were published in the January 28, 2022 *Morbidity and Mortality Weekly Report (MMWR)*. Clarifications to the recommendations were discussed and cost-effectiveness analysis was presented along with Evidence to Recommend (EtR) for three modifications to the recommendations.

The pneumococcal vaccine work group determined there is a distinct advantage to giving a conjugate rather than polysaccharide pneumococcal vaccine. Conjugate vaccines confer longer protection, better effectiveness in immunocompromised persons, and greater protection against vaccine-type pneumococcal pneumonia.

ACIP voted to approve three clarifying recommendations for adult pneumococcal vaccines, including:

1. Adults who have already received a PCV13 dose (because they are immunocompromised, have a cochlear implant or CSF leak, and are ages 19–64 **or** all persons aged 65 and older) should receive either a PCV20 dose at least 1 year after the PCV13 or should receive one to three PPSV23 doses depending on their age and risk condition as previously recommended.

2. Adults who are immunocompromised or have a cochlear implant or a CSF leak and have already received a PCV13 dose and a PPSV23 dose but are not complete on their vaccine series should complete their series by receiving either a PCV20 dose at least 5 years after the last pneumococcal vaccine or by receiving one to three PPSV23 vaccine doses depending on their age at least 5 years after the last PPSV23.

3. Adults who are aged 65 and older who were previously complete in their pneumococcal vaccine series (meaning they had received a dose of PCV13 and a dose of PPSV23, with the PPSV23 having been

administered at age 65 or older) now MAY (with shared clinical decision making) receive a dose of PCV20. If a decision to administer PCV20 is made, it should be administered at least 5 years after the last pneumococcal vaccine dose.

NOTE: This last recommendation applies to 17 million seniors in the U.S. who were previously considered complete with their pneumococcal vaccine recommendations. Currently, CMS only allows for 2 doses of a pneumococcal vaccine to be administered after age 65 years to Medicare recipients. **It is critical that clinicians wait for CMS** and other insurers **to update their coverage** to 3 doses of pneumococcal vaccine prior to instituting this recommendation and administering a third dose of pneumococcal vaccine so that their patients are not inappropriately made responsible for the cost of the vaccine.

Other CDC clarifications provided for the pneumococcal recommendations include:

- A person who has previously received a PCV7 does not count as someone who has "previously received a PCV vaccine" and should be treated as someone who has no history of a PCV vaccine. When indicated due to medical condition or age, they should be given a dose of PCV20 or a dose of PCV15 and PPSV23.
- If a PPSV23 only has been given, either a dose of PCV15 or a dose of PCV20 should be administered at least one year later.
- If a dose of PCV15 and a dose of PPSV23 have been given, no further doses of PPSV23 need to be administered. That is not the case when PCV13 and a dose of PPSV23 have been administered — in that case, recommendation #2 above needs to be followed.
- If a person has received only a single dose of PPSV23 or has inadvertently received a dose of PPSV23 first in a PCV15-plus-PPSV23 series, they should receive either a dose of PCV15 or a dose of PCV20 at least one year later.

A presentation was made proposing use of PCV20 in those needing pneumococcal vaccination after hematopoietic stem cell transplant (HSCT). HSCT recipients have poor immune response to PPSV23 when given during the first year of transplantation or longer, especially in those with chronic grafter versus host disease (GVHD). PCV20 currently has the broadest serotype coverage among available PCVs. In this high-risk population, a regimen that provides broad pneumococcal serotype coverage early on is warranted. Therefore:

- Adults who are HSCT recipients are recommended to receive 3 doses of PCV20 at 4-week intervals starting 3 months after HSCT. This should be followed by a fourth PCV20 dose at least 6 months after the third PCV20 dose, or at least 12 months after HSCT, whichever is later.
- HSCT recipients who have started their pneumococcal vaccine series with PCV13 or PCV15 may complete their 4-dose pneumococcal vaccine series with PCV20.
- If PCV20 is not available, 3 doses of PCV15 at 4-week intervals starting e months after HSCT, followed by a dose of PPSV23 at least 12 months after HSCT may be given. For patients with chronic graft-versus-host disease, a fourth dose of PCV15 can be given in place of PPSV23.

Prelicensure pneumococcal vaccines in development include a 21-valent PCV vaccine by Merck and a 24-valent PCV vaccine by GSK. The FDA approval of PCV20 in children is anticipated during the 2nd quarter of 2023.

COVID-19 Vaccines

Child: It is now almost one year since COVID-19 vaccines were first authorized for children aged 5 years and older and four months since they were authorized for children aged 6 months and older. Over 30 million children and adolescents have received COVID-19 vaccines.

ACIP voted to approve the **Vaccines for Children (VFC) resolution** for COVID-19 vaccines for all eligible children aged 0–18 years. The purpose of the COVID-19 VFC resolution is to ensure ccess to COVID-19 vaccines once they are commercialized. For now, COVID-19 vaccine will continue to be distributed through the federal response. COVID-19 vaccines will not be federally mandated for children. School vaccine requirements are determined at the state or local level.

Adult: The FDA announced and CDC recommended the Emergency Use Authorization (EUA) of a **monovalent booster dose** of the **Novavax** COVID-19 vaccine 6 months after completion of a primary series for adults aged 18+ years if an mRNA bivalent booster dose is not medically or accessibly available **or** if a booster vaccine would otherwise not be received.

Maternal/Infant: Pregnant women who are infected with COVID-19 have a higher chance of preterm birth, ICU admission, or death as well as higher chance of fetal distress, NICU admission, stillbirth, or neonatal death.

COVID-19 vaccination before or during pregnancy protects the mother from severe disease, emergency room visits and hospitalization. Mothers who are fully vaccinated, when they contract a COVID infection during pregnancy, have no higher rate for preterm birth, ICU admission, NICU admission, or stillbirth compared to pregnant women who do not contract COVID infection.

Vaccination during pregnancy results in no increase in stillbirths, infant deaths, preterm birth, or birth defects, and it also protects the aged 0–5 month infant from severe disease and hospitalizations.

For the latest CDC COVID vaccine recommendations, visit the CDC's Clinical Considerations website.

Immunization Schedules

ACIP voted to approve the *Recommended Child and Adolescent Immunization Schedule for Ages 18 Years or Younger, United States, 2023* and the *Recommended Adult Immunization Schedule for Ages 19 Years or Older, United States, 2023*.

Respiratory Syncytial Virus (RSV) Vaccine

Adult: It is estimated that hospitalizations for RSV among adults ages 60 years and older range from 64,000 to 85,000 per year. Bivalent RSV vaccines covering RSV A and RSV B are in clinical trials for adults aged 60 years and older include:

- GSK's adjuvanted 1-dose F protein candidate vaccine (RSVpreF3 OA), containing 120mcg antigen and an ASO1 adjuvant at half the amount of same adjuvant in GSK's Shingrix vaccine
- Pfizer's non-adjuvanted 2-dose F protein vaccine (RSVpreF), containing 120mcg antigen and no adjuvant

Clinic trials of both vaccines showed significant efficacy against lower respiratory tract illness caused by RSV. The GSK candidate had an 82.6% efficacy. The Pfizer candidate had a 66.7% efficacy against respiratory illness with two or more symptoms and efficacy of 85.7% against respiratory illness with three or more symptoms. Efficacy was invariant according to age.

The GSK vaccine was safely and effectively co-administered with influenza vaccine. The Pfizer vaccine trial is currently evaluating co-administration with the COVID vaccine but has not tested co-administration with influenza vaccine.

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Both vaccines had a case or two of Guillain Barre Syndrome in vaccine trial recipients (GSK – 1/15,000 recipients, Pfizer – 2/26,000 recipients), and analyses will need to be done by CDC to further evaluate cases compared to background rates. The RSV workgroup is continuing Evidence to Recommend (EtR) and cost effectiveness analyses in preparation for anticipated licensure next fall.

Maternal/Infant: RSV is the most common cause of hospitalization for healthy full-term infants with 2–3% of all infants being hospitalized for RSV. The RSV workgroup continues to review evidence around novel RSV monoclonal antibody Nirsevimab studies considering if Nirsevimab should be recommended for those listed below and at what dose for each cohort:

- All infants <8 months of age entering their first RSV season
- All infants born during the RSV season
- Children <24 months of age who remain at increased risk of severe disease entering their second RSV season

The question was raised about whether the ACIP should be evaluating non-vaccine preventive therapeutics. A vote is anticipated in June 2023.

Meningococcal Vaccines

The FDA has approved a single-vial, no-need-to-reconstitute version of **Menveo** for persons aged 10 to 55 years. Availability is anticipated in the second half of 2023. The two-vial version is approved for persons as young as 2 months. The off-label use of meningococcal A, C, W, Y vaccine for people aged 55 years and older should continue with this new product.

Both products are administered in 0.5mL doses. The single vial has a pink lid with purple color strip and an 18-month shelf life, with application for approval of a 24-month shelf life. The two-vial version has grey and orange lids, a grey color strip, and a 36-month shelf life.

Pentavalent meningococcal vaccines containing A, C, W, Y and B serogroups manufactured by GSK and Pfizer are currently in clinical trials and being considered. Each vaccine is a combination of an existing MenACWY and existing MenB vaccine.

The GSK pentavalent vaccine is comprised of Menveo (serogroup ACWY) and Bexereo (serogroup B), which are both licensed in the U.S. It is being studied in ages 10 through 25 years using a two-dose schedule with a 6-month interval in both Men ACWY primed and naïve subjects.

The Pfizer pentavalent vaccine is comprised of Nimenrix (serogroup ACWY) not licensed in the U.S. and Trumenba (serogroup B), which is licensed in the U.S.. It is being studied in those aged 10–25 years using two dose schedules at 0, 6 months and 0, 12 months and is being evaluated with two doses in those aged 11–12 (with a booster dose at age 16), or as a single-dose pentavalent alternative to MenACWY vaccine.

The work group is evaluating these following policy questions and anticipates a vote in October 2023:

- Whether the pentavalent vaccine should be included as an option for people currently recommended to receive both MenACWY and MenB vaccines such as 16 year olds
- Whether the pentavalent vaccine should be included as an option for people currently only recommended to receive MenACWY such as 11–12 year olds
- Whether the pentavalent vaccine should be included as an option for people recommended to only receive a MenB vaccine such as during a serogroup B outbreak

Influenza Vaccines

The final vaccine effectiveness (VE) rates for the 2021–2022 influenza season for outpatient influenza illness were 36% overall with:

- 45% for children
- 28% for adults aged 18–64 years
- 50% for immunocompetent adults aged 8–64 years
- 32% for adults aged 65 and older

VE was 31% against pediatric hospitalizations and 11% against adult hospitalizations. Protection was similar to pre-pandemic A-H3N2 dominant seasons.

As part of post-licensure studies, Flublok (RIV) was studied in pregnant woman compared to quadrivalent inactivated influenza vaccines (IIV4). No difference in rates was observed for adverse outcomes of preterm birth <37 weeks, fetal death, neonatal death, spontaneous abortion, or reactogenicity. RIV and IIV vaccines are safe to administer to pregnant women.

Other Topics

Polio – Due to the recent vaccine-derived poliovirus, type 2 (VDPV2) outbreak in New York State, the polio work group is looking at whether adult boosters should be recommended and is evaluating World Health Organization (WHO)-proposed strategies of administering fractional doses of inactivated polio vaccine (fIPV) or novel oral polio vaccine.

Monkeypox – Bavarian Nordic:JYNNEOS orthopoxvirus vaccine is FDA approved and CDC licensed for use as a subcutaneously administered vaccine for at-risk persons aged 18 and older. The Orthopoxvirus Work Group is

gathering evidence on expanded use under EUA, namely, vaccination of those <18 years and intradermal (rather than subcutaneous) administration for the safety and effectiveness of those two emergency use practices.

Dengue – Pfizer: Dengvaxia vaccine is FDA licensed and CDC recommended for prevention of dengue in individuals aged 9–16 years with laboratory confirmation of previous dengue virus infection living in endemic areas. It is a live-attenuated quadrivalent vaccine using a yellow fever backbone given as a 3-dose series (0, 6, 12 months). It has an efficacy of ~80% among seropositive children. Puerto Rico is now administering Dengvaxia.

The dengue vaccine workgroup has started review of the Takeda TAK-003 dengue vaccine, a live-attenuated quadrivalent vaccine with a dengue virus serotype 2 backbone given in two-dose series separated by 3 months.

Chikungunya – Four chikungunya vaccines are in clinical trials:

1) Valneva live-attenuated 1 dose IM vaccine (phase III trial in adults complete). While the virus in this vaccine can replicate, it is attenuated by 60 amino acid deletions in a non-structural protein.
2) Emergent BioSolutions virus-like particle 1 dose IM vaccine.
3) Merck live-attenuated measles-vectored 2-dose vaccine (phase II study complete).
4) Bharat Biotech inactivated whole cell 2-dose vaccine (currently in phase II/III trials).

Most Valneva vaccine recipients developed protective neutralizing antibodies. Results of the Valneva clinical studies include high seroresponse rates (≥98%) at 28 days postvaccination and high seroresponse rates maintained (96%) at 6 months postvaccination. There were mostly mild to moderate adverse events with more arthralgias in the Valneva recipients (17% v. 5%). Valneva is hoping for FDA approval in 2024.

If you have any questions regarding immunization, feel free to contact Tamara Sheffield, MD, MPA, MPH, Senior Medical Director, Preventive Medicine, Intermountain Healthcare, at **801-442-3946**.