Immunization Update and ACIP Highlights – June 2022

July 13, 2022

The Advisory Committee on Immunization Practices (ACIP) of the CDC met virtually on June 22 and 23 for its regular triennial vaccine meeting. For archives of minutes and slides, go to the ACIP meeting website and click on Meeting Materials. The ACIP met the prior week to discuss the use of mRNA vaccines in children ages 6 months through 5 years, and those deliberations are included with information from this meeting's Moderna COVID vaccine for ages 6 through 17 years. COVID Vaccine Recommendations are available on the CDC's Clinical Considerations website. Below are the key highlights:

- ACIP recommends that adults age ≥65 years preferentially receive any one of the **higher-dose or adjuvanted influenza vaccines**: quadrivalent high-dose inactivated influenza vaccine (HD-IIV4 - High-dose Fluzone:Sanofi), quadrivalent recombinant influenza vaccine (RIV4 - Flublok:Sanofi), or quadrivalent adjuvanted inactivated influenza vaccine (aIIV4 - Fluad:Seqirus) over standard dose IIV.
- **PCV15** (VAXNEUVANCE™:Merck) conjugated pneumococcal vaccine has been approved by the FDA and was recommended by the ACIP as an option for children age <19 years according to currently recommended PCV13 dosing and schedules but is not preferred over PCV13 (Prevnar13:Pfizer).
- **MMR** (PRIORIX:GSK) vaccine has been FDA approved and is ACIP recommended according to currently recommended MMR schedules and off-label uses.
- New formulations of **COVID-19 mRNA vaccines** have been recommended for **children and adolescents**. **Pfizer** vaccine was recommended as a 3 dose primary series for ages 6 months through 4 years and **Moderna** vaccine was recommended as a 2 dose primary series for 6 months through 17 years.
- **HPV** vaccination in the U.S. continues to reduce the incidence of HPV infection and resulting diseases and multiple international trials are evaluating a 1 dose schedule with promising results.
- Several prospective **RSV** vaccines for infants are in the pipeline including a new monoclonal antibody in phase 3. Adult RSV vaccine was discussed.
- An informational session was provided concerning **Monkeypox** virus infections in the US since May 2022.

Influenza Vaccines

Vaccine Effectiveness (VE) for the 2021-2022 influenza season was 34%. Of the strains identified, 94% were type A/H3N2. All cases belonged to clade 3C.2a1b subclade 2a.2. The reference virus for the 2021-2022 vaccine was subclade 2a.1, creating some mismatch. The 2022-2023 influenza vaccine will include an updated reference strain for the circulating A/H3N2 subclade 2a.2.

Persons ages 65 years and older have the potential to have a decreased immune response to influenza vaccines. Higher dose or adjuvanted vaccines include High-dose Fluzone:Sanofi (HD-IIV), adjuvanted Fluad:Seqirus (aIIV) indicated for persons age 65 and older, and recombinant Flublok:Sanofi (RIV) indicated for persons age 18 and older. Eighty percent of persons ages 65 and older are already receiving one of these three vaccines.

ACIP voted to recommend that adults aged ≥65 years preferentially receive any one of the higher-dose or adjuvanted influenza vaccines: quadrivalent high-dose inactivated influenza vaccine (HD-IIV4), quadrivalent adjuvanted inactivated influenza vaccine (aIIV4) over standard dose IIV, or quadrivalent recombinant influenza vaccine (RIV4). If none of these three vaccines is available at an opportunity for vaccine administration, then any other age-appropriate influenza vaccine should be used.

Non-whites were less likely to receive high-dose IIV. Preferentially recommending HD-IIV4, aIIV4, and RIV4 in $\geq$ 65 years will possibly increase health equity

Pneumococcal Vaccine

Pneumococcal conjugate vaccine 15 valent (PCV15: VAXNEUVANCE™) by Merck has received FDA approval and ACIP recommendation for use in children ages 18 and younger. PCV20:Prevnar20 by Pfizer is estimated to be approved and recommended by Q2 2023.

The PCV15 non-PCV13 serotypes include 22F and 33F. Acute otitis media (AOM) and invasive pneumococcal disease (IPD) data show that the two additional serotypes included in PCV15 cause 6 to 8% of AOM cases caused by pneumococcus in children age <3 years and 16-17% of IPD in children age less than 18 years. If PCV15 is priced comparably to PCV13, then the use of PCV15 will be a cost-saving strategy in cost-benefit analysis. PCV15 is recommended by ACIP as an option for PCV administration but is not preferred to PCV13.

A supplemental dose of PCV15 is not indicated for children who have received 4 doses of PCV13 or another age appropriate, complete PCV13 schedule.

Children who have **not** received PCV13 or PCV15:

- Either PCV13 or PCV15 is recommended as a 4-dose series at age 2, 4, 6 and 12-15 months.
- PCV13 and PCV15 can be used interchangeably.
- Newborns should begin the schedule at age 2 months, although the first dose can be administered as early as 6 weeks
- Infants receiving their first dose at age 6 months or younger should receive 3 doses at intervals of approximately 8 weeks (the minimum interval is 4 weeks). The fourth (booster) dose is recommended at age 12-15 months at least 8 weeks after the third dose.
- Infants receiving their first dose at age 7-11 months should receive 3 doses with the first 2 doses administered with a minimum interval of 4 weeks. The third dose administered at age 12-15 months, at least 8 weeks after the second dose

- Children receiving their first dose at age 12-23 months should receive 2 doses with a minimum interval of 8 weeks.
- Healthy children receiving their first dose at age 24 months or older should receive a single dose of PCV (either PCV13 or PCV15).
- Children with underlying medical conditions receiving their first dose age 24 through 71 months should receive 2 doses of PCV with a minimum interval of 8 weeks
- Routine use of PCV is not recommended for healthy children ages 5 years and older.
- Children with an immunocompromising condition, asplenia, cochlear implant or CSF leak who have not yet receive a PCV13 or PCV15, should receive one dose of either vaccine regardless of whether they have previously received a dose of PPSV23 or PCV7

Children who have previously received PCV13 or PCV15:

- Infants and children 24 months of age or younger who have received at least 1 dose of PCV (either PCV13 or PCV15) should complete the vaccine series with either PCV13 or PCV15 using the previously recommended series
- Healthy Children ages 24-59 months with an incomplete PCV schedule before age 24 months should receive 1 dose of PCV
- Children ages 24-71 months with underlying medical conditions with and incomplete PCV schedule of <3 doses before 24 months, (with the exception of those who received at least 2 doses between 12-23 months), are recommended to receive 2 doses at least 8 weeks apart.
- Children ages 24-71 months with underlying medical conditions who have received a total of 3 doses of PCV prior to age 12 months, should receive a single dose of PCV at least 8 weeks after the last dose.

PPSV23 use for children ages 2-18 years at increased risk of pneumococcal disease:

- Children ages 2 years and older with underlying medical conditions should receive a dose of PPSV23 after completing all recommended doses of PCV (either PCV13 or PCV 15). These children should receive 1 dose of PPSV23 at age 2 year and older with an 8 week minimum interval from the most recent dose of PCV.
- Children who have received PPSV23 should also receive recommended PCV doses at least 8 weeks after the PPSV23 dose.
- Children ages 2 years and older who have anatomic or functional asplenia including sickle cell disease, HIV or other immunocompromising condition should receive a second dose of PPSV23 at least 5 years after the first dose of PPSV23. No more than 2 PPSV23 doses are recommended before age 65 years.
- Recipients of hematopoietic stem cell transplants are recommended beginning 3 to 6 months after the transplant to receive 3 sequential doses of PCV followed by a dose of PPSV23.

Measles, Mumps, Rubella (MMR) Vaccine

MMR (PRIORIX:GSK) vaccine has been FDA approved for use in persons age 12 months and older and is ACIP recommended according to currently recommended MMR schedules and off-label uses.

(PRIORIX:GSK) has been used in 100 countries outside the U.S. with over 400 million doses distributed. It is a lyophilized vaccine needing reconstitution and is stored refrigerated. It is given as a 0.5 mL dose subcutaneously with the first dose at 12 months, the second dose at age 4-6 years. The second dose can be given at age <4 years with a minimum interval between first and second dose of at least 28 days and can be given at age 7 years and older. Safety and immunologic response were similar when given concomitant with Varicella, Kinrix, Havrix, and PCV13. CDC advises PRIORIX can be fully interchangeable with M-M-R-II.

Off label uses include administration to children ages 6 months through 11 months who are planning to travel or live abroad or during outbreaks, and a third dose administered to persons previously vaccinated with 2 doses who are identified as being at increased risk because of a mumps outbreak, or for measles post exposure prophylaxis.

M-M-R-II contains neomycin and gelatin. PRIORIX contains neomycin but does not contain gelatin.

COVID-19 mRNA Vaccines in Children and Adolescents

New formulations of COVID-19 mRNA vaccines have been recommended for children and adolescents. A 0.3mcg/0.2mL Pfizer vaccine was recommended as a 3 dose primary series for ages 6 months through 4 years and a 25mcg/0.25mL Moderna vaccine was recommended as a 2 dose series for 6 months through 5 years, a 50mcg/0.5mL Moderna vaccine was recommended as a 2 dose series for children ages 6 years through 11 years and a 2 dose series of 100mcg/0.5mL Moderna vaccine was recommended for adolescents ages 12 though 17 years.

For immunocompromised children, a third primary series dose is recommended for all children ages 6 months through 17 years for both Moderna and Pfizer vaccines. All children regardless of their immune status ages 6 months through 4 years receive that third dose with the Pfizer vaccine primary series.

The Pfizer vaccine is the only vaccine that is approved for a booster dose for children and boosting starts with children who are 5 years through 17 years. No booster doses are approved for children younger than 5 years and boosters are only recommended for adults ages 18 and older when using the Moderna vaccine.

The interval between doses for the Pfizer vaccine for ages 6 months through 4 years is 3 to 8 weeks between doses 1 and 2 and at least 8 weeks between doses 2 and 3. The interval between doses for the Moderna vaccine for ages 6 months through 17 years is 4 to 8 weeks, and the minimum interval between doses 2 and 3 for immunocompromised persons is 4 weeks for Moderna.

Immunocompromised children ages 5 through 17 years vaccinated with the Pfizer vaccine may receive a booster dose 3 months after the primary series and those ages 12 through 17 may receive a 2nd booster 4 months after the first booster dose.

The Pfizer 3mcg/0.2mL dose for children ages 6 months through 4 years does not tend to create a sufficient immune response with just 2 doses, particularly during circulation of the Omicron variant. While immunogenicity non-inferiority was met for those ages 6 months to 2 years with 2 doses, it was not met for the 2 to 5-year-olds.

When Pfizer saw these results, they adjusted their study, adding a 3rd dose at least 8 weeks after the second dose, although in the study, the average interval was 16 weeks for the 6 month to < 2 year age cohort and averaged 11 weeks for the 2 through 4-year-olds. Non-inferiority was met at a 1.19 to 1.3 Geometric Mean Titer Ratio of neutralizing antibodies comparing 3 doses of the 0.3mcg dose to 2 doses of the 30mcg adolescent/adult formulation.

Vaccine efficacy (VE) against symptomatic illness for 3 doses given during the Omicron variant phase was 80.3%. But due to few cases to-date and the wide confidence interval of the smaller age cohort of 6 months to 2 years, more data points are needed to have confidence in the VE. Immunogenicity was the primary study endpoint which the FDA and CDC are focused on for moving ahead with their authorization and recommendation. Reactogenicity was low with fever rates similar between doses 1, 2, 3 and placebo.

The Moderna COVID vaccine was studied as a 2 dose primary series for children with a minimum interval of 4 weeks. CDC prefers an 8-week interval due to the potential for lowering the risk for adverse events such as myocarditis. The 25mcg/0.25mL dose for children ages 6 months through 5 years was studied during the Omicron variant period, while studies for ages 6 years through 17 years occurred in Alpha and Delta variant eras. Immunogenicity for was non-inferior compared to young adults ages 18 through 25 years. The vaccine effectiveness with just 2 doses for those age 6 months to 6 years was 43.7% for those in the 6 month to 2 year age group and 37.5% for those ages 2 to 6 years, Vaccine efficacy for the 2 dose primary series was comparable to that of other ages during Omicron periods, but it also may be a harbinger that a 3rd dose will be needed for best protection, since older individuals have needed a 3rd (booster dose) for enhanced protection during Omicron.

There is some protection (VE=16%) from asymptomatic infection in this population, helping mitigate community spread. Local and systemic reactogenicity was common with a rate of fever for any dose ranging from 22-23%.

A 50mcg/0.5mL dose was studied in children ages 6 through 11 years with a Vaccine Efficacy of 80.6% during the Alpha and Delta variant time frame. The vaccine is non-inferior for immunogenicity and the safety profile was similar to the younger age cohort The product that will be used for this population is the blue cap purple, border product that is labeled “Booster Doses Only” so there will need to be staff education that it is also approved for the 6 through 11 year old cohort.

The adolescent 12 through 17 years 100mcg/0.5mL dose vaccine had high efficacy of 89.2% during the alpha variant phase and non-inferior immunogenicity. Because some observational studies have shown

higher rates of myocarditis in young adults receiving Moderna vaccine compared to Pfizer, Moderna vaccine has received more safety scrutiny for adolescents. After 3 million second doses have been given to adolescents, Moderna's global safety database shows that cases of myocarditis are much lower (13.3 cases/million doses) in adolescents ages 12-17 years than in young adults ages 18-24 years (42.7 cases/million doses). Booster doses of Moderna vaccine for children are currently being evaluated with an estimated time of late summer early fall for their authorization.

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

Human Papilloma Virus (HPV) Vaccine

HPV vaccination rates continue to be much lower than Tdap and meningococcal rates. Rates are lowest in whites and persons in rural areas in the US. HPV vaccine has dramatically decreased HPV infections. The prevalence of vaccine type HPV in females has decreased by 88% compared to pre-vaccine era in 14 through 19 year olds and has decreased by 81% in 20 through 24 year olds, and cervical precancer rates have been dropping in young women. Since the pre-vaccine era, juvenile onset recurrent respiratory papillomatosis has decreased from 2.8 cases per 100,000 to 0.7 cases per 100,000.

Multiple vaccine trials of one dose of HPV vaccine in girls, adolescents and young women are showing comparable vaccine efficacy to 2 and 3 doses of vaccine, prompting the WHO's Strategic Advisory Group of Experts on Immunizations to recommend a 1 or 2 dose HPV vaccine schedule for girls age 9 through 14 years.

Respiratory Syncytial Virus (RSV) Vaccine

ACIP is standing up a work group to review RSV vaccine in older adults. Five potential vaccines are in the pipeline. Votes on the first products are anticipated in June 2023. RSV is the most common cause of hospitalizations in U.S. infants and is associated with 58,000-80,000 hospitalizations and 100-300 deaths in children age <5 years annually. RSV is a frequent cause of pneumonia in hospitalized adults and is associated with 177,000 hospitalizations and 14,000 deaths per year in adults ages 65 years and older. Phase 3 studies of novel RSV monoclonal antibody Nirsevimab were discussed.

Monkeypox Information Session

In the U.S. since May 2022, 155 cases of Monkeypox virus have been identified in 24 states predominantly in the MSM population. While first cases were in persons who were infected internationally, local transmission is now occurring. Vaccines which prevent monkeypox include JYNNEOS live attenuated vaccine indicated for persons ages 18 and older (Administration: subcutaneous in 2 doses, 28 days apart). CDC is currently working on an Expanded Access Investigational New Drug Protocol for pediatric populations. ACAM2000 is a live vaccinia virus vaccine administered percutaneously by multiple puncture technique in a single dose. JYNNEOS is preferred for PrEP and PEP due to fewer serious adverse events compared to ACAM2000, but supplies are currently limited. The U.S. government is working with the manufacturer to expand its stockpile.

If you have any questions regarding immunization, feel free to contact Tamara Sheffield, MD, MPA, MPH, Medical Director, Community Health and Prevention, Intermountain Healthcare, at **(801) 442-3946**.