Immunization Update and ACIP Highlights – February 2024

March 6, 2023

The Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control (CDC) met on February 28–29, 2024, 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 ACIP highlights:

SUMMARY

COVID-19 Vaccines – Vote
ACIP recommended the administration of an additional dose of 2023–2024 Formula COVID-19 vaccine to persons ages 65 years and older at least four months after the prior dose of 2023–2024 Formula COVID-19 vaccine. Immunocompromised patients should receive an additional dose of 2023–2024 at least two months after the prior dose.

Chikungunya Vaccine – Vote
ACIP recommends one dose of the live-attenuated chikungunya vaccine (IXCHIQ®: Valneva) for:

- Those persons ages 18 years and older at risk of chikungunya when traveling to a region experiencing an outbreak
- Laboratory personnel working with live virus
- Those persons ages 65 years and older traveling to locations with evidence of Chikungunya virus transmission in the past five years
- Adults with plans to stay six months or longer in locations with evidence of virus transmission

Diphtheria Tetanus DT – Vote
The Vaccines for Children (VFC) program added Td vaccine for use in children ages less than seven years with a contraindication to the pertussis component of the DTaP vaccine. DT vaccine is no longer available.

Influenza Vaccines
Vaccine Effectiveness for the 2023–2024 season is comparable to seasons with good strain match in preliminary analyses. ACIP anticipates that most influenza vaccines will be trivalent for the 2024–2025 influenza season due to the removal of the B/Yamagata strain

Polio Vaccine
ACIP discussed whether two fractional IPV doses administered outside of the U.S. could be counted as a dose toward the U.S. Vaccination schedule.

Respiratory Syncytial Virus (RSV) Vaccine – Adult
ACIP discussed trial results of an mRNA RSV candidate vaccine for persons ages 60 years and older, post-licensure reports of Guillain Barré Syndrome (GBS) in older recipients, the potential for changing to a universal recommendation for adults ages 60 years and older or for an older cohort, the potential for a risk-based recommendation for adults ages 50–59 years, and whether timing vaccination near the respiratory season is preferable.

Meningococcal Vaccines
ACIP continued discussion regarding a revised adolescent meningococcal schedule with a planned

vote at its February 2025 meeting and reviewed a candidate GSK pentavalent meningococcal ABCWY (MenABCWY) vaccine.

Pneumococcal Vaccines
ACIP reviewed considerations of a Merck pneumococcal conjugate, 21-valent (PCV21) candidate vaccine.

Hexavalent Vaccine
ACIP plans to vote in June 2024 on whether Vaxelis® can be used preferentially in American Indian/Alaska Native (AI/AN) infants for *H. influenzae* protection.

COVID-19 Vaccines

COVID-19 hospitalizations peaked in late December/early January; however, there are still approximately 20,000 new hospital admissions and 2,000 deaths due to COVID-19 each week in the U.S. Persons ages 65 years and older have the highest hospitalization rates. Almost all hospitalizations occur among persons who have not received the 2023–2024 Formula COVID-19 vaccine. Persons ages 75 years and older have the highest COVID-19 mortality rates.

Immunosenescence and higher prevalence of vaccine-only immunity in older adults compared to younger adults suggest that more frequent doses may be needed to maintain protection in this population. While there is an uptick in COVID-19 cases during respiratory virus season, COVID-19 hospitalizations and deaths continue throughout the year due to ongoing circulation of SARS-CoV-2. The 2023–2024 Formula COVID-19 vaccine provides protection against the current circulating JN.1 variant and other circulating variants.

The relative vaccine effectiveness (VE) of the 2023–2024 Formula COVID-19 vaccine for hospitalization from COVID in adult recipients compared to those adults who may or may not have received another COVID-19 vaccine or may have infection induced immunity is 43–52%. Thus, those adults who have received the updated vaccine will be half as likely to be hospitalized as those who have not received the vaccine. A large portion of the population has evidence of infection-induced immunity to a COVID-19 virus: 89% of those ages 16–49 years, 84% of those ages 50–64 years, and 72% of those ages 65 years and older.

ACIP concluded that the greatest benefit of a 2023–2024 Formula COVID-19 vaccine dose would be for those who have not yet received a dose, particularly older adults, and those with underlying medical conditions. They also voted to recommend an additional dose of the 2023–2024 Formula COVID-19 vaccine in adults ages 65 years and older to restore protection that may have waned in that population. The recommendations is that the vaccine be administered at least four months after the receipt of the previous dose of the updated 2023–2024 Formula. Considerations for the additional dose may include a person's risk for severe COVID-19 due to age and the presence of underlying medical conditions. Revised *CDC Clinical Considerations* published after the meeting clarify that immunocompromised persons should receive one additional dose of the 2023–2024 Formula COVID-19 vaccine at least two months after the

prior dose of that formula vaccine. Clinicians may use their discretion to administer additional doses to immunocompromised patients if the interval between doses is at least two months.

At the June 2024 meeting, ACIP will make recommendations for the 2024–2025 Formula COVID-19 vaccine based on reviewing World Health Organization (WHO) and Federal Drug Administration (FDA) antigen selections, epidemiology, manufacturer studies, and cost-effectiveness.

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

Chikungunya Vaccine

The FDA approved live-attenuated chikungunya vaccine (IXCHIQ:Valneva) in November 2023 as a single dose primary schedule for use in adults ages 18 years and older to protect against mosquito-borne chikungunya virus. There is a moderate disease burden among U.S. travelers with 100–200 cases reported annually. There is a substantially higher risk for infection if travel occurs to a region during an outbreak.

The vaccine is **immunogenic** with 99% seroprotection at 12 months after vaccination. It is **reactogenic** with arthralgia within 10 days of vaccination in 17% of vaccinees compared to 5% of placebo recipients, but the arthralgia is neither severe nor persistent.

ACIP voted to recommend chikungunya vaccine for:

- Persons 18 years and older traveling to a country or territory where there is a chikungunya outbreak.
- Laboratory workers with a potential for exposure to chikungunya virus; however, vaccination is not necessary for workers handling routine clinical samples. Local biosafety committees should assess the risk for worker exposure to chikungunya.

In addition, the vaccine may be considered for persons ages greater than 65 years, particularly those with underlying medical conditions, who are likely to have at least moderate exposure (2 weeks) to mosquitoes or any adult who is staying for a cumulative period of six months or more in a country or territory without an outbreak, but with evidence of chikungunya transmission among humans within the last five years.

Pregnancy is a precaution for vaccination with live-attenuated chikungunya vaccine because virus can transmit from mother to newborn, causing severe disease in the newborn during the intrapartum period. Clinical guidance for pregnant women includes avoiding travel to an area of potential transmission. In general, vaccination should be deferred until after delivery; however, if exposure risk is high, pregnant women should generally avoid vaccination:

- During the 1st trimester (due to the potential for fever from the vaccine)
- After the 36th week of gestation (to limit the risk of intrapartum transmission of vaccine virus)

Currently, the data are insufficient to recommend deferring breastfeeding for any period after vaccination.

Tetanus and Diphtheria Vaccine

The Vaccines for Children (VFC) program added Td vaccine for use in children ages less than seven years with a contraindication to the pertussis component of the DTaP vaccine. For young children who develop a contraindication to pertussis-containing vaccines, vaccine providers may administer Td for all recommended remaining doses in place of DTaP. The only contraindication specific to the pertussis component in DTaP is encephalopathy within seven days of vaccine, not attributed to another cause. The occurrence of this adverse reaction is extremely rare.

The sole DT vaccine manufacturer in the U.S. discontinued DT protection. DT vaccine is no longer available. MassBiologics has discontinued production of their Td vaccine, TdVax.™ Grifols, who is the exclusive distributor for TdVax™, expects to have product available through approximately June 2024. Sanofi, who manufactures Tenivac®, the only other U.S.-licensed Td vaccine, is taking steps to augment their available Td supply in the U.S.; however, supply may be constrained.

Influenza Vaccines

ACIP reported preliminary vaccine effectiveness (VE) estimates for the 2023–2024 influenza season from four analytical networks as follows:

- Pediatric VE ranged from 59–67% in outpatient settings and 52–61% in inpatients.
- Adult VE ranged from 33–49% and 41–44% in inpatients with comparable or higher rates in seniors.

Due to a lack of cases caused by B/Yamagata lineage viruses over several seasons, the WHO and the FDA Vaccines and Related Biological Products Advisory Committee (VRBPAC) have recommended excluding B/Yamagata from influenza vaccines. As a result, manufacturers are making plans to shift from quadrivalent to trivalent influenza vaccines.

Polio

Fractional Inactivated Poliovirus Vaccine (fIPV) is equal to 1/5 a standard IPV dose and is administered in six countries outside of the U.S. Two fIPV doses are more immunogenic than one full IPV dose. WHO supports the use of two fIPV doses given intradermally in place of a single full IPV dose given intramuscularly.

The Polio Work Group proposed these clinical considerations for persons who received fIPV administered intradermally outside of the U.S.:

- **Two fIPV doses should be considered valid** and counted as one full intramuscular dose of IPV toward the U.S. vaccination schedule.
- **A single dose should not be considered valid** or counted toward the U.S. vaccination schedule.

Respiratory Syncytial Virus (RSV) Vaccines – Adults

Moderna presented phase 3 trial data on its investigational mRNA1345 RSV vaccine for adults ages 60 years and older. The vaccine had a good safety profile with no cases of Guillain Barré Syndrome (GBS) or acute disseminated encephalomyelitis and no imbalance in other neurologic or cardiac conditions compared to an unvaccinated reference population. The vaccine was efficacious at preventing severe RSV disease with continued efficacy through an 8.6-month median follow up with a vaccine efficacy of 63.3%. Boosting was observed with one-year revaccination. RSV-A and RSV-B neutralizing antibody responses were similar among age groups, including those greater than age 80 years. Immunogenicity criteria were met, and there were no new safety signals observed with concomitant administration with influenza vaccine or mRNA COVID-19 vaccine. Studies with high-dose influenza vaccine are still ongoing.

This past season, most RSV vaccines were administered to older individuals in pharmacies, which was most likely due to its status as a Medicare Part D vaccine. ACIP members expressed concern that a pharmacy may be a difficult setting for performing the needed counseling to comply with vaccine's shared clinical decision-making recommendation. RSV vaccine was co-administered with another respiratory vaccine 43% of the time. Data from pre-licensure clinical trials and early findings from post-licensure vaccine safety surveillance suggest the potential for increased risk of Guillain-Barré syndrome (GBS) after RSV vaccination in older adults; however, these early data are insufficient to confirm if there is an increased risk. Active surveillance systems are continuing to collect information.

Currently, the ACIP RSV Work Group continues to endorse the benefits of RSV vaccination for adults 60 and older using shared clinical decision making. However, the Work Group has begun reviewing evidence to discuss potentially changing to a universal recommendation for adults ages 60 years and older and to evaluate whether there should be a risk-based recommendation for adults ages 50 to 59 years.

Age over 75 years continues to be the greatest predictor of risk for hospitalization, ICU admission, and death with RSV. Ninety-four percent of adults with RSV-associated hospitalization have at least one underlying medical condition. Benefits may be maximized by administering RSV vaccine just before the start of RSV season, and the Work Group recommends that timing of vaccine in the late summer, early fall should be part of the shared clinical decision-making discussion.

Meningococcal Vaccines

Because meningococcal disease epidemiology has changed since ACIP made its vaccine recommendations, ACIP is considering revising the adolescent vaccine schedule due to lower incidence and shifting ages of risk. There were 416 cases in 2023 with the greatest rates of disease in children less than 1 year old with a second peak in adolescence. It is estimated that 222 cases of serogroup C, W, and Y disease have been averted in adolescents from 2006–2017 due to vaccination.

The Glaxo Smith Kline (GSK) MenABCWY candidate pentavalent meningococcal vaccine contains Menveo® MenACWY and Bexero® MenB. It has been studied in persons ages 10–25 years and is administered in two doses, at least six months apart. It has the advantage of providing some cross-

protection against gonorrhea. ACIP will use the same framework to evaluate this candidate pentavalent vaccine as it used to evaluate Pfizer's MenABCWY vaccine Penbraya®.

Vaccine-induced protection wanes quickly with meningococcal vaccines: In one to two years following primary vaccination against MenB vaccine and in 3 to 8 years postvaccination with MenACWY vaccine. Therefore, vaccines need to be administered at the most vulnerable times for meningococcus exposure. To achieve acceptable efficacy for disease incidence peak duration in young adulthood, ACIP is considering whether to:

- Remove the recommendation for the age 11–12 years MenACWY dose
- Change MenB vaccine from a shared clinical decision-making recommendation to a routine vaccination or a risk-based recommendation

The new adolescent meningococcal schedule is slated to be voted on in February 2024.

Pneumococcal Vaccines

Each year pneumococcal infections cause approximately 100,000 non-invasive pneumococcal pneumonia hospitalizations, 30,000 invasive pneumococcal disease (IPD) cases, and 3,000 deaths. Eighty percent of IPD cases occur among adults with risk-based indications for vaccination. Serotypes not contained in currently recommended vaccines cause approximately 40% of IPD cases in adults ages 65 years and older.

FDA approval of Merck's 21-valent pneumococcal conjugate vaccine (PCV21) for adults is anticipated in the first half of 2024. PCV21 has significantly greater coverage of the serotypes causing IPD in adults compared to Pneumococcal Conjugate Vaccine 20-valent (PCV20). PCV20 serotypes cover 54–58% of adult IPD, and PCV21 serotypes cover 81–84% of adult IPD cases. Among adults hospitalized with community-acquired pneumonia, 4.1% are infected with an *S. Pneumoniae* serotype included in PCV21 that are not included in PCV15 or PCV20. In a head-to-head analysis, PCV21 was shown to have non-inferior immunogenicity to serotypes shared with PCV20. When PCV21 was co-administered with quadrivalent inactivated influenza vaccine (IIV4), the influenza A:H3N2 subtype did not meet non-inferiority criteria.

Two, 24-valent pneumococcal conjugate vaccines are also currently in phase 1/2 studies.

ACIP plans to vote in June 2024, on recommending PCV21 as a product for pneumococcal protection in adults pending its approval by the FDA. It is also considering whether to lower the age for universal adult pneumococcal vaccination from ages 65 years and above to ages 50 years and above or potentially down to ages 19 years and above.

Hexavalent Vaccine

The ACIP will vote in June 2024 on whether to include hexavalent DTaP-IPV-Hib-HepB vaccine (Vaxelis®:Merck) as a preferred product for use in American Indian/Alaska Native (AI/AN) infants to protect against *Haemophilus influenzae* Type B (Hib). AI/AN infants contract Hib infection at an earlier

age and at a higher rate than other populations. They have a 31-fold higher incidence of invasive Hib disease than non-Native children.

PedvaxHIB® (PRP-OMP) is preferentially recommended in AI/AN infants to provide early protection because this vaccine produces a protective antibody response after the first dose, and other Hib vaccines do not produce this response until later doses. Vaxelis also includes Hib PRP-OMP conjugate, but at a lower concentration than in PedvaxHIB—less than half the concentration of PRP and OMP. A recent study shows post-Dose 1 Geometric Mean Concentrations (GMCs) of Vaxelis appear non-inferior to that of PedvaxHIB among Navajo nation and Alaska Native populations. Including Vaxelis as a second preferred option for AI/AN populations may improve equity and reliability of vaccine supply.

Questions regarding immunization? Contact Tamara Sheffield, MD, MPA, MPH, Medical Director, Immunization Programs, Intermountain Health Canyons Region, at **801-442-3946**.