Doug Campos-Outcalt, MD, MPA
University of Arizona, Phoenix

dougco@email.arizona.edu

The author reported no potential conflict of interest relevant to this article.

doi: 10.12788/jfp.0362

Vaccine update: The latest recommendations from ACIP

Here are the latest recommendations on the hepatitis, pneumococcal, zoster, rabies, and dengue vaccines.

In a typical year, the Advisory Committee on Immunization Practices (ACIP) has three 1.5- to 2-day meetings to make recommendations for the use of new and existing vaccines in the US population. However, 2021 was not a typical year. Last year, ACIP held 17 meetings for a total of 127 hours. Most of these were related to vaccines to prevent COVID-19. There are now 3 COVID-19 vaccines authorized for use in the United States: the 2-dose mRNA-based Pfizer-BioNTech/Comirnaty and Moderna COVID-19 vaccines and the single-dose adenovirus, vector-based Janssen (Johnson & Johnson) COVID-19 vaccine.

TABLE 1[1] includes the actions taken by the ACIP from late 2020 through 2021 related to COVID-19 vaccines. All of these recommendations except 1 occurred after the US Food and Drug Administration (FDA) approved the product using an emergency use authorization (EUA). The exception is the recommendation for use of the Pfizer-BioNTech COVID-19 vaccine (BNT162b2) for those ages 16 years and older, which was approved under the normal process 8 months after widespread use under an EUA.

Hepatitis B vaccine now for all nonimmune adults up through 59 years

Since the introduction of hepatitis B (HepB) vaccines in 1980, the incidence of hepatitis B virus (HBV) infections in the United States has been reduced dramatically; there were an estimated 287,000 cases in 1985[2] and 19,200 in 2014.[3] However, the incidence among adults has not declined in recent years and among some age groups has actually increased. Among those ages 40 to 49 years, the rate went from 1.9 per 100,000 in 2011[4] to 2.7 per 100,000 population in 2019.[5] In those ages 50 to 59, there was an increase from 1.1 to 1.6 per 100,000 population over the same period of time.[4,5]

Recommendations for using HepB vaccine in adults have been based on risk that involves individual behavior, occupation, and medical conditions (**TABLE 2**[6]). The presence of these risk factors is often unknown to medical professionals, who rarely ask about or document them. And patients can be reluctant to disclose them for fear of being stigmatized. The consequence has been a low rate of vaccination in at-risk adults.

At its November 2021 meeting, ACIP accepted the advice of the Hepatitis Work Group to move to a universal adult recommendation through age 59.[7] ACIP believed that the incidence of acute infection in those ages 60 and older was too low to merit a universal recommendation. The new recommendation states that all adults through age 59 years who are not immune to HBV through vaccination or prior infection should receive a HepB vaccine series, as should those 60 years and older with a risk factor (**TABLE 2**[6]). If a patient's immune status is unknown, ACIP recommends administering the vaccine, as there are no documented harmful effects of doing so in an individual with immunity.

Multiple HepB vaccine products are available for adults. Two are recombinant-based and require 3 doses: Engerix-B (GlaxoSmithKline) and Recombivax HB (Merck). One is recombinant based and requires only

TABLE 1

Actions taken by ACIP regarding COVID vaccines[1]

Vaccine *FDA authorization*	ACIP recommendation date	Recommendation	Age
Pfizer-BioNTech COVID-19 (BNT162b2) *EUA*	12-12-2020	2-dose primary series	≥ 16 years
Moderna COVID-19 (mRNA-1273) *EUA*	12-19-2020	2-dose primary series	≥ 18 years
Janssen COVID-19 (Ad.26.COV2.S) *EUA*	2-28-2021	1-dose primary series	≥ 18 years
Pfizer-BioNTech COVID-19 (BNT162b2) *EUA*	5-12-2021	2-dose primary series	12-15 years
Pfizer-BioNTech COVID-19 (BNT162b2) *EUA*	8-13-2021	Additional homologous primary dose ≥ 28 days after receipt of the second dose	Moderately to severely immunocompromised people ≥ 12 years
Moderna COVID-19 (mRNA-1273) *EUA*	8-13-2021	Additional homologous primary dose ≥ 28 days after receipt of the second dose	Moderately to severely immunocompromised people ≥ 18 years
Pfizer-BioNTech COVID-19 (BNT162b2) *BLA*	8-30-2021	Upgraded FDA authorization	≥ 16 years
Pfizer-BioNTech *EUA*	11-2021	Booster	≥ 18 years based on age, risk
Pfizer, Moderna, Janssen *EUA*	11-2021	Booster, including heterologous	≥ 18 years
Pfizer-BioNTech COVID-19 (BNT162b2) *EUA*	11-2-2021	2-dose primary series	5-11 years
Janssen COVID-19 (Ad.26.COV2.S)	12-16-2021	MRNA vaccines are preferred to the Janssen vaccine[a] due to TTS.	≥ 18 years

BLA, biologics license application (the normal process); EUA, emergency use authorization; FDA, US Food and Drug Administration; MRNA, messenger ribonucleic acid; TTS, thrombosis with thrombocytopenia syndrome.

[a] Also known as the Johnson & Johnson vaccine.

2 doses: Heplisav-B (Dynavax Technologies). A new product recently approved by the FDA, PREHEVBRIO (VBI Vaccines), is another recombinant 3-dose option that the ACIP will consider early in 2022. HepB and HepA vaccines can also be co-administered with Twinrix (GlaxoSmithKline).

Pneumococcal vaccines: New PCV vaccines alter prescribing choices

The ACIP recommendations for pneumococcal vaccines in adults have been very confusing, involving 2 vaccines: PCV13 (Prevnar13, Pfizer) and PPSV23 (Pneumovax23, Merck). Both PCV13 and PPSV23 given in series were recommended for immunocompromised patients, but only PPSV23 was recommended for those with chronic medical conditions. For those 65 and older, PPSV23 was recommended for all individuals (including those with no chronic or immunocompromising condition), and PCV13 was recommended for those with

TABLE 2

Risks for hepatitis B infection[6]

Individuals at risk for infection by sexual exposure
• Sex partners of hepatitis B surface antigen (HBsAg)–positive individuals
• Sexually active individuals who are not in a long-term, mutually monogamous relationship (eg, individuals with more than 1 sex partner during the previous 6 months)
• Individuals seeking evaluation or treatment for a sexually transmitted infection
• Men who have sex with men
Individuals at risk for infection by percutaneous or mucosal exposure to blood
• Current or recent injection-drug users
• Household contacts of HBsAg-positive individuals
• Residents and staff of facilities for developmentally disabled individuals
• Health care and public safety personnel with reasonably anticipated risk for exposure to blood or blood-contaminated body fluids
• Hemodialysis patients and predialysis, peritoneal dialysis, and home dialysis patients
• Individuals ≥ 60 years with diabetes, at the discretion of the treating clinician
Others
• International travelers to countries with high or intermediate levels of endemic hepatitis B virus infection (HBsAg prevalence ≥ 2%)
• Individuals with hepatitis C virus infection
• Individuals with chronic liver disease (including, but not limited to, cirrhosis, fatty liver disease, alcoholic liver disease, autoimmune hepatitis, and an alanine aminotransferase or aspartate aminotransferase level greater than twice the upper limit of normal)
• Individuals with HIV infection
• Incarcerated individuals

immunocompromising conditions. Other adults in this older age group could receive PCV13 based on individual risk and shared clinical decision making.[8]

This past year, 2 new PCV vaccines were approved by the FDA: PCV15 (Vaxneuvance, Merck) and PCV20 (Prevnar20, Pfizer). While considering these new vaccines, the ACIP reassessed its entire approval of pneumococcal vaccines. First, they retained the cutoff for universal pneumococcal vaccination at 65 years. For those younger than 65, they combined chronic medical conditions and immunocompromising conditions into a single at-risk group (**TABLE 3**[9]). They then issued the same recommendation for older adults and those younger than 65 with risks: to receive a PCV vaccine, either PCV15 or PCV20. If they receive PCV15, it should be followed by PPSV23. PPSV23 is not recommended for those who receive PCV20. Therefore, PPSV23 is no longer routinely recommended for adults unless PCV15 is the PCV of choice.[9] Clinical guidance on the use of PCV vaccines will be published in early 2022.

Zoster vaccine for younger adults

Recombinant zoster vaccine (RZV) has been licensed and recommended in the United States since 2017 in a 2-dose schedule for adults ages 50 years and older. In the summer of 2021, the FDA expanded the indication for use of RZV to include individuals 18 to 49 years of age who are or will be immunodeficient or immunosuppressed due to known disease or therapy. In October, the ACIP agreed and recommended 2 RZV doses for those 19 years and older in these risk groups (**TABLE 4**[10]).

This recommendation was based on the elevated risk of herpes zoster documented in those with immune-suppressing conditions and therapies. In the conditions studied, the incidence in these younger adults exceeded that for older adults, for whom the vaccine is recommended.[10] There are many immune con-

TABLE 3

Adults younger than 65 for whom PCV[a] is recommended[9]

Chronic medical conditions
• Chronic heart disease (congestive heart failure and cardiomyopathies)
• Chronic liver disease
• Chronic lung disease (chronic obstructive pulmonary disease, emphysema, and asthma)
• Cigarette smoking
• Diabetes
• Cochlear implant
• Cerebrospinal fluid leak
• Alcoholism
Immune-compromising conditions
• Congenital or acquired asplenia
• Chronic renal failure
• Congenital or acquired immunodeficiencies (B- [humoral] or T-lymphocyte deficiency, complement deficiencies, and phagocytic disorders [excluding chronic granulomatous disease])
• Generalized malignancy
• HIV infection
• Hodgkin disease
• Iatrogenic immunosuppression (use of immunosuppressive drugs, including long-term systemic corticosteroids and radiation therapy)
• Leukemia
• Lymphoma
• Multiple myeloma
• Nephrotic syndrome
• Solid organ transplant

[a] Either PCV15 or PCV20. If PCV15 is chosen, it should be followed by PPSV23.

ditions and immune-suppressing medications. The ACIP Zoster Work Group did not have efficacy and safety information on the use of RZV in each one of them, even though their recommendation includes them all. Many of these patients are under the care of specialists whose specialty societies had been recommending zoster vaccine for their patients, off label, prior to the FDA authorization.

Rabies vaccine is now available in 2-dose schedule

People who should receive rabies pre-exposure prophylaxis (PrEP) with rabies vaccine include laboratory personnel who work with rabies virus, biologists who work with bats, animal care professionals, wildlife biologists, veterinarians, and travelers who may be at risk of encountering rabid dogs. The recommendation has been for 3 doses of rabies vaccine at 0, 7, and 21-28 days. The ACIP voted at its June 2021 meeting to adopt a 2-dose PrEP schedule of 0 and 7 days.[11] This will be especially helpful to travelers who want to complete the recommended doses prior to departure. Those who have sustained risk over time can elect to have a third dose after 21 days and before 3 years, or elect to have titers checked. More detailed clinical advice will be published in the CDC's *Morbidity and Mortality Weekly Report* in 2022.

Dengue vaccine: New rec for those 9-16 years

In 2019, the FDA approved the first dengue vaccine for use in the United States for children 9 to 16 years old who had laboratory-confirmed previous dengue virus infection and who were living in an area where dengue

TABLE 4

Those for whom recombinant zoster vaccine is recommended at ages 19-49 years[10,a]

- Hematopoietic stem cell transplant recipients
- Patients with hematologic malignancies
- Renal or other solid-organ transplant recipients
- Patients with solid tumor malignancies
- People living with HIV infection
- Patients with primary immunodeficiencies and autoimmune and inflammatory conditions; patients taking immunosuppressive medications/therapies

[a] This not a comprehensive list of all such conditions.

The incidence of hepatitis B infection among adults has not declined in recent years and has actually increased in some age groups.

is endemic. The CYD-TDV dengue vaccine (Dengvaxia) is a live-attenuated tetravalent vaccine built on a yellow fever vaccine backbone. Its effectiveness is 82% for prevention of symptomatic dengue, 79% for prevention of dengue-associated hospitalizations, and 84% against severe dengue.[12]

Dengue viruses (DENV) are transmitted by Aedes mosquitoes. There are 4 serotypes of dengue, and all 4 appear to be circulating in most endemic countries. Clinical disease varies from a mild febrile illness to severe disease. The most common clinical presentation includes sudden onset of fever, headache, retro-orbital pain, myalgia and arthralgia, abdominal pain, and nausea.

Severe disease includes plasma leakage, shock, respiratory distress, severe bleeding, and organ failure. While severe dengue can occur with a primary infection, a second infection with a different DENV increases the risk of severe dengue. A small increased risk of severe dengue occurs when dengue infection occurs after vaccination in those with no evidence of previous dengue infection. It is felt that the vaccine serves as a primary infection that increases the risk of severe dengue with subsequent infections. This is the reason that the vaccine is recommended only for those with a documented previous dengue infection.

At its June 2021 meeting, the ACIP recommended 3-doses of Dengvaxia, administered at 0, 6, and 12 months, for individuals 9 to 16 years of age who have laboratory confirmation of previous dengue infection and live in endemic areas.[12] These areas include the territories and affiliated states of Puerto Rico, American Samoa, US Virgin Islands, Federated States of Micronesia, Republic of Marshall Islands, and the Republic of Palau. Puerto Rico accounts for 85% of the population of these areas and 95% of reported dengue cases.[12]

The reason for the delay between FDA approval and the ACIP recommendation was the need to wait for a readily available, accurate laboratory test to confirm previous dengue infection, which is now available. There are other dengue vaccines in development including 2 live-attenuated, tetravalent vaccine candidates in Phase 3 trials. JFP

References

1. ACIP. COVID-19 vaccine recommendations. Accessed February 8, 2022. www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/covid-19.html
2. CDC. Division of viral hepatitis. Disease burden from viral hepatitis A, B, and C in the United States. Accessed February 8 2022. www.cdc.gov/hepatitis/PDFs/disease_burden.pdf
3. CDC. Surveillance for viral hepatitis – United States, 2014. Hepatitis B. Accessed February 8, 2022. https://www.cdc.gov/hepatitis/statistics/2014surveillance/commentary.htm#:~:text=HEPATITIS%20B-,Acute%20Hepatitis%20B,B%20cases%20occurred%20in%202014
4. CDC. Viral hepatitis surveillance: United States, 2011. Hepatitis B. Accessed February 8, 2022. www.cdc.gov/hepatitis/statistics/2011surveillance/pdfs/2011HepSurveillanceRpt.pdf
5. CDC. Viral hepatitis surveillance report, 2019. Hepatitis B. Accessed February 8, 2022. www.cdc.gov/hepatitis/statistics/2019surveillance/HepB.htm
6. Schillie S, Harris A, Link-Gelles R, et al. Recommendations of the Advisory Committee on Immunization Practices for use of a hepatitis B vaccine with a novel adjuvant. *MMWR Morb Mortal Wkly Rep*. 2018;67:455-458.
7. CDC. Advisory Committee on Immunization Practices. Meeting recommendations, November 2021. Accessed February 8, 2022. www.cdc.gov/vaccines/acip/index.html
8. Matanock A, Lee G, Gierke R, et al. Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine among adults aged ≥65 years: updated recommendations of the Advisory Committee on Immunization Practices. M*MWR Morb Mortal Wkly Rep*. 2019;68:1069-1075.
9. Kobayashi M. Considerations for use of PCV15 and PCV20 in U.S. adults. Accessed February 8, 2022. www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-02/24-25/05-Pneumococcal-Kobayashi.pdf
10. Anderson TC, Masters NB, Guo A, et al. Use of recombinant zoster vaccine in immunocompromised adults aged ≥19 years: recommendations of the Advisory Committee on Immunization Practices — United States, 2022. *MMWR Morb Mortal Wkly Rep*. 2022;71:80-84.
11. CDC. ACIP recommendations. June 2021. Accessed February 8, 2022. www.cdc.gov/vaccines/acip/recommendations.html
12. Paz-Bailey G. Dengue vaccine. Evidence to recommendation framework. Presented to the ACIP June 24, 2021. Accessed February 8, 2022. www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-06/03-Dengue-Paz-Bailey-508.pdf