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Immunization Update

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Introduction

The Center for Disease Control and Prevention's (CDC) Advisory Committee on Immunization Practices (ACIP) makes recommendations regarding the use of immunizations in the United States. The committee's evidence-based recommendations are published in the CDC's Morbidity and Mortality Weekly Report (MMRW) and incorporated into the annual CDC Immunization Schedules for children and adults. ACIP meets three times per year to review clinical research, pharmacoeconomic studies, and other data related to vaccines, and recommendations can change with the same frequency.

In addition to regularly evaluating and updating recommendations for the clinical use of vaccines currently on the market in the US, ACIP reviews data related to new vaccines following licensing approval by the FDA. Currently, there are dozens of vaccines in various stages of development including late-phase clinical trials. One of those likely to be reviewed by the FDA in the near future is a novel type of herpes zoster (shingles) vaccine whose trial results have been promising. Remaining up-to-date in this rapidly changing field ensures that practice is consistent with the best and most current evidence available.

The updates discussed below provide a review of substantive changes to ACIP recommendations during the last 18 months, and are further summarized in Table 1. Pharmacists are also encouraged to periodically review CDC publications as well as other professional and patient resources that are updated frequently. Important sources of comprehensive vaccine-related information include the MMWR (www.cdc.gov/mmwr/index.html) and the Immunization Action Coalition (www.immunize.org), both of which are freely available to the public.

Influenza

The intranasal live attenuated influenza vaccine (LAIV, FluMist®) was FDA approved in 2003. Research during multiple seasons prior to 2010 compared the efficacy of trivalent live attenuated influenza vaccine (LAIV3) and trivalent inactivated influenza vaccine (IIV3). These studies indicated that, in adults and children, LAIV3 was statistically at least as effective as IIV3.[1-4] LAIV was reformulated as a quadrivalent vaccine (LAIV4) in 2012 with an H1N1 vaccine virus that was different from the 2009 pandemic virus included in all other influenza vaccine formulations. Studies and analysis of observational data conducted after this change found no significant efficacy at preventing influenza infection, particularly H1N1 influenza.[5,6] For this reason, ACIP recommended against the use of LAIV4 in all populations for the 2016-17 flu season.[6] During the June 2017 ACIP meeting, the committee voted to continue this recommendation for the 2017-18 flu season as minimal impact on overall vaccination rates was noted for 2016-17.[7,8]

Aside from LAIV4, there are a multitude of types and formulations of tri- and quadrivalent flu vaccines available. Each is approved for specific age groups, so familiarity with the particular product being administered is important. In 2016, a quadrivalent cell culture-based IIV4 (ccIIV4, Flucelvax®) was approved by the FDA for use in ages 4 years and older. The previously marketed formulation, trivalent ccIIV, was only approved for individuals over age 18 years.[6]

Human papilloma virus (HPV)

As of December 2016, ACIP recommends a simplified two-dose series of nine-valent HPV vaccine (9vHPV, Gardasil-9®) administered at 0 and 6 months for individuals who receive the first dose prior to their 15th birthday.[9] This recommendation is based on recent evidence of non-inferiority of the two-dose series compared to the standard three-dose series (administered at 0, 1-2, and 6 months) in study participants between the ages of 9 and 14 years.[10]

Routine vaccination with HPV vaccine is recommended between 11 and 12 years of age, but girls and boys as young as 9 years may begin the two-dose series. A three-dose series is still recommended for adolescents and young adults who initiate vaccination at age 15 years or later. Individuals who were

previously vaccinated with 2vHPV, 4vHPV or 9vHPV vaccine on a schedule consistent with the current recommendations should be considered adequately vaccinated. Incomplete series can be completed with 9vHPV, the only formulation currently available, regardless of the initial product(s) used and need not be restarted.[9] A simplified schedule is significant due to its potential to improve rates of complete vaccination and cost effectiveness.

Meningococcal serogroups A, C, Y, W-135

During the past two decades, a growing body of evidence has indicated an increased risk of meningococcal disease among HIV-positive persons.[11,12] As a result, ACIP reviewed available data on the immunogenicity, safety, and cost-effectiveness of quadrivalent meningococcal vaccines in this population. In the Fall of 2016, the committee subsequently recommended that all HIV-positive individuals 2 months and older receive conjugated quadrivalent meningococcal vaccines (MenACWY-D, Menactra® or MenACWY-CRM, Menveo®) to reduce the risk of serogroups A, C, Y, and W-135 infection. This recommendation is aligned with recommendations for the use and dosing of meningococcal vaccines in patients with other specific types of immunocompromising conditions.[13]

Meningococcal serogroup B

The populations for whom serogroup B meningococcal vaccines are recommended continue to be somewhat narrower than those for the quadrivalent meningococcal vaccines. Vaccination with either of two available formulations, MenB-FHbp (Trumenba®) or MenB-4C (Bexsero®), is recommended by ACIP for individuals age 10 years and older at increased risk and during serogroup B outbreaks. Additionally, there is a permissive recommendation for adolescents and young adults between the ages of 16 and 23 years.[14,15]

In October 2016, ACIP considered data regarding the immunogenicity of a simplified two-dose regimen for MenB-FHbp as compared to a three-dose series. This followed an April 2016 change in the FDA approved dosing schedule to include use as either a two- or three-dose series with doses at 0 and 6 months and 0, 1-2, and 6 months, respectively. Based on published and unpublished data, ACIP aligned its recommendation with the FDA licensed dosing such that a two-dose series may be used for healthy individuals age 16-23 years. While the two-dose series has the same dosing timeline as MenB-4C, the two vaccines are not interchangeable and a single formulation must be used to complete all doses in the series.[16]

ACIP continues to recommend that the three-dose series be used for patients at increased clinical risk for meningococcal infection and in outbreak situations. However, in the case that the second dose is administered 6 months or longer after the first dose, the series may be considered complete.[16]

Cholera

Oral cholera vaccines have been available internationally for some time; however, it was only recently that one was licensed in the United States. Lyophilized cholera serogroup O1 vaccine (CVD 103-HgR, Vaxchora®) received FDA approval in 2016.17 ACIP recommends this vaccine in addition to personal protective measures for adults age 18-64 years who plan to visit areas of active cholera transmission. While this is typically not applicable to most tourist itineraries, individuals who may be at risk of cholera exposure include healthcare workers and other humanitarian workers as well as those who are visiting friends and relatives.[18]

Yellow Fever

Based on clinical research, the World Health Organization (WHO) amended International Health Regulations to such that a single dose of yellow fever is considered protective for the life of the person vaccinated. Prior to this 2014 change, revaccination was recommended every 10 years for individuals at continued risk and was required as a condition for entry into certain countries.[19-21]

ACIP aligned its recommendation with the WHO in 2015, and the new international health regulation officially took effect in July 2016.[21,22] A recently published systematic review provides further evidence of lifelong immunity following a single dose of yellow fever vaccine.[23] Specific patient populations, including those vaccinated during pregnancy, those who are HIV positive, and some hematopoietic stem cell recipients may still require revaccination if they remain at continued risk.[22]

Due to manufacturing complications and a transition to a new production facility, Sanofi Pasteur is anticipating a complete depletion of supply of YF-VAX® from mid-2017 until 2018. Until Sanofi's new facility is operational, the FDA, CDC, and U.S. Department of Defense have worked with the company to implement an emergency IND protocol under which certain clinics may administer Stamaril®, a live yellow fever vaccine product similar to YF VAX® that is licensed in many countries and produced in France.[24]

Table 1. Summary of recent updates to ACIP vaccine recommendations:

Vaccine	ACIP recommended for:	Update(s)
Influenza	All individuals over age 6 months (FDA approval for different age groups varies by formulation)	• ACIP recommends against use of live attenuated influenza vaccine (LAIV, Flumist Quadrivalent®). • Cell culture inactivated influenza vaccine (Flucelvax®) is now quadrivalent and approved for children and adults 4 years and older.
Human Papilloma Virus (HPV)	• Females age 9-26 years • Males age 9-21 years (up to age 26 may be vaccinated)	• A two-dose series is recommended for adolescents who initiate vaccination before their 15th birthday. • Nine-valent HPV vaccine (Garadasil-9®) is the only HPV vaccine currently on the market.
Meningococcal Serogroups ACYW	• Routine pediatric and adolescent vaccination • First-time college students • Certain immunocompromised patients • Persons at risk due to an outbreak or international travel to a high-risk area • Certain laboratory workers • Military recruits	ACIP now recommends quadrivalent meningococcal vaccine for all HIV-positive patients 2 months and older.
Meningococcal Serogroup B	• Certain immunocompromised patients • Persons at risk due to an outbreak • Certain laboratory workers • Permissive recommendation for adolescents and young adults age 16-23 years	MenB-FHbp (Trumenba®) may now be administered as a two-dose series in certain patients.
Cholera	Adults age 18-64 years traveling internationally to an area with active cholera transmission	A new vaccine, lyophilized CVD 103-HgR covering cholera serogroup O1 (Vaxchora®), was approved in 2016 and is recommended by ACIP for a select patient.
Yellow Fever	Persons age 9 months and older traveling to or residing in an area with yellow fever virus transmission	• A single dose is now considered to be protective for life - revaccination is not necessary for most travelers. • A severe shortage of the only FDA approved vaccine, YF VAX®, is expected to continue through mid-2018.

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