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Vaccine Update 2016

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The Advisory Committee on Immunization Practices (ACIP) meets three times a year to discuss research focused on vaccine safety and efficacy. Their recommendations serve as public health guidance for storage, handling and administration of immunizations. The ACIP 2016 adult vaccine schedule includes updates for the human papillomavirus (HPV), pneumococcal and meningococcal vaccinations. In addition, ACIP revised some of their previous influenza recommendations for the upcoming 2016-17 season. A summary of ACIP immunization recommendations from the past year will be reviewed in this article.

Influenza Vaccine - Nasal Spray not recommended for 2016-17 flu season

In June 2016, ACIP reviewed its annual influenza vaccine recommendations. The committee voted to continue recommending all people 6 months and older be vaccinated annually against influenza. In a change from previous recommendations, ACIP voted that the live attenuated influenza vaccine (LAIV) nasal spray formulation not be used during the 2016-17 season.[1] The committee also voted to remove LAIV from the Vaccines for Children (VFC) program. This is an interim recommendation, as data may be subject to change in future influenza seasons. Final ACIP recommendations for the 2016-17 influenza season can be accessed at this web site: http://www.cdc.gov/mmwr/volumes/65/rr/rr6505a1.htm?s_cid=rr6505a1_w

The vote was based on data collated by the U.S. Influenza Vaccine Effectiveness Network demonstrating poor efficacy of LAIV from 2013 through 2016. The Center for Disease Control (CDC) conducts vaccine effectiveness studies every flu season to evaluate the efficacy of the current influenza vaccine. Vaccine effectiveness can vary widely from season to season depending on the circulating viruses and the antigens contained in the vaccine manufactured for each influenza season. The CDC estimate of LAIV effectiveness against any influenza virus during the 2015-16 season amongst children 2 through 17 years of age was 3% (95% Confidence Interval (CI): -49 to 37). In other words, no protective benefit could be measured. In contrast, the inactivated influenza vaccine (IIV) contained in the intramuscular flu shot had a vaccine effectiveness estimate of 63% (95% CI: 52 to 72) in the same age group and time frame.[2] From 2010 through 2013, the influenza nasal spray was a trivalent vaccine. In late 2013, the quadrivalent formulation of the nasal spray was developed for influenza prophylaxis. In a CDC retrospective review it was noted that the LAIV formulation was substantially less effective than the IIV form of the vaccine in preventing Influenza A(H1N1)pdm09 in the 2010-11, 2013-14 and 2015-16 influenza seasons.[3]

Possible reasons for poor performance of LAIV in 2015-16 were theorized as follows:

- Suboptimal performance of the A/Bolivia/559/2013 (H1N1)pdm09 HA vaccine component[3]
- Potential interference among viruses in the quadrivalent vaccine [i.e., additional B vaccine component inhibits viral replication of A(H1N1)pdm09 virus][3]
- Reduced immunogenicity of LAIV as a result of more highly vaccinated population in recent years; compared with populations of earlier studies, in which it is likely that a higher proportion of children were vaccine-naïve[3]

Three recent studies evaluated the seasonal effectiveness of LAIV compared to IIV. A retrospective analysis of the U.S. Influenza Effectiveness Network data from 2010 through 2014 evaluated the relative effectiveness of LIAV compared with IIV in preventing influenza.[4] The odds of influenza were not statistically different between 2010 through 2013 between LAIV and IIV for all types of influenza. However, in the 2013-14 season the odds of influenza were significantly higher for LAIV compared to IIV in patients aged 2-17 years (OR = 2.88; 95% CI: 1.62-5.12) and for patients aged 2-8 years (OR = 5.36, 95% CI: 2.37-12.13).[4] Notably, for the age range between 9 and 17 the odds ratio was not statistically significant.

When the odds ratios were calculated by virus type, a higher proportion of LAIV patients aged 2-17 years tested positive for Type A(H1N1)pdm09 virus compared to the IIV patients (OR = 5.53, 95% CI: 1.35-22.76) in 2010-11.[4] Similar patterns were seen in 2013-14 in the same age range (OR = 2.65, 95% CI: 1.34-5.27).[4] There were no statistically significant differences noted for A/H3N2 or Type B viruses. This analysis suggests lower effectiveness of LAIV was related to the influenza type A(H1N1)pdm09 virus.[4] Current circulating strains of influenza A are subcategorized as either H1N1 or H3N2 viruses. In the spring of 2009, a new strain of influenza A(H1N1) was identified as causing the first flu pandemic in over 40 years.[5] This particular viral strain replaced the previously circulating influenza Type A virus and continues to circulate each season. Influenza Type A tends to cause more severe disease and mortality in older patients, while children and young adults seem to be more susceptible to influenza Type B infections.

An observational trial was conducted in 1033 children aged 2-17 years during the 2013-14 influenza season at 4 separate geographic sites.[6] Seventy four percent of the influenza cases were due to A(H1N1)pdm09 strains, 21% were due to influenza B, and 4% were due to influenza H3N2. LAIV did not show significant effectiveness against A(H1N1)pdm09 (Vaccine effectiveness (VE) = 13%, 95% CI: −55 to 51) but was effective against B strains (VE = 82%, 95% CI: 12–96).[6] Inactivated influenza vaccine was effective against A(H1N1)pdm09 (VE = 74% , 95% CI: 50–86) and type B (VE = 70%, 95% CI: 18–89).[6] The authors concluded LAIV provided significant protection against type B influenza but not against A(H1N1)pdm09 in children aged 2–17 years during the 2013–2014 season.

In another observational trial, influenza vaccine effectiveness was evaluated during the 2013-14 season against the Type A(H1N1)pdm09 strain of the influenza virus at 5 different sites in adults and children.[7] Of the 1197 confirmed influenza cases assessed in the study, 85% were positive for A(H1N1)pdm09, 9% had the A/H3N2 virus, and 6% tested positive for the Type B strain. Vaccine effectiveness for LAIV was estimated in children aged 2–17 years as very few adults received LAIV. The LAIV VE against A(H1N1)pdm09-related respiratory illness was 18% (95% CI, −38% to 51%) and not statistically significant. LAIV VE against A(H1N1)pdm09 was not significant in any age-stratified model. Among the youngest children, aged 2–4 years, 11% of those who were negative for influenza virus had received LAIV4, compared with 18% of those with confirmed A(H1N1)pdm09; this difference was not statistically significant (p = 0.23).[7]

A recently published randomized controlled trial (RCT) directly compared the trivalent formulation of LAIV to IIV in a rural Canadian population to assess if one formulation provided more effective protection against influenza than the other.[8] A total of 4611 participants were enrolled in the study over a 3 year period from 2012 through May, 2015. The primary outcome was the presence of laboratory confirmed influenza A or B. Influenza infection occurred in 5.3% of the LAIV group compared to 5.2% of the IIV group.[8] The nonsignificant hazard ratio comparing LIAV to IIV was 1.03 (95% CI 0.85-1.24).[8] The investigators concluded immunizing with LAIV does not provide better community protection again influenza than IIV.[8] When comparing the results of this RCT to observational trials it must be noted that the study period took place during different years (2012-2015) and with the trivalent

forms of the flu vaccine. The poor performance of LAIV in the United States was observed in the 2015-16 season with the quadrivalent formula. Finally, the study population was a small, isolated rural community which may not reflect influenza transmission in larger, urban populations.

In conclusion, there is mounting evidence that the influenza nasal spray does not provide adequate effectiveness in preventing influenza when compared to the injectable form. For this reason, the ACIP Advisory Committee voted 13-1 that the nasal spray should not be used during the 2016-17 influenza season. However, annual flu vaccination with the injectable flu vaccine continues to be an ACIP recommendation for everyone over the age of 6 months. The Oregon Health Authority (OHA) supports the ACIP recommendations and is advising against using the nasal spray. The nasal spray will NOT be supplied through the Vaccines For Children (VFC) population. Medicaid Fee-For-Service will not be paying for administration of the nasal spray for patients aged 2 through 18 years old. OHA has stated that the inactivated injectable form is preferred for all ages.[9] The 2016-17 Oregon immunization protocols can be accessed at the following web link:
https://public.health.oregon.gov/PreventionWellness/VaccinesImmunization/ImmunizationProviderResources/Documents/PharmIIV.pdf

Human Papillomavirus (HPV) Vaccine - New formulation added to adult schedule

Human papillomavirus is a common sexually transmitted infection and is associated with cervical cancer. HPV infection is also associated with oropharyngeal cancer and other anogenital cancers. There are 3 HPV vaccines in the United States. The newest vaccine, Gardasil-9® was recently added to the adult vaccination schedule. This nine valent vaccine targets five additional strains of the HPV virus that account for 15% of cervical cancers.[10] The differences between the 3 vaccines are outlined in Table 1. Of note the bivalent vaccine (Cervarix®) is only approved for use in women for prevention of cervical cancer and pre-cancers. The quadrivalent vaccine (Gardasil®) has additional approval for prevention of genital warts. The vaccines will not have a therapeutic effect on existing HPV infection, genital warts or cervical lesions. Three HPV vaccine doses are recommended starting at age 11 or 12. Vaccination is recommended through age 26 for all females, through age 21 for all males and through age 26 for immunocompromised males including those with HIV and men who have sex with men.[11]

Table 1 – HPV Vaccines licensed in the United States

Brand Name	HPV Types	Sex	Age Groups	Schedule
Cervarix®	16,18	Females	9-25 years	3 doses (0, 1, 6 mo.)
Gardasil®	6,11,16,18	Females and Males	9-26 years	3 doses (0, 2, 6 mo.)
Gardasil-9®	6,11,16,18,31, 33,42,52, 58	Females and Males	9-26 years	3 doses (0, 2, 6 mo.)

Adult Pneumococcal Vaccine – New scheduling recommendations

The US Food and Drug Administration (FDA) has approved two pneumococcal vaccines for adults: conjugate PCV13 (Prevnar®) and polysaccharide PPSV23 (Pneumovax®). The two pneumococcal vaccinations should not be given at the same time and should be administered in a specific order at specific intervals. ACIP recommends administering PCV-13 first to provide optimal immune response to the vaccine. For most healthy adults aged 19- 64 years, PPSV23 can be given one year after the initial PCV 13 dose.[12] However, for adults of all ages with immunocompromising conditions, functional or anatomic asplenia, cerebrospinal fluid leaks, or cochlear implants PCV13 and PPSV23 should be administered at least 8 weeks apart.[11] PCV 13 is only recommended to be administered one time. Revaccination with PPSV23 five years after the first dose is recommended for: 1) children and adults younger than 65 of age who are at high risk for serious pneumococcal infection and 2) adults 65 years and older who have received their first PPSV23 dose for any reason when they were younger than 65 years old.[12] Adults who receive PPSV23 after the age of 65 only need a single dose. The risk of administering pneumococcal vaccines too soon is increased injection site swelling and pain.[13]

Meningococcal Vaccine - Additional meningitis vaccine added to adult schedule

The meningococci that can cause invasive meningitis are one of five bacterial serogroups: A, B, C, W or Y. Serogroup prevalence varies by geographic area. For example, epidemics of serogroup A meningococcal disease have frequently occurred in sub-Saharan Africa. The major causes of meningococcal disease in the United States are due to serogroups B, C and Y. Three meningitis vaccines are available that provide immunity to serogroups A, C, W and Y (MenACWY): Menactra®, Menveo® and Menomune®. These formulations have been available for several years. Until late 2014, there was no vaccine available for serogroup B. Due to recent outbreaks of serogroup B meningococcal disease on college campuses, the development of vaccines targeted towards Group B meningococcal vaccines was fast tracked by the FDA. The first serogroup B meningococcal vaccine, Trumenba® was introduced in late 2014. In early 2015 a second serogroup B meningococcal vaccine, Bexsero® received FDA approval. Trumenba® is a 3 dose vaccine while Bexsero® is a 2 dose series. Table 2 provides a comparison of all meningococcal vaccines available in the United States.

Table 2- Meningococcal Vaccines Licensed in the United States

Brand Name	Type of Vaccine	Serogroups	Year Licensed	Age Range
Menomune®	Polysaccharide	A,C,W,Y	1981	≥ 2 years
Menactra®	Conjugate	A,C,W,Y	2005	9 mo. - 55 yrs.
Menveo®	Conjugate	A,C,W,Y	2010	2 mo.– 55 yrs.
MenHibrix®	Conjugate	C,Y and H influenzae type B (Hib)	2012	6 wks. – 18 mo.
Trumenba®	Recombinant Protein	B	2014	10 – 25 yrs.
Bexsero®	Recombinant Protein	B	2015	10 – 25 yrs.

The recent ACIP recommendations provide guidance as to who should receive the meningococcal B (MenB) vaccines. The products are not interchangeable and the same product must be used to complete the two- or three-dose series. MenB vaccine series **should** be administered to persons aged ≥10 years who are at increased risk for serogroup B meningococcal disease. Patients with persistent genetic deficiencies, receiving eculizumab, or with anatomic asplenia are at risk for meningococcal disease and have a higher mortality rate (40-70%) then healthy people.[14] MenB vaccine series **may** be administered to adolescents and young adults aged 16 through 23 years (preferred age is 16 through 18 years) to provide protection against most strains of serogroup B meningococcal disease.[15] ACIP did not recommend all adolescents routinely receive the MenB vaccine because there is still limited data on the effectiveness and safety of these new vaccines. In addition, the increasing rarity of meningitis type B infections limited ACIP from making administration of MenB vaccine a universal recommendation. At-risk microbiologists (those who might be exposed through work) also need both types of meningococcal vaccinations. MenACWY vaccine may be administered at the same time as the MenB vaccine, but at a different anatomic site.

In conclusion, vaccines are one of the best defenses in preventing hospitalizations and complications from communicable diseases. Insuring the appropriate vaccine formulation is administered to target populations at recommended intervals are important components of effective immunization

strategies. Staying updated on ACIP guidelines can assist health care practitioners in providing their patients with reliable vaccine information.

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