**IMMUNIZATIONS NEWSLETTER**

**PROVIDING GSA MEMBERS WITH UPDATES ON ADULT IMMUNIZATIONS**

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**FEATURES**

**News**

- Addressing questions about **seasonal influenza vaccination of pregnant women**, Getahun et al. report in *Vaccine* no safety concerns and fewer adverse outcomes among vaccinated than unvaccinated mothers (2019;37(13):1785–1791). “The lack of increased adverse outcomes associated with influenza vaccination suggests that the benefits of vaccination during pregnancy to the woman and her child far outweigh any risk, if there is one, from the vaccination,” the group concluded. Among the benefits associated with influenza immunization were a 51% reduction in influenza, 60% less risk of maternal fever, 7% reduction in risk of preeclampsia, 11% reduction in placental abruption, 12% fewer stillbirths, and 11% less risk of the child requiring neonatal intensive care.

**Resources**

- In response to last month’s *NAVP Immunizations Newsletter* article on the vaccine industry, GSA Past President Leonard Hayflick of the University of California, San Francisco, wrote to share with readers a recent review of the **important WI-38 cell line** that is used in commercial production of many human virus vaccines. Published in *AIMS Public Health* (2017;4(2):127–138), the article estimates that WI-38–related vaccines have averted 198 million cases of and 450,000 deaths from poliomyelitis, measles, mumps, rubella, varicella, adenovirus, rabies, and hepatitis A in the United States and 4.5 billion cases and 10.3 million deaths globally. Dr. Hayflick was a pioneer in the discovery and development of the WI-38 cell line, which catalyzed development and marketing of live attenuated viral vaccines.
While the numbers of older adults who have received the 13-valent pneumococcal conjugate vaccine (PCV13) in the past 5 years has increased, those receiving the second dose of 23-valent pneumococcal polysaccharide vaccine (PPSV23) have not seen similar increases despite Centers for Disease Control and Prevention (CDC) recommendations to receive both vaccines.

One tool to help patients remember that they are due for another dose of pneumococcal vaccine is a reminder-recall system. Various types of reminder-recall systems have been shown to significantly improve immunization rates, and they don’t have to take a lot of time. Voicemail, email, text, and mailings are all options, with several third parties offering support.

This tool from a Quality Innovation Network–Quality Improvement Organization provides a few ways for health care professionals to implement a reminder-recall system. Among the factors to consider in choosing a system are a clinic’s vaccination workflow, the amount of staff time and resources available, and the cost.

ACHIEVING CLARITY ON PNEUMOCOCCAL VACCINES

The currently recommended pneumococcal vaccines for protecting older and other susceptible adults from Streptococcus pneumoniae continue to generate debate and discussion. In recent weeks, a clinical study was published that shows very high vaccine effectiveness (VE) for the 13-valent product against vaccine-type community-acquired pneumonia (CAP). At February's meeting of the Advisory Committee on Immunization Practices (ACIP), members received updates on this vaccine, the CAP study, and options that will form the basis of votes at the group’s June sessions.

As reported in the December 2018 issue of this newsletter, ACIP in 2014 added a single dose of the 13-valent pneumococcal conjugate vaccine (PCV13; Prevnar 13—Pfizer) to its recommended immunization schedule for adults aged 65 years or older. This created the recommendation for two pneumococcal vaccinations, with the 23-valent pneumococcal polysaccharide vaccine (PPSV23; Pneumovax 23—Merck Vaccines) administered second because that timing increases the host response to PCV13. The current discussion focuses on whether PCV13 has shown sufficient effectiveness and safety to merit continuation of that recommendation.
Writing in *Clinical Infectious Diseases*, researchers reported results of the first assessment of real-world VE of PCV13. A test-negative design was used to conduct a case–control study of adults in Louisville, Kentucky, who were hospitalized for CAP and agreed to have their pneumococcal vaccination history confirmed using health insurance records. The study was supported by Pfizer.

In this test-negative study, those hospitalized patients with vaccine-specific serotypes of *S. pneumoniae* served as cases (n = 68). Other hospitalized patients with CAP were controls (n = 1,966). A urine antigen detection assay was used to identify serotypes; blood cultures were used to detect bacteremia (invasive pneumococcal disease, or IPD). Among all 2,034 study participants, 288 had received PCV13 and 432 had received PPSV23. Median age was 76 years (range, 65–102 years), and more than one-third (35.4%) were 80 years or older. All demographic and clinical characteristics were similar between cases and controls except for receipt of PCV13 in the past 5 years (4.4% of cases; 14.5% of controls), risk level (controls had more high-risk and/or immunocompromising conditions), and body mass index category (controls had greater overweight/obesity).

The unadjusted VE against vaccine-type CAP was 72.8% (95% confidence interval, 12.8%–91.5%). Further analysis showed no confounding factors and an adjusted VE range of 71.1% to 73.3%. Against IPD, VE was 70%. The VE figures against vaccine-type CAP are higher than those shown in the pivotal Community-Acquired Pneumonia Immunization Trial in Adults (CAPiTA) randomized trial (46%) and comparable to the VE against IPD (75%) in CAPiTA.

As their names suggest, the two available pneumococcal vaccines differ both in the number of bacterial serotypes they cover and the way they are constructed (and therefore the way they interact with the immune system).

PCV13 induces immunity against serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F, as reported in the January 2016 NAVP Immunizations Newsletter. It is a conjugate vaccine, one in which the antigen is combined with a carrier molecule. By linking pneumococcal polysaccharides to carrier protein CRM197, the vaccine elicits a T-cell–dependent immune response, providing the signal needed for maturation of the B-cell response. This provides protection against meningitis, bacteremia, and lung infections.

PPSV23 works in a complementary way. In addition to the serotypes covered by PCV13, this product adds protection against *S. pneumoniae* serotypes 2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 20, 22F, and 33F but omits serotype 6A. This is a polysaccharide vaccine, which works by presenting large molecules from the organism’s biocapsule directly to B cells, inducing antibody formation without the need for T-cell involvement. Because T cells are not involved in fighting this organism, the effects cannot be boosted by later doses. That is the reason PCV13 is given first—which effects are boosted by the later PPSV23 dose.

A major clinical concern is with serotype 3. Even though it is covered by PCV13, VE is lower for serotype 3 disease in the United States and other countries that use this vaccine. This reduces the clinical benefit of the vaccine impact and lowers cost-effectiveness figures in economic analyses.
To make recommendations for national vaccine schedules, ACIP considers safety and effectiveness first but is also concerned about the impact of decisions on the cost of medical care, health communications, and general understanding and acceptance of its recommendations.

ACIP heard presentations on the above real-world study during the February meeting and also reviewed cost-effectiveness analysis (CEA) for PCV13. Three models for cost-effectiveness of pneumococcal vaccines have been developed; a Pfizer model assumes the highest VE, a Pittsburgh model the lowest, and a CDC model in the middle. The resulting CEA figures are strongly influenced by the VE assumption, with cost per quality-adjusted life–year in the range of $46,000 to $650,000 with the Pfizer model, $112,000 to $2.3 million for the CDC model, and $461,000 to $2.2 million for the Pittsburgh model.

Further complicating the situation is that three investigational pneumococcal vaccines are in development. These include a CRM197 conjugated product, PCV15 (PCV13 with the additional 22F and 33F serotypes), and PCV20 (PCV13 with seven additional serotypes—8, 10A, 11A, 12F, 15B, 22F, and 33F). Clinical trials of these products in adults are expected to be finished in the third quarter of 2020 for PCV15 and late this year or in early 2020 for PCV20.

As with many of ACIP’s decisions, members often factor in the difficulty of communicating decisions to health professionals and the public. In the case of PCV13 for older adults, ACIP will consider these policy options at its next meeting in late June:

- We do not recommend the intervention: PCV13 in series with PPSV23 no longer recommended for immunocompetent adults ≥65 years old.
- We recommend the intervention for individuals based on clinical decision-making: PCV13 in series with PPSV23 would be given to immunocompetent adults ≥65 years based on patient–provider judgment.
- We recommend the intervention: continue PCV13 in series with PPSV23 for immunocompetent adults ≥65 years old.

The wide variability in available data will make this a difficult decision, one that could be influenced by the need for more experience with the vaccine and the prospects of newer vaccines in development that could replace PCV13 in the near future. The discussion so far has been interesting and unpredictable; the June meeting promises more of the same.