IMMUNIZATIONS NEWSLETTER

PROVIDING GSA MEMBERS WITH UPDATES ON ADULT IMMUNIZATIONS

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FEATURES

News

• Why do adult parents get vaccinations for their children but not for themselves? That’s a central question posed in a Kaiser Health News article that addresses concerns about vaccine hesitancy and its possible effects on uptake on the new, highly effective shingles vaccine (zoster vaccine recombinant, adjuvanted; Shingrix—GlaxoSmithKline). The article quotes neurologist Anne Louise Oaklander, MD, PhD, of Massachusetts General Hospital: “What’s remarkable [about the new vaccine] is that the high level of immunity persists even in the very old. It’s pretty hard to get the immune system of older people excited about anything.” In addition to older people, Shingrix is indicated and recommended for adults aged 50 years or older.

• Licensed by the U.S. Food and Drug Administration (FDA) in November 2017, the new hepatitis B vaccine was recommended in February 2018 for inclusion in the adult immunization schedule by the Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control and Prevention (CDC). Heplisav-B (Dynavax Technologies) is a recombinant, adjuvanted vaccine indicated for prevention of all known subtypes of hepatitis B virus in adults 18 years of age or older. The first new vaccine against this pathogen in a quarter century, Heplisav-B has the advantage of being administered in two doses 1 month apart; existing vaccines require three doses over a 6-month period. The CDC generally adopts ACIP recommendations, which should mean an update to the adult immunization schedule during its next revision. While the new vaccine has demonstrated higher efficacy rates than older products, especially in populations with low response figures, ACIP did not express a preference for any specific vaccine product.

Resources

• Plan now for promotional activities during Older Americans Month (May), National Immunization Awareness Month (August), Healthy Aging Month (September), Grandparents Day (September 9), and National Influenza Vaccination Week (December 2–8).
The 2017–18 influenza season holds the dubious distinction of the highest hospitalization rates ever recorded by the CDC for those aged 65 years and older. With new data available such as those described in the main article of this newsletter, it’s the perfect time to consider new messages reinforcing the severity of influenza disease and the benefits of vaccination.

The recent media attention on influenza vaccine has focused on its low efficacy. While efficacy is certainly far from ideal, the reasons are complicated, including the unpredictable nature of influenza disease itself. In briefing calls with media and partners, Dan Jernigan, MD, MPH, a long-time CDC influenza researcher, stated that he is continually humbled by what influenza disease is capable of. It’s a disease worthy of awe and respect.

Kwong and colleagues emphasize this point, publishing data showing the increased risk for myocardial infarction immediately following influenza disease (see "Health Sciences" section of main article). If the risk of influenza itself is not enough to convince patients to vaccinate, perhaps its impact on the risk of other serious health consequences of influenza will sway people. Incorporating messages about the risk of heart attack, stroke, and other thromboembolic conditions will demonstrate concrete benefits of the vaccine in those with doubt about vaccine efficacy.

**IMPROVING INFLUENZA VACCINES: INFORMATION FOR ADVOCATES**

Influenza vaccine has long been the black sheep of the immunization world. It’s not the smallpox vaccine that eradicated the pathogen worldwide. It’s not the polio vaccine that has largely eliminated one of the most dreaded human diseases. It’s not any of several childhood vaccines that are nearly 100% effective in protecting against disease.

This image of influenza vaccine is at least partly—and perhaps mostly—responsible for the lack of progress in getting more people vaccinated each year. Even without the urban myths surrounding flu vaccine, it is admittedly a tough sell to get healthy adults to get a flu shot when its effectiveness is at best 65%—and each season’s formulation never seems to hit even that low target.

Have we hit a wall with influenza vaccine, a shifty pathogen that makes immunization difficult? Recent research says no and reinforces why it’s important not to give up. When planning for the 2018–19 influenza season, here is important information to reinforce with patients and the public.
A potentially promising direction for influenza vaccine research comes from clues that products made using cell cultures or recombinant techniques may avoid problems related to egg-based cultures. As explained in a *New England Journal of Medicine* editorial earlier this year, the viral hemagglutinin (HA) protein is the primary target of neutralizing antibodies during the body’s infection-fighting processes. Because the influenza virus used for producing vaccines acquires amino acid changes (that is, mutations) that facilitate egg production, including some in the HA protein, the vaccine’s effectiveness is thought to be reduced.

During the 2016–17 influenza season, circulating influenza A (H3N2) viruses had HA characteristics that did not match well with one specific egg-culture HA mutation, T160K. Cell-based vaccines for that season also used a seed virus that had undergone egg passage, and as a result, the T160K mutation was present. The immunologic result was that both human and ferret antibodies (which are used in testing) produced by these vaccines did not neutralize circulating viruses. The clinical result was low vaccine effectiveness for egg- and cell-based vaccines, but not those from recombinant DNA baculovirus systems.

During the current influenza season, the same influenza A (H3N2) culture was used for egg-based vaccines, and when this strain turned out to be the predominant one in circulation, this likely contributed to the severe season. Cell-culture vaccines used a seed virus without the T160K mutation, and efficacy results for those and recombinant products could show increased efficacy when product-specific data become available.

The T160K mutation problem will extend into next season, as the A (H3N2) strain is being included in the 2018–19 influenza formulation. Some people are likely to begin asking about which product they are receiving—much as they already do regarding the trivalent versus quadrivalent products, high-dose formulations for older adults, and recombinant products.

The long-term answer to problems associated with seasonal influenza vaccine is a universal vaccine, the editorialists wrote: “Although targeted research to improve current vaccine antigens, platforms, and manufacturing strategies may in the short term lead to enhanced effectiveness of seasonal influenza vaccines, to achieve the ultimate objective of a universal influenza vaccine, a broad range of expertise and substantial resources will be required to fill gaps in our knowledge and develop a transformative approach to influenza-vaccine design.”

Another report in the *New England Journal of Medicine* reinforces just how important it is to prevent influenza and other respiratory illnesses. Confirming results from previous observational studies, a case–control analysis from Ontario that used high-specificity laboratory methods shows a 6-fold increase in the risk of acute myocardial infarction in the 7 days after a positive influenza test, compared with the prior 52 weeks and the subsequent 51 weeks.

Prior research lacked the rigor and methodology of the current study. The investigators linked 19 laboratory databases with the provincial hospitalization data to identify 364 hospitalizations in adults aged 35 years or older occurring 1 year before or 1 year after laboratory testing for respiratory viruses.
While getting vaccinated is a simple and brief medical intervention, the decision leading up to that moment is a complex one. Sandra Crouse Quinn, PhD, of the University of Maryland School of Public Health presented research on this process to the National Vaccine Advisory Committee at its February meeting in Washington, DC.

For influenza, vaccine hesitancy is associated with perceptions of the importance of getting vaccinated, confidence in the vaccine and vaccine process, and convenience (including affordability), Quinn said. According to a national panel survey that explored vaccines and the vaccine process, Americans trust physicians the most, followed by the CDC, FDA, and lastly pharmaceutical companies. Blacks have less trust in these vaccine players than do whites, but in this same order.

Looking further into differences in racial beliefs and associated disparities in vaccination rates, Quinn said that individuals who are conscious of their race in a health care setting, and those who feel that discrimination has affected their care, are more likely to have less trust in the vaccine process. They also have a higher perceived risk of adverse effects to vaccines, less knowledge about these products, greater use of naturalism, belief in conspiracies, and greater vaccine hesitancy.

An important finding in this research is that a significant predictor of influenza immunization for everyone was a perceived moral obligation to other people to get vaccinated. This finding reinforces the value of community- and family-centered vaccine promotion messages, Quinn said. Ideas for applying these findings included the following:

- Work with community organizations and social media to promote vaccination to protect the broader community.
- Talk about getting the vaccine as a means of protecting family members.
- Change social norms by talking about the importance of influenza vaccination with friends and family members.

Outside the “risk interval” of 7 days following a positive test for influenza virus, patients were hospitalized for heart attack at a rate of 3.3 admissions per week. During the risk interval, the rate was 20 admissions per week. This translates into 10.11-fold increased risk for influenza B and 5.17-fold for influenza A.

The study also showed increased risk of hospital admission for acute myocardial infarction in patients with other respiratory infections: 3.51 for respiratory syncytial virus (RSV), 2.77 for viruses other than influenza or RSV, and 3.3 when no virus was identified.

“These results suggest that influenza is illustrative of the role that acute respiratory infections have in precipitating acute myocardial infarction,” the authors concluded. “Our findings, combined with previous evidence that influenza vaccination reduces cardiovascular events and mortality, support international guidelines that advocate for influenza immunization in persons older than 65 years of age to protect against ischemic coronary events.”
As vaccine providers place orders for the 2018–19 influenza season and begin planning promotional campaigns for the fall, considering news, research, and information in the public discourse is a good idea. Articles in the lay media have questioned the need for getting the influenza vaccine and criticized its vaccine effectiveness. Vaccine advocates need to be ready to explain why immunization is important, outline what steps are being taken to make the vaccine better, and use messages that target the perceptions at the heart of vaccine hesitancy for each individual.

A topic with the potential to create confusion and conversation in coming months is the ACIP’s February recommendation to restore the nasally administered live attenuated influenza vaccine (LAIV; FluMist Quadrivalent—AstraZeneca/MedImmune) to its immunization schedule for children aged 2 years or older and adults through age 49 years. The panel expressed a number of concerns about the product but ultimately voted 12–2 in favor of reinstatement. This will generate discussion, as will the fact that the vote came after orders were placed for the Vaccines for Children (VFC) program for this season. While an effort is underway to allow supplemental VFC orders, usage will likely be limited—and therefore extend the time required to generate enough data to know whether the product’s effectiveness problem has been solved.

**SOURCES AND RESOURCES**


