News

• Among fee-for-service Medicare beneficiaries, several demographic and clinical variables are associated with higher use of vaccination benefits, according to a study published in *Vaccine* (2019;37:1194–1201). Shen et al. found these significant associations with seasonal influenza, pneumococcal, and herpes zoster vaccination in 2014 to 2017: black beneficiaries were less likely to receive any of the vaccines compared with white beneficiaries; Native American beneficiaries were most likely to receive pneumococcal vaccine; beneficiaries using preventive services—particularly cardiovascular screening, other vaccinations, and the Medicare Annual Wellness Visit—were more likely to receive all three vaccines; and beneficiaries in rural settings and those who were dually eligible for Medicare and Medicaid were more likely to receive the herpes zoster vaccine.

• Given results of a study showing significant elevations in risk of meningococcal B infections among U.S. college students (*Pediatrics*. 2019;143:e20182130), is it time to reconsider recommendations for the MenB vaccine? MenB vaccines are currently recommended by the Advisory Committee on Immunization Practices (ACIP) for high-risk groups in the appropriate age category (Category A recommendation) and can be considered on an individual basis for other adolescents and young adults (Category B recommendation). Editorialists commenting on the study (*Pediatrics*. 2019;143:e20183372) describe the scope and consequences of six outbreaks in 2014 to 2016 on college campuses and note the large relative risk of serogroup B infections among college versus noncollege students (3.54, 95% CI 2.12–5.41). Given this scenario, the editorialists conclude that ACIP is unlikely to change its current Category B recommendation for all adolescents and young adults, as the increased risk is limited to an identifiable cohort (college students) and the absolute risk of a meningococcal B infection is small (0.17 cases per 100,000 people aged 18–24 years).

Resources

• The Centers for Disease Control and Prevention has released the 2019 immunization schedules for pediatric and adult patients. Changes in the adult schedule include restoration of the intranasal live attenuated influenza vaccine (FluMist Quadrivalent—AstraZeneca) for adults through age 49 years; addition of the 2-dose, single-antigen recombinant hepatitis B vaccine with a novel cytosine-phosphate-guanine 1018 oligodeoxynucleotide adjuvant (Heplisav-B—Dynavax) for prevention of hepatitis B virus infection in adults aged 18 years or older; and addition of homelessness as an indication for routine hepatitis A vaccination with a 2-dose series of single-antigen hepatitis A vaccine (Havrix—GlaxoSmithKline; Vaqta—Merck) or a 3-dose series of combination hepatitis A and B vaccine (Twinrix—GlaxoSmithKline). The presentation and usability of the information is much improved as a result of major changes in the schedules’ format and graphics.
Communicating ever-changing and evolving science can be difficult for providers who interact with patients and make recommendations for vaccination each day. The public places responsibility on providers to communicate the science, asking them to strike a balance between giving a confident recommendation and being absolute. And yet most scientists are never trained in communication. One group of scientists has proposed ideas for undergraduate and graduate faculty seeking to fill this need by incorporating more communication content throughout their curricula:

- Teach communication in the context of basic science.
- Recognize that practice doesn’t make perfect, but it does improve skills.
- Encourage real-world application of coursework to boost student motivation.
- Expand training to include oral communication.

The need to better communicate science with a lay audience is real in patient care settings as well as in the media. Academic communities have a concrete opportunity to contribute to this effort through better training of health sciences students and practicing health professionals.

IT'S COMPLICATED: INTERACTIONS BETWEEN PEOPLE AND INFLUENZA VACCINE

Until the day comes when the perfect influenza vaccine is produced, microbiologists, immunologists, and vaccine developers will continue trying to ferret out the complexities of protecting people from this sometimes deadly disease. Two recent lines of research are yielding fruit and helping to clarify some promising approaches in producing better immunologic protection against influenza: immunologic imprinting and vaccine priming.

Results of these studies call into question several common assumptions. When a vaccinated individual comes down with the flu, the problem may lie with the person, not the vaccine as it is usually assumed. Similarly, while immunosenescence is real, older age is actually protective against some viral strains. And the continued use of eggs in manufacturing influenza vaccine is causing real problems in the clinical setting, but other factors also contribute to poor vaccine responses.
The National Institute of Allergy and Infectious Diseases (NIAID) is in the final stages of awarding a $5 million grant to fund a study of the "Impact of Initial Influenza Exposure on Immunity in Infants." When its results are known 7 years from now, the longitudinal registry could help transform what has been a conundrum—immunologic imprinting, also known as the "original antigenic sin"—into better vaccine design for people across the lifespan.

Since the days of the Spanish H1N1 influenza pandemic 100 years ago, researchers have noticed unusual patterns of age-related susceptibility to influenza viruses. Instead of the expected J- or U-shaped mortality curves showing susceptibility at the extremes of the age range, some pandemics have had patterns that look like W’s or inverted U’s. It turns out that people with prior exposure to similar strains many years earlier were not as susceptible to the pandemic virus as those in other age cohorts, both younger and older. The person’s first influenza virus exposure was critical in determining later vaccine responses.

This "imprinting" helps produce stronger vaccine responses to similar antigens, especially to strains of the influenza A virus that were similar to the first one. Similarly, influenza A antigens that are different from the initially imprinted ones produce poorer antibody responses. Studies by Danuta M. Skowronski of the British Columbia Centre for Disease Control and others have shown that the initial vaccine response, even in older adults, is more important than any waning effects during the influenza season.

The NIAID study will seek to determine whether vaccines can have the same imprinting effect as does natural infection. If so, vaccines might be designed that would imprint infants for all major influenza A types—giving them the capability of mounting strong responses to all types throughout life.

Liu et al., looking at individual antibody profiles of more than 300 young and middle-aged adults over the 2010–11 through 2015–16 seasons, identified vaccine-response factors associated with immunologic imprinting and use of eggs or cell cultures in manufacturing.

The three age-specific priming patterns were based on a person’s likely initial exposure to influenza A(H1N1): a 1977 virus from the Soviet Union, the 1986 Taiwan strain, or the 1999 New Caledonia strain. Vaccine responses correlated with whether strains had a specific mutation in the hemagglutinin protein (amino acid substitution from lysine to glutamine at position 163). This position is in the antigenic site of the protein—the region that the complementary antibody would recognize.

The egg-production problem was related to a mutation at position 223 on the hemagglutinin protein in viruses grown in eggs. Presence of this mutation was associated with low vaccine responses to the pandemic A(H1N1)pdm09 component of influenza vaccine used during those seasons.
Some advantages of cell culture in vaccine production were further demonstrated in another study, one of older adults, but other factors also seemed to be involved with responses. Similar advantages accrue from use of recombinant influenza vaccines over egg-based products.

Izurieta et al. analyzed Medicare records for the 2017–18 influenza season and found a significant but modest difference in vaccine effectiveness (VE) between vaccines produced in eggs versus cell cultures. Based on VE for avoiding influenza-related hospital encounters, cell-cultured quadrivalent vaccine and high-dose trivalent egg-produced vaccine were significantly more effective than egg-based adjuvanted and egg-based standard-dose trivalent products.

The difference in relative VE was approximately 10% in these comparisons, leading the authors to conclude, “The modest VE difference between cell-cultured and egg-based vaccines only partially explains the low overall VE reported by the Centers for Disease Control and Prevention, suggesting that egg adaptation was not the main contributor to the low VE found among individuals aged ≥65 years.”

So which is more important—immunologic imprinting and other factors that affect a person’s response to influenza vaccine or the specifics of product preparation?

In a 2008 article, Skowronski et al. sided with the person’s immunologic history and called for reconsideration of the idea that antibody levels decline rapidly in older adults during the influenza season. Combining data from 8 studies of older adults, the investigators showed that when antibody levels were high enough after vaccination, seroprotection rates were 70% to 100% “not just at 4 months (2 studies) but also at 5 months (2 studies) and even at >6 months (4 studies), for the H3N2 and H1N1 vaccine components.”

In conveying these concepts to patients, the facts can be boiled down to core messages about influenza vaccine:

• You’re better off vaccinated than not, regardless of the specifics of the vaccines and the season.
• You should get vaccinated at the first opportunity. The virus can start circulating early, and your protection is very likely to last throughout the season.
• Even if you’re vaccinated, be sure to avoid illness through healthy habits: cough or sneeze into your elbow area; wash your hands frequently; avoid others who are ill whenever possible; stay home when you’re sick; avoid touching your eyes, nose, or mouth; and practice other good health habits regarding sleep, physical activity, stress, fluids, and nutrition.
• Older adults should receive high-dose influenza vaccine or either cell culture–based or recombinant vaccine, when available. While the ACIP has not expressed a preference based on its population view, the individual practitioner has a wealth of data to rely on when choosing these more effective products for use in patients aged 65 years or older.
The NAVP Immunizations Newsletter is produced monthly by The Gerontological Society of America and is supported in part by Merck and Pfizer. Copyright © 2019 by The Gerontological Society of America. All rights reserved.

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