IMMUNIZATIONS NEWSLETTER

PROVIDING GSA MEMBERS WITH UPDATES ON ADULT IMMUNIZATIONS

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FEATURES

News

• Influenza vaccination and early antiviral therapy are important interventions in patients with transplants, according to a study of 616 participants with confirmed influenza infections published in Clinical Infectious Diseases and an accompanying editorial. The multicountry study included recipients of solid organ grafts and hematopoietic stem cells over a 5-year period. Participants vaccinated during the current influenza season had less severe disease based on presence of pneumonia, and those receiving early antiretroviral therapy had improved outcomes.

Resources

• New resources on influenza immunizations for those with chronic illness are available from the National Foundation for Infectious Diseases. The online toolkit is designed to increase awareness of the dangers of influenza in this population. It offers a video, infographics, a “call to action” report, and fact sheets for health care professionals and consumers as well as continuing education programs for health professionals.

• In GSA's Journal of Gerontology Series A, the December 2018 Translational Section features three articles on influenza and vaccination. Topics include the value of flu vaccines beyond influenza prevention, influenza illness and hip fracture hospitalizations in nursing home residents, and age-related respiratory epithelial responses to influenza infection.

COMMUNICATIONS

Communicating about vaccines, especially with patients who are deeply hesitant about vaccinations, often requires understanding of highly technical processes and distilling it into comprehensible (and brief!) explanations for patients. In 2019, you’ll see the NAVP Immunizations Newsletter tackle some of those technical processes in order to better explain the background and reasons for vaccination to patients. In this first edition, we cover understanding the science used to develop vaccines, balancing safety profiles and effectiveness, and recognizing that some vaccines have room for improvement. Ultimately, vaccines remain the best way to protect against these diseases, and your strong recommendation, with more explanation if necessary, is the best predictor of patients receiving them.
VACCINES: MODULATING MICROBE/IMMUNE CELL INTERACTIONS

Similar to landmark events in the history of microbiology that led to development of rabies vaccine and diphtheria antitoxin in the 19th century, paradigm-shifting discoveries are changing the face of vaccinology in the new millennium. While vaccines have always required empiric evidence of safety and effectiveness—“show me the data in humans” remains the mantra—new vaccines now can be much more directed and incorporate new evidence.

The developments rely on today’s advanced microbial and immunologic methods, high-throughput “omics,” recombinant technologies, availability of computers powerful enough to analyze large datasets, and new manufacturing processes. Medical researchers are using these tools to make new scientific discoveries about the pathogenic mechanisms of disease and protective immune mechanisms. Yet, they are reminded by challenging influenza seasons and baffling diseases such as acute flaccid myelitis just how much we do not understand and cannot predict about viruses and other pathogens and their effects on the human body. With this dichotomy in mind, the first two 2019 issues of the NAVP Immunizations Newsletter will provide overviews of vaccinology (this month) and the vaccine industry (in February).

BIOLOGICAL SCIENCES

The development of some early vaccines preceded scientific discoveries establishing the role of microorganisms as causative agents in some diseases. Many of these were viruses, and a full century would pass after Jenner’s use of cowpox as a vaccine against smallpox (1795) before the term “virus” was used to describe a “filterable agent” associated with tobacco mosaic disease. Even then, another 20 years would go by before virology became a recognized field.

Several basic methods were used to make vaccines during most of the 20th century. Most of the successful vaccines used inoculation of people with attenuated microbial strains: polio (Sabin), measles, mumps, rubella, varicella, zoster vaccine live (Merck), rotavirus, and the original rabies vaccine. Attenuation occurs by multiple passages of a virus in a nonhuman host taking advantage of Darwinian genetics to select mutants that have a growth advantage in the new species and a disadvantage in humans. By the 1950s, scientists showed that cell cultures could be used for growing polioviruses, creating a much better and consistent method for maintenance of organisms used in vaccine production.

Another approach—“an empiric ‘isolate–inactivate–inject’ paradigm,” Poland and colleagues wrote last year in a Vaccine review—produced tetanus, diphtheria, and pertussis vaccines. This technology became somewhat more sophisticated as investigators learned more about pathogenic factors of bacteria and protective mechanisms in the human immune response. Hence, the bacterial polysaccharide replaced the whole organism in the pneumococcal vaccine, and inactivated pertussis toxin in the acellular pertussis vaccine began to replace the earlier whole-cell pertussis vaccine. In some cases, though, the technology traded better safety profiles for decreased effectiveness.

HEALTH SCIENCES

Adjuvants were recognized as important components early in vaccine development, but how aluminum salts and other agents worked was poorly understood. As recombinant products came onto the market starting in the 1980s, these adjuvants became much more important in maximizing the immune response to antigens. At the same time, advances in knowledge of the immune system were shedding light on how the host’s T and B cells interacted with vaccine antigens.
Today, products such as the new shingles vaccine (herpes zoster subunit vaccine from GlaxoSmithKline) and cell-culture vaccines against influenza and other pathogens have resulted from advances in vaccinology. “The new fields of vaccinomics and adversomics provide models that permit global profiling of the innate, humoral, and cellular immune responses integrated at a systems biology level,” the Vaccine article explains. Such advances promise a world with a more personalized approach to vaccines. As Poland told the National Vaccine Advisory Committee in a February 2017 presentation and explained in the April 2017 issue of this newsletter, the new vaccine model will be “discover → validate → characterize → apply.” Systems-level analyses will enable better understanding of immune responses across age, sex, race, and comorbidities, and gene signatures will be used for monitoring vaccines in clinical trials. Adversomic data can reveal genetic drivers of aberrant immune, autoimmune, or nonimmune responses to a vaccine.

It may take 20 years—or more—to work out the details, but the result of this research will be safer and more effective vaccines. That is key. Despite the noise created by small groups of parents concerned about childhood vaccines, the fact is an overwhelming majority of children are fully vaccinated. Why? Because the vaccines are highly effective and very safe. Similarly, the demand for the new shingles product shows that older adults will seek out and take vaccines with effectiveness rates exceeding 90% against a disease they want to avoid. Despite these notable successes and advances in decreasing disease with vaccines against conditions such as pertussis, influenza, and varicella, there remains room to improve vaccine effectiveness. For flu vaccine in particular, elicitation of a robust immune response to a new vaccine to confer protection against all influenza A viruses (a “universal vaccine”) would be an enormous advance.

The need for vaccine advocates to promote the advantages of vaccines and to identify and counter misinformation is perhaps greater today than ever. Social media and other digital innovations have enabled geographically dispersed individuals to connect with others who have concerns about vaccines and to amplify myths and personal experiences and beliefs. Such “n of 1” connections can be strong in people’s minds despite availability of well-conducted trials that disprove links between vaccines and adverse outcomes such as deaths, cancer, immune disorders, and autism and other developmental disorders.

Given all that is known about the benefits of vaccinations, public health practices and governmental policies are often built on broad immunization of at-risk populations. When vaccine hesitancy or refusal reduces immunization rates, more people get sick, some unnecessarily die or have life-changing sequelae, and health care costs rise. In pandemics or when large populations are threatened by conditions such as bird flu or severe acute respiratory syndrome, restrictions on travel or destruction of livestock can produce real economic damages to people, companies, and countries. Situations such as the influenza pandemic following World War I can even contribute to societal unrest and changes in and among nations.
The care with which the World Health Organization and national organizations such as the Centers for Disease Control and Prevention approach decisions about vaccines is evident given the balance needed in such a high-stakes situation. The science, the costs of action versus no action, the effects of a vaccine on people’s health, and even the difficulty of communicating the decision or applying a recommendation in practice—all must be considered in coming to the best possible decision. It is not an easy or smooth process, and someone is bound to be upset.

More may be known today about disease, pathogens, immunology, and the vaccines, but a difficult decision must be made based on incomplete and sometimes imperfect information. Yet, one truism has not changed: public health officials and decision makers must recommend an optimal course of action based on the best available evidence. This remains the most important task of those in the vaccination community, whether yesterday, today, or tomorrow.

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**SOURCES AND RESOURCES**


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