• Recent articles make it clear that the varicella zoster virus (VZV) is not the “generally nonthreatening virus” that many think it is. In the June 15 issue of The Journal of Infectious Diseases, a study demonstrates the association between VZV infection and giant cell arteritis in the aorta—the latter being a reactivation of latent virus as is classic herpes zoster, but without the characteristic skin rash and pain (2016;213:1866–71). There may be manifestations of gastrointestinal infections as well. This makes VZV infection even more serious than previously thought and the case for the shingles vaccine even stronger (2016;213:1859–61).

• November is National Diabetes Month and National COPD Awareness Month. Being fully vaccinated is especially important for people with diabetes and lung diseases such as chronic obstructive pulmonary disease (COPD). Talk to patients, colleagues, and friends with these conditions about staying up to date on their vaccinations.

INFLUENZA ANTIGENIC DRIFT: NEW CAPABILITIES FOR EARLY IDENTIFICATION, INTERVENTION

Many different factors affect whether a person develops influenza, including that individual’s natural or acquired immunity, the viral strains in circulation, and even travel patterns and other considerations about those in the community. But all of these variables get reduced to a couple of observations by most people: “I haven’t had the flu vaccine for 3 years and I didn’t get sick,” or “I had the flu last year even though I got the vaccine.” Countering such oversimplifications through one-on-one recommendations and public health promotions is difficult. One thing is for sure though: If we could find better predictive approaches to influenza vaccination and better explanations of why it works sometimes and not others, then people could talk about facts rather than perceptions.
A research article and accompanying editorial published last month in *The Journal of Infectious Diseases* show how science can help in the ongoing effort to make more accurate predictions about the clinical impact of antigenic drift and produce better vaccines and faster responses when something in the virus begins changing.

Seeking to explain what happened during the problematic 2014–15 U.S. influenza season, researchers turned to newly expanded genetic tools.

During that season, antigenic drift resulted in a “mismatch” between a large proportion of the circulating influenza viruses and the antigens in the vaccine. Influenza viruses have a gene for the protein hemagglutinin (HA). Its function is to facilitate entry of the virus into the host cell, and the current vaccination strategy is to stimulate host antibodies that bind to HA and thereby stop entry of the influenza virus.

A change in just one base pair in the HA gene can result in a different amino acid at important places in the protein structure. If that change affects the binding affinity of the vaccine-stimulated antibodies, then the vaccine effectiveness (VE) is reduced and illness can result.

Researchers from the Centers for Disease Control and Prevention (CDC) have now used a new tool—pyrosequencing assay with high throughput—to genetically characterize circulating influenza strains. Among 1,397 viruses in the type A(H3N2) category, 1,134 (81%) had an amino acid change at position 159 (phenylalanine replaced by tyrosine) that was associated with lack of protection by the seasonal vaccine.

Other circulating strains had amino acid changes caused by mutations in the HA gene that were associated with lack of VE, but these affected smaller numbers of patients. By sequencing thousands of clinical isolates using this assay, CDC researchers were able to put together a phylogenetic tree showing how dozens of influenza strains varied at the base pair level and what impact the resulting amino acid changes had on effectiveness of that season’s vaccine (Figure 1).
Clinicians remember the 2014–15 influenza season for the early and widespread impact of the antigenically drifted strains. By December, cases of infection caused by the most common mismatched A/H3N2 strain were the cause of about half of the illness among Americans. This illness, however, was not evenly spread across the country. As shown by the pie charts in Figure 2, strains isolated from various states and localities differed greatly in terms of their phylogenetic categorizations. For instance, Pennsylvania is one of five locations in the U.S. Influenza Vaccine Effectiveness Network (see the upper map in Figure 2); the prevalence of the drifted category 3C.2a was much lower in Pennsylvania than at the other four sites. Data on influenza strains from public health laboratories show state-to-state variations (lower map in Figure 2).

**HEALTH SCIENCES**

Combined with the new ideas presented in the October issue of this newsletter, this type of data could enable public health authorities, pharmaceutical manufacturers, and clinicians to make timely responses to antigenic drift in circulating influenza strains, including the following:

- The seasonal vaccine could be changed if the new strain is circulating late in the prior season, or an additional monovalent vaccine—one against the drifted strain—could be manufactured and distributed if the situation is obvious by June.
- Given their important role in transmission of influenza, schoolchildren might be the best target group for reducing local antigenic drift and stopping spread to young siblings and older grandparents.
- Antiviral medications could be used more aggressively in locations known to be affected by low VE.

Such strategies would be new to Americans, and effective public health mechanisms would be required to educate people to the problems and the solutions developed by CDC and others.

**FIGURE 2.** Geographic distribution of genetic groups of influenza A(H3N2) viruses in the United States and from patients enrolled in the U.S. Influenza Vaccine Effectiveness Network study.

A. Viruses from influenza A(H3N2) virus–positive patients enrolled from November 10, 2014, through April 10, 2015 (n = 1,397). Pie charts present the proportional distribution of hemagglutinin (HA) genetic group, based on the number of genetically characterized influenza A(H3N2) viruses from patients enrolled at each study site.

B. Viruses identified by U.S. public health laboratories from November 10, 2014, through April 10, 2015, and submitted to the Centers for Disease Control and Prevention for genetic characterization (n = 1,633). Pie charts present the proportional distribution of HA genetic group, based on the number of genetically characterized influenza A(H3N2) viruses from each state or territory.

Source: *J Infect Dis*. 2016;214:1010–9. Figure is in the public domain in the United States.
Communications and health promotions will be key activities when increased and timelier responses to antigenic drift are possible. Health professionals and their patients would need information on which to base decisions about individual vaccines.

As noted by the authors of the editorial in *The Journal of Infectious Diseases*, “Continuous large-scale monitoring of genetic variability of circulating influenza viruses may provide us with insights on how antigenic drift is affected by environmental and social factors, such as population density, number of school holidays, intercommunal and intracommunal mobility, and vaccine uptake, and allow us to influence antigenic drift by measures taken at the community level.”

**SOURCES AND RESOURCES**