NEWS

• Influenza activity at the national level often gets the most media coverage and attention, but state-level data often show wide divergences. As illustrated in two recent articles in *Morbidity and Mortality Weekly Report*, such geographic data are often more relevant to practitioners and public health planners. In Utah, the severity of the 2017–18 influenza season prompted a field investigation involving two large health care systems in the state [2019;68(50):1158–1161]. National data were applied to estimate how many Utah residents had tested positive for influenza, been hospitalized, or died from influenza infections. The estimates were then confirmed using local data that provided information and useful statistics for health professionals, planners, media, and health promotions. Separately, a report creating alarm about the current influenza comes from Louisiana [2020;69(2):40–43]. A highly pathogenic subclade of the influenza B/Victoria virus identified in the Bayou State has been associated hospitalizations of children and one pediatric death.

• During the *severe 2017–18 season*, influenza vaccine, while not well matched with circulating strains, nevertheless “reduced a substantial burden of influenza-associated illness, medical visits, hospitalizations, and deaths” [*Clin Infect Dis.* 2019;69(11):1845–1853]. Authors of this U.S. research study wrote, “When modeled with burden and vaccine coverage, we estimated that influenza vaccination prevented 7.1 million illnesses, 109,000 hospitalizations, and 8,000 deaths related to influenza.”

RESOURCES

• *The Antigen*, a new Pfizer podcast, is an 8-part, audio-documentary style resource covering the *scientific, cultural, and social elements of vaccination*. The host is Yasmeen Agosti, MD, a pediatrician who is Pfizer’s Global Medical Lead for Viral Vaccines. She interviews leading vaccine researchers, public health experts, global advocates, journalists, and people who have been personally impacted by vaccine-preventable diseases for the podcasts. Episodes posted thus far discuss Vaccines 101; The History of Vaccines; and Global Perspectives, Barriers, and Solutions.
“She doesn’t feel well today. I’m sure it’s the flu.”

It’s winter, and the influenza virus is spreading widely. The presumption would be that when older adults present with flu-like symptoms, influenza is the cause. But if they test negative, what other conditions might this be? For many patients, the cause of symptoms that can be just as severe as influenza is respiratory syncytial virus (RSV). Developing a vaccine for this potentially lethal pathogen has vexed researchers and companies for decades. And while RSV infections are not readily diagnosed, no treatment is available for older adults, and these infections can be severe and even fatal.

Progress in vaccinology and manufacturing techniques has renewed interest in prevention of RSV infections. Let’s take a look at the need for and status of RSV vaccines.

**IMPORTANCE OF RECOGNIZING RSV**

RSV is a well-recognized pathogen in pediatrics, but these infections in adults can be confusing. Clinically, the symptoms of RSV are very similar to those of influenza. The scenario is further complicated by lack of an inexpensive, widely available clinical test for RSV. When samples are tested, numerous assays are emerging, and these vary from simple cultures to RNA-based and polymerase chain reaction–based tests. These new diagnostic tests and a reorganization of diagnostic codes could feasibly give clinicians a better picture of the incidence of RSV and better differentiation from influenza virus and other respiratory pathogens.

Despite the confusion, RSV is a virus that can cause serious illness as people age. When RSV is confined to the upper respiratory tract, symptoms are usually mild. If it reaches the lower respiratory tract in conditions such as tracheobronchitis, bronchitis, or hospital- or community-acquired pneumonia, patients often require hospitalization and secondary bacterial infections are common. Death can result.

In skilled nursing facilities, RSV attack rates reported in 2005 were 5% to 10% per year with significant rates of pneumonia (10%–20%) and death (2%–5%). The highest risk of severe RSV disease is among those with underlying medical conditions such as chronic obstructive pulmonary disease, functional impairment, and low neutralizing antibody titers.

**DEVELOPING EFFECTIVE, SAFE RSV VACCINES**

A member of the Paramyxoviridae family, RSV is a single-strand, reverse-sense RNA virus (Figure 1). Two of its transmembrane surface proteins, denoted F and G, are the targets of many of the vaccines developed to date. Following deaths of two children who received a formalin-inactivated RSV vaccine developed in the early 1960s, interest lagged in developing candidate products for this virus.

As the morbidity and mortality of RSV in infants, young children, and older adults became better understood and new types of vaccines emerged, researchers turned again to developing a product to protect against RSV. As shown in Figure 2, several companies and organizations are actively researching the clinical utility of vaccines of various types. The only product that has reached phase 3 of testing is being developed by Novavax; to date, results in these large clinical trials have been disappointing.
As the U.S. Food and Drug Administration (FDA) receives applications for RSV vaccines, the agency is expediting their review. A live attenuated RSV vaccine, MV-012-968 (Meissa Vaccines), is in phase 1 testing; it was recently granted fast-track designation by FDA. A Janssen RSV vaccine that uses the company’s adenovector platform was granted breakthrough therapy designation in late 2019; it is listed as phase 2 on the PATH chart in Figure 2.

Even as an effective RSV vaccine has proven difficult to develop, progress has been made in monoclonal antibody and antiviral therapy in patients with RSV infections. Approved in 1998 for prophylaxis (not treatment) in high-risk infants, palivizumab is a humanized mouse monoclonal antibody to the F protein of RSV. The agent has been used in immunocompromised patients as a single agent or in combination with ribavirin and/or steroids. Other treatments in development include presatovir, an oral entry inhibitor being tested in infants; ALS-008176, a nucleoside analogue; and ALX-0171, a nanobody therapy for blocking RSV fusion to cells that is being tested in infants.

Ribavirin is the only approved antiviral agent indicated for use in infants, young children, and special populations with RSV. Use in other adults, including those of advanced age, is unstudied.

With the amount of research devoted to RSV and protective treatments, prospects for finding an effective and safe approach should be increasing. However, clinicians caring for infants and older adults remember being disappointed over the decades with promises regarding this vexing pathogen. Until better tests, vaccines, and treatments are available, those caring for older adults will need to beware that everything that looks like the “flu” is not influenza and oftentimes, RSV will be prominent in the differential diagnosis.

<table>
<thead>
<tr>
<th>VACCINE TYPE</th>
<th>PRECLINICAL</th>
<th>PHASE 1</th>
<th>PHASE 2</th>
<th>PHASE 3</th>
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<tr>
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</tbody>
</table>

**FIGURE 2.** Number of investigational RSV vaccines and monoclonal antibodies by stage of development. Integers in green indicate one or more products under study for use in older adults.

SOURCES AND RESOURCES