Testimony before the Committee on Energy and Commerce Subcommittee on Oversight and Investigations United States House of Representatives

U.S. Public Health Preparedness for Seasonal Influenza: Has the Response Improved?

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For Release upon Delivery
Thursday, November 19, 2015
Expected at 10:00 a.m.

Introduction

Good morning Chairman Murphy, Ranking Member DeGette, and Members of the Subcommittee. I am Dr. Anne Schuchat, Principal Deputy Director of the Centers for Disease Control and Prevention (CDC). We thank the Committee for its continued interest in seasonal influenza. Seasonal influenza is a serious public health problem. As I discussed with you last February, the 2014-2015 season underscored that this respiratory illness should not be characterized as "just the flu." Our concerns about seasonal and pandemic influenza keep many of us in public health awake at night as time and again, this virus is a worthy adversary to our best science. I look forward to discussing with you today ways in which we are working with our partners to continue to improve influenza prevention and control.

Influenza is unpredictable because flu viruses are constantly changing. Each flu season, different flu viruses can spread, and can affect people differently based on their individual immune systems. We cannot say in advance of a season how severe it will be, which viruses will predominate, or who will be most affected. Between five percent and 20 percent of Americans are sickened by the virus annually – hundreds of thousands of those who fall ill with the disease end up hospitalized and thousands or tens of thousands die from influenza-related illness.[1] Looking at three decades of data from 1976 to 2007, we estimate that flu deaths in the United States during any one season have ranged from about 3,000 to 50,000 Americans[2]. Direct medical costs for influenza are estimated to exceed $10 billion each year in the U.S., with more than $80 billion indirect costs[3].

Despite everything that we cannot predict about influenza viruses, the single best thing you can do to protect yourself and your family from influenza is to get vaccinated. For the last decade, CDC has supported studies to determine the effectiveness of flu vaccines. Results have shown that the effectiveness of the vaccine varies. When most circulating flu viruses are similar to the viruses used to develop vaccine, vaccination can

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[1] Influenza-Associated Hospitalizations in the United States 1979 Through the 2000-2001 Respiratory Seasons ." *Journal of American Medical Association's* September 14, 2004 issue (volume 292, no. 11).
[2] Estimates of deaths associated with seasonal influenza—United States, 1976–2007. MMWR Morbidity Mortality Weekly Report 2010;59(33):1057–62
[3] Molinari NA, Ortega-Sanchez IR, Messonnier ML, Thompson WW, Wortley PM, Weintraub E, Bridges CB. The annual impact of seasonal influenza in the US: measuring disease burden and costs. Vaccine. 2007 Jun 28;25(27):5086-96

reduce the risk of flu illness by 50 percent to 60 percent. But vaccine effectiveness can be lower in certain people, or against viruses that have changed, or "drifted" from the vaccine viruses used to develop vaccine as we saw last season with H3N2 viruses, which had become significantly different or "drifted from" the H3N2 virus used to develop vaccine. While these studies show the need for continued progress toward making better flu vaccines, they also help us to see the impact that vaccines have each year. Studies show flu vaccine helps prevent illnesses. It helps prevents medical visits for flu-related illness. It helps prevents hospitalizations. It helps protect a pregnant woman from influenza. Flu vaccine is a valuable public health tool, yet only about half of Americans get vaccinated each year.

While flu vaccine is the best way to prevent influenza illness and protect against its potentially deadly consequences, if a person becomes sick with flu antiviral flu drugs are a treatment option. Since 1999 a large and growing body of observational data, including in hospitalized patients, shows there are benefits to using antiviral drugs beyond the treatment of uncomplicated illness. In medical practice, these drugs have been documented to reduce serious flu complications. In 2008, CDC began recommending these drugs for early treatment of severely ill and high risk patients based on that data. During and after the 2009 H1N1 pandemic, clinical studies in medical practices continued to show that people very ill with flu who got antiviral drugs fared better than those who did not; sometimes these drugs were associated with preventing severe illness and death. For that reason, CDC continues to recommend that the neuraminidase inhibitor influenza antiviral drugs be used for early treatment of people who are very sick with influenza or of people who are sick who are at high risk of serious influenza-associated complications. Most previously healthy people will recover from flu without treatment.

CDC's recommendations for using influenza antiviral medications aim to protect the people who are most vulnerable to serious complications from flu. The recommendations for antiviral drugs are based on data from randomized clinical trials as well as from observational studies of patients receiving treatment in medical

practice. CDC recognizes that currently recommended influenza antiviral drugs have limitations; however, these drugs are the only influenza-specific therapy approved by FDA with activity against circulating influenza viruses.

Influenza viruses are constantly changing; therefore, unlike other vaccines, annual immunization with seasonal influenza vaccine is recommended. There are two types of changes we continually monitor for in influenza viruses. "Antigenic shift" Is an abrupt, major change in influenza A viruses, resulting in a new influenza A subtype that is so different from circulating human flu viruses that most people do not have immunity to the new (e.g. novel) virus. "Antigenic drift" refers to small changes in the genes of influenza viruses that happen continually as the viruses spread and infect people. These small genetic changes can accumulate over time. This results in the emergence of viruses that are sufficiently different antigenically from previously circulating viruses. When this happens, the body's immune system may not recognize those viruses. Because of antigenic drift, twice a year the World Health Organization (WHO) convenes a consultation with the Directors of WHO Collaborating Centers and representatives of key national laboratories. They review the results of surveillance, laboratory and clinical studies, and the availability of vaccine viruses, and make recommendations on the composition of the influenza vaccine. These meetings take place in February for selection of the upcoming Northern Hemisphere's seasonal influenza vaccine and in September for the Southern Hemisphere's vaccine. WHO recommends specific vaccine viruses for inclusion in influenza vaccines, but then each individual country makes their own decision about which viruses should be included in influenza vaccines licensed in their country. In the United States, the Food and Drug Administration (FDA) makes the final decision about vaccine viruses for influenza vaccines sold in the United States.

2014-2015 and 2015-16 Influenza Seasons

H3N2 viruses were the most predominant by far last season. In the past, H3N2 seasons have been associated with more illnesses and deaths in certain populations in relation to H1N1-predominant seasons. The

2014-2015 season was severe for the elderly in particular. We saw the highest hospitalization rates ever documented since this type of record-keeping began (in 2005-06) among people 65 and older, while hospitalization rates in other age groups were within the range seen in other H3N2-dominant years. Exacerbating the situation last season was the fact that most of the H3N2 viruses that circulated in the United States last season had changed, or "drifted," from the viruses which had circulated during the prior season and which had been selected to develop the 2014-15 Northern Hemisphere seasonal flu vaccines. This resulted in reduced vaccine effectiveness against circulating H3N2 viruses last season, which in turn caused greater susceptibility to infection among vaccinated persons, particularly older adults. The drifted H3N2 viruses are difficult to characterize using traditional antigenicity tests and are difficult to grow in eggs. This makes surveillance more difficult, and it also make creating a candidate vaccine virus more difficult. Most of the vaccine supply manufactured for the United States continues to rely on egg-based technology.

Currently, influenza circulation is low, and the 2015-2016 influenza season has not begun. The most recent CDC FluView report indicated that flu activity in the United States remains low. CDC has received reports of early institutional outbreaks of flu. In the United States, flu outbreaks can happen as early as October and can last as late as May. The flu season is said to have begun when certain key flu indicators (for example, levels of influenza-like illness [ILI], hospitalization and deaths) rise and remain elevated for a number of consecutive weeks. Usually ILI increases first, followed by an increase in hospitalizations, which is then followed by increases in flu-associated deaths. We cannot predict exactly when this threshold will be crossed or which viruses will circulate most widely in the coming months; we have seen a predominance of H3N2 viruses in surveillance.

2015-16 Vaccine

While we cannot predict how effective this season's influenza vaccines will be, the composition of this season's vaccine has been updated to better match circulating viruses. Both the influenza A H3N2 and influenza B components in the 2015-16 vaccine were updated from the 2014-15 formulation. While we wait to gather and analyze epidemiologic information and to conduct field studies of vaccine effectiveness, laboratory data can give some indication of how well the vaccine might work. Current global laboratory data indicate that most

circulating influenza viruses are similar to the reference vaccine viruses used for development of the 2015-2016 U.S. vaccines. These data suggest that vaccination with Northern Hemisphere influenza vaccine should offer protection against the majority of circulating viruses. CDC will continue to carefully review results of laboratory studies of currently circulating viruses to look for evidence that viruses are changing. We are committed to ongoing, transparent communication about the characteristics of seasonal influenza viruses and vaccine effectiveness. Our weekly interactive influenza surveillance report appears each Friday on the CDC website (http://www.cdc.gov/flu/weekly/).

Last Spring, manufacturers projected that between 171 million and 179 million doses of flu vaccine would be supplied to the U.S. market this season. While early supply projections can differ from the actual number of vaccine doses distributed at the end of the season, manufacturers report having shipped more than 123.7 million doses of flu vaccine as of October 30, 2015, a figure similar to what had been distributed by this time last season. Some manufacturers have reported shipping delays of certain vaccine formulations; however, overall, we are not aware of vaccine shortage issues at this time.

Next Steps

We appreciate the opportunity to talk with you about how we are working with HHS colleagues to better prevent influenza through more effective vaccines. CDC has a lead role in several improvement initiatives that have been identified within HHS. Particularly, we are working to improve global surveillance and virus characterization to detect emergent viruses more quickly and use this information to inform vaccine virus selection. Globally-coordinated surveillance is the foundation of the influenza vaccine virus development and selection process. It is important to ensure that the best available technologies are being used to analyze influenza viruses and likewise that the best technologies are employed in the production of influenza vaccines. The World Health Organization (WHO) Global Influenza Virus Surveillance and Response System (GISRS) is a global network that provides year-round surveillance of human and animal influenza viruses, makes recommendations on the composition of seasonal influenza vaccines, and provides candidate vaccine viruses for manufacturers to use in the production of seasonal influenza vaccines. GISRS works closely with vaccine

manufacturers through the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) to provide regular updates on virus characterization, including the emergence of drifted virus that may warrant changes in vaccine formulation and the availability of new candidate vaccine viruses. CDC has served as a WHO Collaborating Center (CC) for Surveillance, Epidemiology, and Control of Influenza since 1956. CDC's Influenza Division is currently the largest global resource and reference center supporting public health interventions to control and prevent seasonal and pandemic influenza. CDC is always working to strengthen its ability to conduct epidemiologic and virologic surveillance. We are expanding the use of new technologies - including Advanced Molecular Detection –to better identify and characterize influenza viruses, as well as optimizing antigenic characterization assays. CDC also is in the process of restructuring laboratory processes to first characterize incoming virus samples using high-throughput nucleotide gene sequencing, affording a quicker and more comprehensive picture of circulating viruses and what changes they may have acquired so that we can better foresee newly emerging drifted viruses for vaccine virus development. Over a 10 year period -- in large part due to CDC'S capacity building efforts in low and middle income countries through cooperative agreements bilaterally and with all WHO Regional offices -- we have increased the numbers of countries that submit samples to the GISRS to inform vaccine strain selection process from 66 countries in 2004 to 107 countries submitting into the system in 2014. During this same period, the actual numbers of virus submissions to GISRS has increased from approximately 9,000 to almost 15,000 per year. Despite major advances made by CDC and its partners in building GISRS during the last decade, surveillance gaps remain. Expansion of GISRS through capacity building remains a CDC priority. It is critical for us to continue to support bilateral cooperative agreement partners around the world to maintain and build upon gains in global influenza surveillance and laboratory capacity.

CDC also is working to develop U.S. laboratory networks to generate and share whole influenza virus genome data. In addition, CDC is collaborating with other HHS partners to incorporate technological improvement to enhance and speed vaccine production. The improvements I've just mentioned are ones we're

making right now – we look forward to being part of the push toward the development of a universal influenza vaccine with our colleagues across the department.

Conclusion

Unlike other vaccine preventable pathogens, influenza viruses are constantly changing. The investments made by the U.S. government for the diagnosis, prevention, and control of influenza have led to increased domestic and global viral surveillance, an increase in knowledge about how the flu virus works, more choices of vaccine types, increases in the number of cases averted due to vaccination, expanded recommendations of influenza vaccination to all age groups (above the age of six months) and increased use of influenza vaccine among children and pregnant women. Although many gains in seasonal and pandemic influenza preparedness and control have been made over the years, continued improvements are needed. We will work, along with our government colleagues, academic, and industry partners, to improve use of antiviral treatment, to make more effective influenza vaccines, and to speed production of existing vaccines for all Americans.

Thank you for the opportunity to talk about CDC's role in the 2015-2016 influenza season. I am happy to answer any questions you may have.