KEY POINTS: Potential for Circulation of Drifted Influenza A (H3N2) Viruses and CDC Recommendations for 2014-2015 Influenza Season

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Background

- On December 4, 2014, CDC held a telebriefing highlighting flu activity in the United States so far this season and reviewing the agency's influenza vaccination and treatment recommendations.
- A CDC Health Advisory was distributed via the CDC Health Alert Network on December 3, 2014, and is available at http://emergency.cdc.gov/HAN/han00374.asp.
- Overall, influenza activity remains low, but is beginning to increase in parts of the United States. CDC is getting reports of increased flu illnesses, flu hospitalizations and flu deaths. Five pediatric deaths have been reported this season already.
- Surveillance data indicate that influenza A (H3N2) viruses have predominated so far, with lower levels of detection of influenza B viruses and very few H1N1 viruses detected.
    - Higher influenza-associated hospitalization rates and increased mortality have been observed during seasons when H3N2 viruses have predominated compared with seasons during which H1N1 or influenza B viruses have predominated.
    - H3N2 seasons are especially hard on people who are at high risk of serious flu complications, including older people, very young children, and persons with certain chronic medical conditions.
- Of the H3N2 viruses that have been collected and analyzed in the United States from October 1 through November 22, 2014, about half (52%) are different (or "drifted") from the H3N2 vaccine virus.
    - During the week ending November 22, 1,123 (91.4%) of the 1,228 influenza-positive tests reported to CDC were influenza A viruses and 105 (8.6%) were influenza B viruses.

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- Of the 85 H3N2 viruses collected by U.S. laboratories and antigenically or genetically characterized at CDC since October 1, 2014, 44 (52%) are significantly different (drifted) from A/Texas/50/2012, the U.S. H3N2 vaccine virus.
- Drifted H3N2 viruses were first detected in late March 2014, after World Health Organization (WHO) recommendations for the 2014-2015 Northern Hemisphere influenza vaccine had been made in mid-February. At that time, a very small number of these viruses had been found among the thousands of specimens that had been collected and tested, but these viruses have become more predominant over time.
- Most of the drifted H3N2 viruses are A/Switzerland/9715293/2013 viruses, which is the H3N2 virus selected for the 2015 Southern Hemisphere influenza vaccine. Initially, A/Switzerland viruses appeared only sporadically, but became more common over time.
- Note: A new FluView will be published on Friday, December 5, 2014.

- **Because of the detection of drifted H3N2 viruses, CDC is urging influenza vaccination of unvaccinated patients and reminding clinicians about the importance of the use of neuraminidase inhibitor antiviral medications when indicated for the treatment of influenza illness, as an adjunct to vaccination.**

Recommendations for Health Care Professionals

- Health care professionals should encourage all patients 6 months and older who have not yet received an influenza vaccine this season to be vaccinated against influenza. There are several influenza vaccine options for the 2014-15 influenza season. (See http://www.cdc.gov/flu/protect/vaccine/vaccines.htm)
- Health care professionals should encourage all persons with influenza-like illness who are at high risk for influenza complications (see list below) to seek care promptly to determine if treatment with influenza antiviral medications is warranted. (See http://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm.)
- CDC recommends prompt treatment of high risk or severely ill patients with suspected influenza with flu antiviral medications without waiting for confirmatory testing.

OVERARCHING INFLUENZA MESSAGES

1) CDC CONTINUES TO RECOMMEND A FLU VACCINE AS THE BEST WAY TO PROTECT AGAINST THE FLU

- We cannot know which viruses will circulate over the season.
- Flu vaccination can still reduce flu illnesses, doctors' visits, and missed work and school due to flu, as well as prevent flu-related hospitalizations and deaths.
- The influenza vaccine protects against three or four different influenza viruses, depending on which vaccine you got (trivalent or quadrivalent).

- Antibodies created through vaccination with one influenza virus can sometimes offer protection against drifted influenza viruses (this is called cross-protection).
- While a sub-optimal match can reduce the vaccine's effectiveness, the vaccine can still protect many people and prevent flu-related complications.
- If we have a severe season (with H3N2 viruses predominating) getting a vaccine that provides even partial protection may be more important than ever.

2) EVERYDAY ACTIONS LIKE COVERING YOUR COUGH, STAYING AWAY FROM SICK PEOPLE AND WASHING YOUR HANDS OFTEN CAN HELP PREVENT THE SPREAD OF RESPIRATORY VIRUSES LIKE THE FLU

- Cover your nose and mouth with a tissue when you cough or sneeze—throw the tissue away after you use it.
- Stay away as much as you can from people who are sick.
- If you get the flu, stay home from work or school. If you are sick, do not go near other people so that you don't make them sick too.
- Wash your hands often with soap and water, especially after you cough or sneeze. If you are not near water, use an alcohol-based hand cleaner.
- Try not to touch your eyes, nose, or mouth. Germs often spread this way.

3) ANTIVIRAL MEDICATIONS ARE AN IMPORTANT SECOND LINE OF DEFENSE AGAINST THE FLU AND ARE ESPECIALLY IMPORTANT FOR PEOPLE AT HIGH RISK OF SERIOUS FLU COMPLICATIONS OR PEOPLE WHO ARE VERY SICK

- There are prescription drugs, called "influenza antiviral drugs" that can be used to treat the flu or to prevent infection with flu viruses.
- Treatment with antivirals works best when begun within 48 hours of getting sick, but can still be beneficial when given later in the course of illness.
- Treatment with flu antiviral drugs can make your illness milder and shorter. Treatment with antivirals can also lessen the risk of being hospitalized or dying from flu.
- Antiviral drugs become even more important when circulating flu viruses are very different from the vaccine viruses; which can mean that the vaccine's effectiveness is reduced against those viruses.
- Antiviral drugs are effective across all age and risk groups.
- Prescription antiviral drugs are under-prescribed for high risk people who get flu.
- Treating high risk people or people who are very sick with flu with antiviral drugs is very important. It can mean the difference between having a milder illness instead of very serious illness that could result in a hospital stay.

- Two FDA-approved influenza antiviral agents are recommended for use in the United States during the 2014-2015 influenza season: oseltamivir (Tamiflu®) and zanamivir (Relenza®).
- Visit http://www.cdc.gov/flu/professionals/antivirals/index.htm for information about how antiviral medications can be used to prevent or treat influenza when influenza activity is present in your community.

4) HOW WELL THE FLU VACCINE WORKS CAN VARY

- Vaccine effectiveness (VE) can vary depending on vaccine match and the health and age of the person getting vaccinated.
- If the influenza viruses spreading are very different from the vaccine viruses, the vaccine may not work as well.
- Another factor that influences VE is the age and health of the person being vaccinated.
- This means that VE can vary by season; it can vary based on the virus and it can vary from person to person, depending on how well they respond to vaccination.

5) INFLUENZA VIRUSES ARE ALWAYS CHANGING

- Influenza viruses are constantly changing – they can change from one season to the next or they can even change within the course of the same season. This kind of gradual change is called "antigenic drift."
- Experts must pick which viruses to include in the vaccine many months in advance in order for vaccine to be produced and delivered in time for the upcoming flu season.
- Because of these factors, there is always the possibility of a sub-optimal match between circulating viruses and the viruses in the vaccine.

6) DRIFTED H3N2 VIRUSES APPEARED AFTER IT WAS TOO LATE TO INCLUDE THEM IN THE VACCINE

- In order for any vaccine to be delivered in the fall, the viruses in the vaccine must be chosen in February.
- When the vaccine strains for 2014-2015 were selected, A/Texas/50/2012 was representative of the predominant circulating influenza H3N2 viruses.
- The drifted H3N2 viruses that account for about half of circulating H3N2 viruses now had NOT yet been detected through virologic surveillance.
- Drifted H3N2 viruses were first detected in March 2014, and appeared only sporadically at first.

7) IT'S POSSIBLE THAT PROTECTION AGAINST DRIFTED H3N2 VIRUSES MAY BE REDUCED

- About half of H3N2 viruses collected domestically characterized at CDC since October 1, 2014 are antigenically different from the H3N2 vaccine component.
- They are drifted viruses.

- It's possible that vaccine effectiveness against these drifted viruses may be reduced.
- However seasonal influenza vaccination can sometimes induce antibodies and/or T cells capable of cross-reacting with antigenically distinct viruses.
- Influenza vaccination still offers the best protection we have against seasonal flu.
- In the context of reduced vaccine effectiveness, the use of influenza antiviral drugs as a second line of defense against the flu becomes even more important, especially for high risk people and people who are very sick (hospitalized).

Additional Information

Antiviral Treatment

- Influenza antiviral treatment not a substitute for vaccination; it is an important second line of defense to treat flu illness in the event of infection.
- Evidence from past influenza seasons and the 2009 H1N1 pandemic has shown that treatment with antiviral medications can have clinical and public health benefit in reducing severe outcomes associated with influenza when they are initiated soon after illness onset.
- Antiviral drugs can shorten the duration of fever and illness symptoms; reduce the risk of complications from influenza (e.g., otitis media in young children and pneumonia requiring antibiotics in adults); and reduce the risk of death among hospitalized patients.
- Clinical benefit is greatest when antiviral treatment is administered early. When indicated, antiviral treatment should be started as soon as possible after illness onset, ideally within 48 hours of symptom onset. However, antiviral treatment might still be beneficial in patients with severe, complicated or progressive illness and in hospitalized patients when started after 48 hours of illness onset, as indicated by observational studies.
- Antiviral treatment with oseltamivir or zanamivir is recommended as early as possible for any patient with confirmed or suspected influenza who
    - is hospitalized;
    - has severe, complicated, or progressive illness; or
    - is at high risk for influenza complications. This list includes:
        - children aged younger than 2 years;
        - adults aged 65 years and older;
        - persons with chronic pulmonary (including asthma), cardiovascular (except hypertension alone), renal, hepatic, hematological (including sickle cell disease), and metabolic disorders (including diabetes mellitus), or neurologic and neurodevelopment conditions (including disorders of the brain, spinal cord, peripheral nerve, and muscle such as cerebral palsy, epilepsy [seizure disorders],

stroke, intellectual disability [mental retardation], moderate to severe developmental delay, muscular dystrophy, or spinal cord injury);

- persons with immunosuppression, including that caused by medications or by HIV infection;
- women who are pregnant or postpartum (within 2 weeks after delivery);
- persons aged younger than 19 years who are receiving long-term aspirin therapy;
- American Indians/Alaska Natives;
- persons who are morbidly obese (i.e., body-mass index is equal to or greater than 40); and
- residents of nursing homes and other chronic-care facilities.

- Antiviral treatment also can be considered for any previously healthy, symptomatic outpatient not at high risk with confirmed or suspected influenza on the basis of clinical judgment, if treatment can be initiated within 48 hours of illness onset.
- Treatment of persons with suspected influenza should not wait for laboratory confirmation of influenza.
- When there is clinical suspicion of influenza and antiviral treatment is indicated, antiviral treatment should be started as soon as possible, along with use of appropriate infection control measures.
- Use of antiviral medications for chemoprophylaxis to control outbreaks in institutional settings also is recommended. Chemoprophylaxis may also be considered for all employees, regardless of their influenza vaccination status.
    - For more information on the control of institutional outbreaks, please see CDC's Interim Guidance for Influenza Outbreak Management in Long-Term Care Facilities and the IDSA guidelines web site.
- While influenza vaccination is the first and best way to prevent influenza, a history of influenza vaccination does not rule out the possibility of influenza virus infection in an ill patient with clinical signs and symptoms compatible with influenza.
- Two FDA-approved neuraminidase inhibitor antiviral medications are recommended for use in the United States during the 2014-2015 influenza season: oseltamivir (Tamiflu®) and zanamivir (Relenza®).
- More information about antiviral drugs can be found at http://www.cdc.gov/flu/antivirals/index.htm.
- Antiviral information for health care professionals is available http://www.cdc.gov/flu/professionals/antivirals/index.htm.

Influenza Vaccination

- Flu vaccination continues to offer the best protection against influenza infection.
- How well the flu vaccine works depends in part on the match between vaccine viruses and circulating flu viruses. If the viruses are well-matched, vaccine effectiveness tends to be higher (see Vaccine Effectiveness section below).
- Decreased vaccine efficacy typically occurs during flu seasons when drifted influenza viruses predominate. Therefore, if drifted H3N2 viruses continue to circulate broadly in the United States this season, this could translate into reduced vaccine effectiveness against circulating H3N2 viruses.
- Even when drifted viruses are found to be circulating, CDC continues to recommend influenza vaccination for all people age 6 months and older because:
    - the vaccine can still offer protection against different but related strains of influenza viruses. Studies have shown evidence that seasonal influenza vaccination can sometimes induce antibodies and/or T cells capable of cross-reacting with antigenically distinct viruses. This is called "cross-protection."
    - more than one type or subtype of influenza usually circulates during a single season and flu vaccination offers protection against circulating flu viruses that have not drifted from the vaccine viruses (such as H1N1 and B viruses). Depending on which vaccine is given, vaccines will protect against three or four different influenza viruses.
- **Health care professionals should continue to vaccinate patients who have not yet received influenza vaccine this season.**

Vaccine Effectiveness

- Influenza viruses are constantly changing – they can change from one season to the next or they can even change within the course of the same season. This kind of gradual change is called "antigenic drift."
- It is because of drift that the composition of the flu vaccine is reviewed annually and updated as needed to keep up with circulating viruses.
- Each year experts pick which viruses to include in the vaccine many months in advance (usually February) in order for vaccine to be produced and delivered in time for the upcoming flu season.
- Because flu viruses are constantly changing and it takes a long time to manufacture flu vaccine, there is always the possibility of a sub-optimal match between circulating viruses and the viruses in the vaccine.
    - While a less than optimal virus match can reduce the vaccine's effectiveness, vaccination can still protect enough to make illness milder and prevent flu-related complications.
    - Such protection is possible because antibodies created through vaccination with one strain of influenza viruses will often cross-protect against different influenza viruses.

Conclusions

CDC recommends a three-pronged approach to fighting flu:

1) **influenza vaccination.** The influenza vaccine contains three or four influenza viruses depending on the influenza vaccine—an influenza A (H1N1) virus, an influenza A (H3N2) virus, and one or two influenza B viruses. Therefore, even if vaccine effectiveness is reduced against drifted circulating viruses, the vaccine will protect against non-drifted circulating vaccine viruses. Further, there is evidence to suggest that vaccination may make illness milder and prevent influenza-related complications. Such protection is possible because antibodies created through vaccination with one strain of influenza viruses will often "cross-protect" against different but related strains of influenza viruses;

2) **use of neuraminidase inhibitor medications when indicated for treatment or prevention**. Antiviral treatment with oseltamivir or zanamivir is recommended as early as possible for any patient with confirmed or suspected influenza who: is hospitalized; has severe, complicated, or progressive illness; or is at higher risk for influenza complications. Antiviral chemoprophylaxis should be used for prevention of influenza when indicated for institutional influenza outbreaks, and may be considered for those who have contraindications to influenza vaccination.

3) **use of other preventive health practices that may help decrease the spread of influenza**, including respiratory hygiene, cough etiquette, social distancing (e.g., staying home from work and school when ill, staying away from people who are sick) and hand washing.

For more information, visit www.cdc.gov/flu, or call CDC at
800-CDC-INFO (English and Spanish) or 888-232-6348 (TTY).

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