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Influenza Update
FINAL SCRIPT

I would like to begin the program with an update on influenza. I'll begin with a summary of current influenza activity, then discuss vaccine issues.

Let me first briefly describe the influenza surveillance system in the United States.

CDC uses four systems to monitor influenza activity in the U.S. The first system is a group of about 120 WHO and National Respiratory and Enteric Virus Surveillance Laboratories throughout the country. These laboratories, many of which are in state health departments, help monitor influenza virus activity and the emergence of new influenza strains. These laboratories send information on virus isolates and a subset of the isolates to CDC to be characterized further.

The second system consists of reports from state and territorial epidemiologists who report the level of influenza activity in their area each week. These epidemiologists report the activity level as either sporadic, local, regional, or widespread.

The third system consists of about 1,000 sentinel providers located throughout the United States. These physicians report the percentage of all patient visits for influenza-like illness in their practice.

The fourth system consists of 122 cities that report the percentage of all deaths in their cities attributable to pneumonia or influenza. During severe seasons the percentage of such deaths will exceed the expected baseline or so-called epidemic threshold.

This graph summarizes influenza virus surveillance information collected in the U.S. through January 3, 2004, the most current data that is available (influenza surveillance updates are issued weekly in October through May, and are available on the CDC influenza website). The stacked bars represent the number of viruses which have been isolated by week. The black line represents the percentage of clinical specimens which are testing positive for influenza in the surveillance laboratories.

The 2003-04 season has been dominated by influenza A viruses. The yellow bars indicate the number of influenza A isolates that have not yet been subtyped. The red bars which represent influenza A (H3N2) viruses. Through the week ending January 3, national surveillance laboratories have reported detecting about 16,000 influenza A viruses and 109 B viruses.

The proportion of specimens testing positive for influenza virus peaked at about 40% in week 47, and is now falling.

Although this graph suggests that activity peaked in week 50, in mid-December, there is some lag in reporting. It won't be clear exactly when the peak occurred for a few weeks.

To date, more than 99% of all influenza viruses isolated in the U.S. have been type A viruses.

3,927 A viruses have been subtyped. All were A (H3N2) viruses except one H1N1 virus.

454 of the H3N2 viruses have been further characterized for strain typing. 22% have been Panama-strain viruses and 78% have been Fujian-strain viruses.

As you know, influenza vaccine normally contains three viruses: an influenza A (H3N2) virus, an influenza A (H1N1) virus and a B virus. The H3N2 strain contained in the 2003 vaccine is a Panama virus and not a Fujian virus. There are several important reasons for this situation that I would like to discuss.

The strains used in the U.S. vaccine are usually selected each year between February and March at a meeting held by the Food and Drug Administration. The strains must be chosen by this time each year to provide manufacturers with enough time to produce and distribute vaccine and the Food and Drug Administration with enough time to test lots before they're released.

In 2003 global surveillance detected A/Fujian-like viruses late- in January. Due to the late detection there was not enough time to find a suitable Fujian-like virus that had been passaged and grown completely in eggs. Most surveillance laboratories worldwide now use cell cultures to isolate influenza viruses. However, by law only viruses grown solely in embryonated hens eggs can be used for vaccines. Because the virus emerged so late this year, there was not enough time to identify a suitable Fujian strain, so the decision was made to retain Panama as the H3N2 virus in the vaccine.

The A/Fujian-like viruses represent drift variance or mutated viruses that evolved from the A/Panama viruses. Antibodies to A/Panama viruses will cross react with A/Fujian-like viruses but at lower levels.

Because antibodies to A/Panama cross react with Fujian viruses it is expected that this year's vaccine will provide some degree of protection against A/Fujian viruses. However, cross-reactivity in a laboratory doesn't necessarily correlate with the actual protection provided by the vaccine. Vaccine effectiveness can only be estimated by clinical vaccine effectiveness studies. CDC has performed several vaccine effectiveness studies in the last few weeks, some of which are still in progress.

In December, CDC and the Colorado Department of Public Health and Environment performed a retrospective study of vaccine effectiveness among employees of a hospital in Colorado. The outcome measure was influenza-like illness, defined as fever plus either cough or sore throat.

Using 2 different methods of analysis, the investigators were not able to demonstrate effectiveness against influenza-like illness for this year's vaccine. Keep in mind that influenza-like illness is a broad category of illnesses that includes bad colds and other respiratory illnesses not caused by influenza virus. Influenza vaccine will not protect against these other illnesses, many of which cause "flu-like" symptoms. So this initial study may underestimate true vaccine effectiveness.

This study could not address the effectiveness of the vaccine against laboratory confirmed influenza, influenza A (H1N1) or influenza B, or against severe complications of influenza, such as pneumonia or death. In past years, when the vaccine and circulating viruses have not been well matched, the vaccine usually still afforded some protection against influenza-related complications.

This study's results do not change our recommendation that people, particularly those who are at highest risk of severe complications from influenza, get vaccinated if they have not yet done so. The 2003-2004 influenza A (H1N1) and B strains in the current vaccine are well matched to most circulating strains, which may cause illness later in the influenza season.

Additional studies to determine the effectiveness of the vaccine against laboratory confirmed influenza and influenza-related hospitalization are in progress now. Results from these studies may be available in late Spring or early Summer.

Details about the Colorado study will be published in the January 16 2004 edition of Morbidity and Mortality Weekly Report, which will be available electronically later today.

This map shows state influenza activity levels as reported by state and territorial epidemiologists. In week 53, 38 states shown here in red were reporting widespread activity. Nine states shown in blue were reporting regional activity.

This level of activity is a considerable improvement from mid-December when widespread influenza activity was reported by as many as 45 states.

This graph shows the percentage of patient visits being made to sentinel providers for influenza-like illness. The 2003 season is represented by the red line which clearly shows that activity began early this year. Two other seasons, the 1999-2000 season in green, and the 2002 and 2003 season in purple are shown for purposes of comparison.

In week 53, 6.3% of patient visits to U.S. sentinel providers were due to influenza-like illness. This is a decrease from week 52, but still above the national baseline of 2.5%. Visits for influenza like illness were highest in the West South Central region that includes Arkansas, Louisiana, Oklahoma, and Texas.

This graph shows pneumonia and influenza mortality reported by 122 cities in the United States. The sinusoidal baseline represents the expected pneumonia and influenza deaths

throughout the year as a percent of all deaths. The jagged line shows the actual percent of deaths which occurred.

You can see from this graph that there's a great deal of variability in pneumonia and influenza mortality by season, and from year to year. For example, if you look to the left you can see that for the 1999-2000 season there was a high peak in deaths between weeks 10 and 15. In the years between 2001 and 2003 there were small peaks.

This year is represented at the far right of the graph and you can see that during week 53, 9.4% of all deaths reported by the vital statistics offices of these cities were due to pneumonia and influenza. This is above the epidemic threshold of 8% for week 53. However, increases in deaths typically lag other markers by about a few weeks, so we will continue to watch this line carefully.

I also want to briefly discuss reports of influenza-associated deaths in children which have occurred this year. There has been a lot of media coverage about these deaths in children.

From October through January 6, 2004, CDC has received reports of 93 deaths in children age younger than 18 years.

The median age of these children is four years, with a range of 4 weeks to 17 years.

55% of children whose sex was reported were female.

Deaths have been reported from 31 states.

Influenza virus infection has been confirmed by rapid antigen testing or other laboratory testing in all children who have died.

Among the children reported to date, 38% had an underlying chronic medical condition, and 44% were reported to have no known medical condition. The medical status of 18% is unknown. Underlying medical conditions include 12 with developmental delay, 9 with cerebral palsy or other neurologic conditions, 8 with asthma or other chronic lung disease, 5 with heart disease, such as pulmonary stenosis or heart transplant, and 4 who were immunosuppressed.

Vaccination status is known for 45 children. Only 1 had been adequately vaccinated and 6 were partially vaccinated, meaning they had received 1 of 2 doses.

Pneumonia was a reported complication in 25 children. 15 children had secondary infections with a variety of bacteria including Staphylococcus aureus, Streptococcus pneumoniae, group A Streptococcus, and gram negatives, such as E. coli, Pseudomonas, and Klebsiella.

A summary of these data appeared in the January 9 issue of MMWR. The MMWR report also contains a request for states to report all such influenza-associated deaths to CDC.

The number of deaths being reported to CDC this year is striking. However, childhood death from influenza is not a reportable condition. So we do not have a baseline of such deaths and it is uncertain whether this is an unusual number of cases to occur in an H3N2 year. Mathematical models have estimated that on average about 92 deaths each year occur from influenza in children younger than five years. CDC will be investigating whether the deaths being reported this year are unusual and whether this is a more severe year for influenza than usual.

Now a few comments about the influenza vaccine supply and vaccine recommendations.

During the 2003-2004 influenza season, CDC awarded contracts to both manufacturers of inactivated influenza vaccine and to the manufacturer of live attenuated influenza vaccine.

All of the pediatric and adult influenza vaccine manufactured by Aventis Pasteur has been distributed.

About 75 thousand doses of the Evans/Chiron vaccine are still available on the federal contract. This vaccine is available only in 10-dose vials and contains thimerosal.

About 2 million doses of LAIV are still available from Wyeth/Medimmune.

A common question we have received is whether Aventis pediatric vaccine can be administered to a person older than the labeled age range of 6 to 35 months. Two pediatric doses of Aventis vaccine can be used for a person 3 years of age or older. Two 0.25 mL doses can be administered at the same visit and can be counted as a single valid 0.5 mL dose. However, there are no data as to the effectiveness or safety of this practice.

Providers who use two pediatric doses to vaccinate persons aged 3 years and older should do so using two separate injections at two different sites during the same visit. Under no circumstances should vaccine be transferred from one syringe into another syringe to administer two 0.25 mL doses with a single injection. Transfer of vaccine in this manner greatly increases the chance for contamination.

The Evans/Chiron vaccine Fluvirin is not approved for children younger than 4 years of age because data to demonstrate the efficacy and safety of this vaccine in younger children have not been provided to FDA.

We do NOT recommend that Fluvirin be administered off-label to children 6 to 47 months of age. Only Aventis vaccine should be used for this age group.

Adult doses of Aventis vaccine cannot be divided into two pediatric doses. Single dose 0.5 mL syringes filled by the manufacturer cannot be split. Under no circumstances should vaccine be transferred from one syringe into another syringe to administer two 0.25 mL doses from a single dose 0.5 mL pre-filled syringe. Transfer of vaccine in this manner greatly increases the chance for contamination and the distribution of the active components of the vaccine may not be equal within the syringe, even after shaking. Therefore, splitting the 0.5 mL volume may result in unequal amounts of active vaccine ingredients in the two halves.

Similarly, a single dose 0.5 mL syringe filled by the manufacturer should not be used to give a single 0.25 mL dose, either by discarding half the volume prior to administration or by injecting only half the volume.

The only exception to the use of adult vaccine for children is for vaccine supplied in a 10 dose vial. In this situation it is acceptable to remove a 0.25 mL dose from a 10 dose vial.

We have received many questions about live attenuated influenza vaccine, or LAIV.

LAIV is licensed for use only in healthy people 5 to 49 years of age. It should not be administered to a person younger than 5 years, older than 49 years, or to anyone with an underlying medical illness.

LAIV may be administered to healthy people 5-49 years of age who have a household contact with an underlying medical condition. However, because of the unknown risk of transmission of vaccine virus, ACIP prefers the use of inactivated vaccine for persons who have an immunosuppressed household contact, and for healthcare workers who may be in contact with immunosuppressed people.

When LAIV is administered, environmental contamination with live attenuated influenza vaccine virus is probably unavoidable. There are no data on the risk of infection with vaccine virus for the person administering the vaccine. Until such data are available, it seems prudent that providers who are immunosuppressed avoid administering the vaccine.

We believe that healthcare workers with underlying medical conditions not associated with immunosuppression may administer LAIV. Gloves should be worn when administering the vaccine, and the person administering the vaccine should have already received inactivated influenza vaccine.

Finally, on December 31, 2003 Wyeth and MedImmune announced that FDA had approved a change in the storage requirement for live attenuated influenza vaccine shipped after December 31, 2003. LAIV shipped after this date can be stored in a conventional frost-free freezer unit without the use of a freezer insert, which Wyeth calls a Freezebox. This applies only to vaccine shipped since December 31, 2003. Vaccine shipped before this time must continue to be stored in the Freezebox.

LAIV must be kept in a unit with a separate freezer compartment. It may NOT be stored in a unit without a separate freezer, such as a dorm-style refrigerator-freezer unit.

It is important to note that LAIV kept in a freezer without a freezebox must be used by March 31, 2004. Any vaccine stored without a freezebox remaining after March 31, 2004 must be returned to the manufacturer or destroyed.

Contact Wyeth if you have questions about the storage of your LAIV supply.

Here is contact information for the National Immunization Program. If you have immunization questions you can call the National Immunization Information Hotline at 800.232.2522. The Hotline is staffed Monday through Friday, 8 am until 11 pm Eastern Time.

You can contact us by Email at nipinfo @ cdc.gov. Please use this email address for questions or comments specifically about this program, or about obtaining continuing education credit. The Hotline staff will not have this information.

Please visit our website at www.cdc.gov/nip. Among many other things, the slides, script, resources, and questions and answers for this program will be available on this website.