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SHARON: This afternoon I'd like to give you some additional information about the live attenuated influenza vaccine (which we abbreviate as L-A-I-V). Unlike the intramuscular trivalent inactivated influenza vaccine, which has been around for years, LAIV is a new vaccine that was first used last flu season. LAIV was licensed one year ago in June 2003. It is produced by MedImmune and marketed as FluMist.

SHARON: LAIV is an intranasally-administered trivalent vaccine that contains the same 3 virus strains as the inactivated influenza vaccine (which is abbreviated as TIV for trivalent inactivated influenza vaccine). The live viruses in LAIV are attenuated and, therefore, produce mild or no signs and symptoms of influenza. The LAIV viruses are also temperature-sensitive, meaning that they do not replicate efficiently at the temperature in the lower airways. Finally, the viruses are cold-adapted, so that they do replicate efficiently at the temperature in the upper airways. Therefore, LAIV viruses are able to replicate in the mucosa of the nasopharynx, which produces protective immunity against the viruses in the vaccine. However, the LAIV viruses are temperature-sensitive and attenuated and do not replicate efficiently in the lungs, so they do not produce influenza disease.

SHARON: Because LAIV contains live viruses that replicate in the nasopharynx, these vaccine viruses can be shed in respiratory secretions for 2 or more days after vaccination, although in lower titers than typically occur with shedding of wild-type influenza viruses. Shedding should not be equated with person-to-person transmission of vaccine viruses, although, in rare instances, shed vaccine viruses can be transmitted from vaccinees to nonvaccinated persons.

SHARON: One unpublished study in a childcare center assessed transmissibility of vaccine viruses from 98 vaccinated to 99 unvaccinated children, all aged 8-36 months. 80% of the vaccinated children shed one or more virus strains for an average of 7.6 days. In this study, there was only one documented instance of transmission of a vaccine virus to an unvaccinated contact. The contact did not exhibit symptoms that were different from those experienced by the vaccine recipients. Furthermore, the transmitted virus retained its attenuated, temperature-sensitive, cold-adapted characteristics, as did all the viruses shed by the children. The researchers estimated that the probability of acquiring vaccine virus following close contact with a single LAIV recipient in this childcare population was 0.6-2.4%.

SHARON: The frequency and duration of LAIV viral shedding by persons 5-49 years of age has not been established. However, studies of live attenuated influenza vaccine in adults and children using an earlier version of LAIV made of the same master donor strain as FluMist found that adults shed less vaccine virus and for substantially fewer days than children. The maximum period of shedding in adults was 6 days. Furthermore, because the viruses are attenuated, it is unlikely that typical influenza symptoms would develop even if a vaccine virus were transmitted to another person.

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SHARON: This table shows the vaccination schedule for LAIV based on age and prior influenza vaccination history. A dose of LAIV is 0.5 mL, regardless of age, divided equally between each nostril. Children 5-8 years of age who have never previously received either LAIV or TIV should receive 2 doses of LAIV separated by 6 to 10 weeks. Note that this is a longer interval than the 1 month recommended between the first two doses of TIV. Two doses of influenza vaccine are recommended for satisfactory antibody responses in young children. The first dose acts as an immunologic primer to get the immune system used to recognizing the influenza virus. The second dose increases serum antibody levels. The Advisory Committee on Immunization Practices (or ACIP) recommends that children 5-8 years of age who have been previously vaccinated with either LAIV or TIV should receive 1 dose of LAIV. They do not require a second dose of LAIV during the same flu season because they have already been primed by the earlier vaccination. This recommendation is different than the manufacturer's labeling, which recommends that children 5-8 years of age who have not previously received LAIV should receive 2 doses, regardless of whether they were previously vaccinated with TIV. Persons 9 through 49 years of age should receive only 1 dose of LAIV. By this age it's assumed that they have already been primed, either by exposure to wild-type influenza virus or by previous vaccination.

SHARON: So, how does the vaccine efficacy of LAIV compare to that of TIV? Well, researchers have compared the ability of LAIV and TIV to protect adults against laboratory-confirmed influenza illness following experimental challenge with wild-type viruses. The overall efficacy of LAIV was 85%. The efficacy of TIV was 71%. However, the difference between the two vaccines was not statistically significant. At this time, there is no evidence that LAIV reduces culture-confirmed influenza any more or less effectively than TIV.

SHARON: LAIV is an option for vaccinating healthy persons 5-49 years of age, including those in close contact with high-risk groups. The only exceptions are household members, healthcare workers, and others who have close contact with severely immunocompromised persons in protected isolation. This group of persons should receive TIV. Otherwise, any healthy person 5-49 years of age who wishes to reduce the risk of acquiring influenza may use LAIV. However, LAIV has a number of contraindications you need to be aware of.

SHARON: LAIV should not be given to persons younger than 5 years of age or older than 49 years of age. Persons in these age groups should receive TIV. LAIV should also not be administered to anyone with an underlying medical condition that increases the risk for complications of influenza. There are few data concerning the safety of LAIV among these high-risk persons. Therefore, until additional data are available, persons with high-risk medical conditions should continue to receive TIV. These high-risk medical conditions include all those conditions for whom TIV is recommended. They are…

SHARON:

- Pulmonary disease, such as emphysema and asthma;
- Cardiovascular disease, such as congestive heart failure;
- Metabolic disease, such as diabetes;
- Renal disease, such as chronic renal failure and nephropathy;
- Hemoglobinopathies, such as sickle cell disease; and
- Immunosuppression, such as HIV.

SHARON: Other persons who should not receive LAIV include children or adolescents receiving long-term aspirin therapy or other salicylates because of the theoretical association of Reye syndrome with LAIV viruses. Pregnant women should also not receive LAIV. Both children taking chronic aspirin therapy and pregnant women should get TIV. LAIV should not be administered to persons with a history of a severe allergy to egg or a severe allergy to any other vaccine component. Finally, LAIV should not be administered to persons with a history of Guillain Barre syndrome. In addition to these contraindications, a moderate or severe acute illness at the time of vaccination is a precaution.

SHARON: Because of the potential for shedding and transmission of vaccine virus and the lack of data concerning the frequency and safety of LAIV virus transmission to severely immunosuppressed persons, ACIP prefers that LAIV NOT be administered to people (such as HCWs) in close contact with those who are severely immunosuppressed during those periods in which the immunosuppressed person requires care in a protective environment (such as patients with hematopoietic stem cell transplants). ACIP has no preference for either LAIV or TIV use by healthcare workers or other close contacts of persons with lesser degrees of immunosuppression (such as those with diabetes, those with asthma taking corticosteroids, and those infected with HIV). Similarly, ACIP has no preference for LAIV or TIV use by close contacts of persons with other high-risk conditions, such as pregnant women, children aged 2 years and younger, or adults aged 50 years and older.

SHARON: If a healthcare worker receives LAIV, that worker should refrain from contact with severely immunosuppressed patients in protective isolation for 7 days after receiving the vaccine. Hospital visitors who have received LAIV should also refrain from contact for 7 days. However, such persons need not be excluded from visiting other patients who are not severely immunosuppressed.

SHARON: Low-level introduction of vaccine viruses into the environment is likely unavoidable when administering LAIV. The risk of acquiring vaccine viruses from the environment is unknown but likely to be limited. Severely immunosuppressed healthcare workers should not administer LAIV. However, other healthcare workers at high risk for influenza complications may administer LAIV. These include healthcare workers with high-risk medical conditions (such as asthma), pregnant healthcare workers, and healthcare workers 50 years of age and older.

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SHARON: The safety of LAIV has been assessed in 20 pre-licensure clinical trials involving approximately 6000 healthy participants in the approved age range of 5-49 years. Among healthy children there does not appear to be a significant increase in upper respiratory illness symptoms, fever, or other systemic symptoms. Unpublished data from a study including subjects aged 1-17 years indicated an increase in asthma or reactive airways disease in the subset aged 12-59 months. Because of this, LAIV is not approved for use in children younger than 5 years of age. LAIV should also not be used in persons with asthma, reactive airways disease, or other chronic pulmonary diseases. Among healthy adults, a significantly increased rate of cough, runny nose, nasal congestion, sore throat and chills was reported in 10-40% of LAIV recipients. However, there was no increase in the occurrence of fever. No statistically significant increase in serious adverse reactions has been identified in LAIV recipients, either in children or in adults.

SHARON: Therefore, LAIV is a safe and efficacious vaccine and is a useful alternative to TIV for healthy persons 5-49 years of age.