

Health Update:

2009 H1N1 Influenza Update 14: Antiviral Drugs from the SNS, Key Issues Concerning Antivirals, Peramivir Availability, H1N1 Vaccines, Clinical Support Line for Providers of Care to Pregnant/Postpartum Women

November 13, 2009

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**Health Update
November 13, 2009**

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SUBJECT: 2009 H1N1 Influenza Update 14: Antiviral Drugs from the SNS, Key Issues Concerning Antivirals, Peramivir Availability, H1N1 Vaccines, Clinical Support Line for Providers of Care to Pregnant/Postpartum Women

This Health Update provides information on: 1) antiviral medications from the SNS; 2) key issues concerning antivirals; 3) availability of peramivir; 4) 2009 H1N1 influenza vaccines; 5) CDC clinical support line for medical providers caring for pregnant/postpartum women.

Antiviral Medications from the Strategic National Stockpile (SNS)

Missouri has received antiviral medications from the Strategic National Stockpile (SNS): Tamiflu 30 mg, 45 mg, and 75 mg capsules; Tamiflu oral suspension; and Relenza inhalation powder. These medications are intended for treatment of persons with known or suspected influenza, and should only be utilized when all local resources have been exhausted. Exhausted local resources may include the unavailability of the drug in area pharmacies and hospitals, and also the patient's inability to pay for the drug. Antivirals obtained from the SNS cannot be used for chemoprophylaxis.

Most of the antiviral medications received from the SNS have been transferred to local public health agencies (LPHAs) throughout the state. Each LPHA has developed antiviral dispensing plans, and identified community partners to dispense these drugs. These plans include written agreements with physicians, pharmacies, hospitals, and other healthcare facilities which dispense medication. Plans may vary by jurisdiction depending on the availability of healthcare resources, and the partnerships that have been developed with dispensers. For a listing of community partners who are dispensing SNS antiviral medications, contact your LPHA. A listing of these agencies can be found at: <http://www.dhss.mo.gov/LPHA/LPHAs.html>.

Key Issues for Clinicians Concerning Antiviral Treatments

The Centers for Disease Control and Prevention (CDC) has stated that most healthy persons who develop an illness consistent with uncomplicated influenza, or persons who appear to be recovering from influenza, do not need antiviral medications for treatment. However, for some individuals antiviral treatment is recommended. (See the current CDC antiviral guidance at <http://www.cdc.gov/h1n1flu/recommendations.htm>. See also information on antiviral safety at http://www.cdc.gov/H1N1flu/antivirals/safety_info.htm)

CDC has found that among ill persons who would be recommended to receive antiviral treatment, not all are being treated. To help address this situation, CDC has recently issued a document entitled "Key Issues for Clinicians Concerning Antiviral Treatments for 2009 H1N1" (<http://www.cdc.gov/H1N1flu/HAN/110609.htm>), whose content is reproduced here:

Although use of influenza antiviral drugs in the United States has increased during the 2009-2010 flu season, not all people recommended for antiviral treatment are getting treated. Listed below are important facts to consider when deciding whether a patient needs to be treated with antiviral medication.

It is critical to remember that it is not too late to treat, even if symptoms began more than 48 hours ago. Although antiviral treatment is most effective when begun within 48 hours of influenza illness onset, studies have shown that hospitalized patients still benefit when treatment with oseltamivir is started more than 48 hours after illness onset. Outpatients, particularly those with risk factors for severe illness who are

not improving, might also benefit from treatment initiated more than 48 hours after illness onset.

Recommendations for Clinicians

Many 2009 H1N1 patients can benefit from antiviral treatment, and **all hospitalized patients with suspected or confirmed 2009 H1N1 should receive antiviral treatment with a neuraminidase inhibitor – either oseltamivir or zanamivir – as early as possible** after illness onset. Moderately ill patients, especially those with risk factors for severe illness, and those who appear to be getting worse, can also benefit from treatment with neuraminidase inhibitors. A full listing of risk factors for severe influenza is available at: <http://www.cdc.gov/h1n1flu/highrisk.htm>.

Although antiviral medications are recommended for treatment of 2009 H1N1 in patients with risk factors for severe disease, **some people without risk factors may also benefit from antivirals**. To date, 40% of children and 20% of adults hospitalized with complications of 2009 H1N1 did not have risk factors. Clinical judgment is always an essential part of treatment decisions.

When treatment of persons with suspected 2009 H1N1 influenza is indicated, it **should be started empirically. If a decision is made to test for influenza, treatment should not be delayed while waiting for laboratory confirmation**. The earlier antiviral treatment is given, the more effective it is for the patient. Also, rapid influenza tests often can give false negative results. If you suspect flu and feel antiviral treatment is warranted, treat even if the results of a rapid test are negative. Obtaining more accurate testing results can take more than one day, so treatment should not be delayed while waiting for these test results. For more information on influenza testing, please see: http://www.cdc.gov/h1n1flu/guidance/diagnostic_tests.htm.

Although commercially produced pediatric oseltamivir suspension is in short supply, **there are ample supplies of children's oseltamivir capsules, which can be mixed with syrup at home. In addition, pharmacies can compound adult oseltamivir capsules into a suspension for treatment of ill infants and children**.

Additional information on compounding can be found at: <http://www.cdc.gov/H1N1flu/pharmacist/>.

For More Information

Updated Interim Recommendations for the Use of Antiviral Medications in the Treatment and Prevention of Influenza for the 2009-2010 Season: <http://www.cdc.gov/H1N1flu/recommendations.htm>.

Questions & Answers: Antiviral Drugs, 2009-2010 Flu Season: <http://www.cdc.gov/h1n1flu/antiviral.htm>.

Influenza Diagnostic Testing: http://www.cdc.gov/h1n1flu/diagnostic_testing_clinicians_qa.htm.

Updated Interim Recommendations for Obstetric Health Care Providers Related to Use of Antiviral Medications in the Treatment and Prevention of Influenza for the 2009-2010 Season:

http://www.cdc.gov/H1N1flu/pregnancy/antiviral_messages.htm.

Antiviral Drugs: Summary of Side Effects: <http://www.cdc.gov/flu/protect/antiviral/sideeffects.htm>.

General information for the public on antiviral drugs is available in “2009 H1N1 and Seasonal Flu: What You Should Know About Flu Antiviral Drugs” at <http://www.cdc.gov/H1N1flu/antivirals/geninfo.htm>.

Downloadable brochures and informational flyers, including one on antiviral drugs, are available at <http://www.cdc.gov/h1n1flu/flyers.htm>.

For the FDA page on antiviral influenza drugs:

<http://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm100228.htm>.

For additional information, you can also call CDC's toll-free hotline, 800-CDC-INFO (800-232-4636) TTY: (888) 232-6348, which is available 24 hours a day, every day.

Availability of Intravenous Peramivir

The Food and Drug Administration (FDA) has recently issued an Emergency Use Authorization (EUA) to allow use of the neuraminidase inhibitor peramivir for the treatment of certain hospitalized patients with known or suspected 2009 H1N1 influenza. For more information on peramivir, see <http://www.cdc.gov/h1n1flu/eua/peramivir.htm> and http://www.cdc.gov/h1n1flu/EUA/pdf/peramivir_qa.pdf.

Peramivir can be requested through CDC by going to <http://emergency.cdc.gov/h1n1antivirals/>. Note that as part of this request, the clinician must acknowledge his/her compliance with the terms and conditions of the EUA.

Information on 2009 H1N1 Influenza Vaccines

Supplies of 2009 H1N1 vaccines are now coming into Missouri, and more will become available in the coming weeks. See http://www.dhss.mo.gov/BT_Response/provider_listing.html for current information on 2009 H1N1 and seasonal influenza vaccines in the state. Knowing that initial supplies of 2009 H1N1 vaccines would be limited, the Advisory Committee on Immunization Practices (ACIP) has recommended that vaccination efforts first be directed to certain priority groups (see <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5810a1.htm>). Contact your LPHA for recommendations on how vaccine is being distributed in your area.

The following are sources of information for clinicians on 2009 H1N1 influenza vaccines:

- DHSS Issues Exemption for 2009 H1N1 Influenza Vaccine (DHSS)
<http://www.dhss.mo.gov/NewsAndPublicNotices/2009/h1n1vaccinewaiver.html>
The Missouri Department of Health and Senior Services (DHSS) recently issued an exemption (which applies only to 2009 H1N1 influenza vaccine) that temporarily sets aside a statute which prohibited pregnant women and children under three from receiving vaccine containing thimerosal.
- Update on Influenza A (H1N1) 2009 Monovalent Vaccines (CDC)
<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5839a3.htm>
- Monovalent Influenza Vaccine Dosage, Administration, and Storage (CDC)
<http://www.cdc.gov/h1n1flu/vaccination/dosage.htm>
- Influenza A (H1N1) 2009 Monovalent (FDA)
<http://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm181950.htm>
Includes links to the package insert for each of the licensed vaccines.
- Vaccine Information Statements: 2009 H1N1 Influenza Vaccines (CDC)
<http://www.cdc.gov/vaccines/pubs/vis/default.htm#h1n1live>
- Model Standing Orders for Administering 2009 H1N1 Vaccine and for Treatment of Post-Vaccination Reactions (DHSS)
http://www.dhss.mo.gov/BT_Response/model_standing_orders.pdf

CDC has developed several sets of questions and answers on 2009 H1N1 influenza vaccines. A selection of these questions and answers, arranged by category, is found in the Appendix beginning on the next page.

CDC Clinical Support Line for Medical Providers Caring for Pregnant/Postpartum Women

As mentioned in Health Update 13, CDC has established a new clinical support line to provide technical assistance to medical providers caring for seriously ill pregnant or immediately postpartum (within 6 weeks of delivery) women with influenza. The telephone number is 404-368-2133. Clinical support is available from board-certified OB/GYN subject matter experts 24 hours a day, 7 days a week. Note that this number should only be used for consultation on seriously ill pregnant or postpartum patients, or to report seriously ill pregnant or immediately postpartum patients who are admitted to an intensive care unit (ICU) or who die (see Health Update 12). For questions regarding pregnant women who are not seriously ill, providers can call 1-800-232-4636.

Links to comprehensive information and guidance for medical professionals on 2009 H1N1 influenza are available at http://www.dhss.mo.gov/BT_Response/MedProfs.html. Links to comprehensive information and guidance on seasonal influenza are found at <http://www.dhss.mo.gov/PandemicInfluenza/MedSeasonalFlu.html>.

Missourians, including Missouri medical professionals, now have access to a toll-free H1N1 influenza information line. Named the **H1N1 InfoLine**, and sponsored by DHSS, it can provide information and guidance on 2009 H1N1 influenza and H1N1 vaccine to both the public and medical providers. This service is available 24 hours a day, seven days a week at 1-877-FLU-4141 (1-877-358-4141).



APPENDIX

Questions and Answers on 2009 H1N1 Influenza Vaccines

The following questions and answers on the 2009 H1N1 influenza vaccines are from materials prepared by the Centers for Disease Control and Prevention (CDC), and are arranged in the following categories:

- **2009 H1N1 Live Attenuated (LAIV) Vaccine** 1
- **Use of 2009 H1N1 Vaccine in Children 6 Months Through 9 Years of Age** 2
- **Pregnant Women** 2
- **Vaccinating Persons Who Have Had Influenza-Like Illness** 4
- **Simultaneous and Sequential Administration of 2009 H1N1 Vaccines and Other Vaccines** 4
- **Adverse Reactions** 5

2009 H1N1 Live Attenuated (LAIV) Vaccine

See also the section below entitled “Simultaneous and Sequential Administration of 2009 H1N1 Vaccines and Other Vaccines”

Can the nasal-spray flu vaccine be used together with influenza antiviral medications?

If a person is taking an influenza antiviral drug (including Tamiflu® or Relenza®), then the nasal spray flu vaccine should not be given until 48 hours after the last dose of the influenza antiviral medication was given.

If a person takes antiviral drugs within two weeks of getting the nasal spray flu vaccine, that person should get revaccinated. (The antiviral drugs will have killed the vaccine viruses that are supposed to cause the immune response against those viruses.)

Antiviral drugs can be taken with the inactivated (i.e. killed) flu vaccine.¹

Can people receiving the nasal-spray flu vaccine LAIV pass the vaccine viruses to others?

In clinical studies, transmission of vaccine viruses to close contacts occurred only rarely. The current estimated risk of getting infected with vaccine virus after close contact with a person vaccinated with the nasal-spray flu vaccine is low (0.6%-2.4%). Because the viruses are weakened, infection is unlikely to result in influenza illness symptoms since the vaccine viruses have not been shown to change into typical or naturally occurring influenza viruses.¹

Can contacts of people with weakened immune systems get the nasal-spray flu vaccine?

People who are in contact with others with severely weakened immune systems when they are being cared for in a protective environment (for example, people with hematopoietic stem cell transplants), should not get the nasal spray vaccine, including the 2009 H1N1 nasal spray vaccine if they will come into contact with the severely immunocompromised person within 7 days of vaccination. People who have contact with others with lesser degrees of immunosuppression (for example, people with diabetes, people with asthma taking corticosteroids, or people infected with HIV) can get the nasal spray vaccine.¹

Can a person who has received LAIV test positive on a rapid influenza diagnostic test?

The live attenuated influenza vaccine viruses in LAIV (seasonal vaccine and 2009 H1N1 monovalent vaccine) can cause a positive result on a rapid influenza diagnostic test. The tests are designed to detect influenza viruses and cannot differentiate between live attenuated and wild-type influenza viruses. A positive test in a person who recently (in the previous 7 days) received LAIV and who also has an influenza-like illness could be caused by either LAIV or wild-type influenza virus.²

Can health care providers get the live attenuated influenza vaccine?

Yes. LAIV is a very good option for most health care providers who are healthy, younger than 50 years old, and not pregnant. However, health care providers should not get LAIV if they are providing medical care for patients who require special environments in the hospital because they are profoundly immunocompromised (e.g., those who work in bone marrow transplant units). Although no immunocompromised patient has been shown to be harmed by use of LAIV among health care workers, the recommendation against the use of LAIV in health care workers with this type of patient contact is intended as an extra precaution for fragile immunocompromised patients. Health care workers with this type of patient contact can get LAIV, but if they do, they should wait 7 days after being vaccinated before returning to duties that include care of severely immunocompromised patients in special environments.¹

Can health care personnel in a neonatal intensive care unit (NICU) get LAIV?

Yes. Either the inactivated injectable influenza vaccine or the LAIV can be given to health care personnel working in a neonatal intensive care unit (NICU). Nearly all healthy, non-pregnant health care workers, including those who come in contact with newborn infants, pregnant women, persons with a solid organ transplant, persons receiving chemotherapy (not in preparation for a bone marrow transplant), and persons with HIV/AIDS, may receive LAIV if otherwise eligible. However, LAIV should not be

used for health care personnel who care for patients undergoing bone marrow transplantation (i.e., patients who require a protected environment).

No special precautions (e.g., masks or gloves) are necessary for health care personnel who have been vaccinated with the LAIV and who do not work with patients undergoing bone marrow transplantation. However, for health care personnel that were vaccinated with LAIV and who work with patients undergoing bone marrow transplantation, the ACIP recommends, as a precautionary measure, that those health care personnel avoid providing care for such patients for 7 days after vaccination.¹

Can health care workers who cannot receive the nasal spray vaccine (e.g., pregnant women, older adults, persons with chronic medical conditions) administer this vaccine to others?

Yes. Health care workers who cannot get the nasal spray vaccine themselves can administer the vaccine to others.¹

What personal protective equipment is recommended for health care workers who are giving the 2009 H1N1 nasal spray vaccine?

Personal protective equipment (gloves and masks) are not needed when administering the nasal spray vaccine, including the 2009 H1N1 nasal spray vaccine.¹

Use of 2009 H1N1 Vaccine in Children 6 Months Through 9 Years of Age

Children ages 6 months through 8 years receiving seasonal influenza vaccination for the first time are recommended to receive 2 doses. However, in the prescribing information (package inserts) for 2009 H1N1 monovalent influenza vaccines, children ages 6 months through 9 years are recommended to receive 2 doses. Does CDC recommend that clinicians follow the recommendation in the 2009 H1N1 monovalent vaccine package inserts or use the standard seasonal vaccine recommendations?

The recommendations for use of seasonal vaccine are unchanged – children 6 months through 8 years receiving seasonal influenza for the first time are recommended to receive 2 doses. Other children just need one dose of seasonal influenza vaccine.

Using the 2009 H1N1 monovalent influenza vaccine schedule presented in the prescribing information is recommended (6 months through 9 years receive 2 doses regardless of earlier vaccination with seasonal influenza vaccine).³

The interval between doses stated in the 2009 H1N1 monovalent influenza vaccine prescribing information is "approximately 1 month". What does "approximately 1 month" mean?

CDC recommends that the two doses of 2009 H1N1 monovalent vaccines be separated by 28 days (4

weeks).³

The 2009 H1N1 monovalent influenza vaccine trials that are currently underway have often used a 21 day (3 week) interval between doses. Is a 21 day interval acceptable for inactivated 2009 H1N1 monovalent vaccines?

CDC recommends that the two doses of 2009 H1N1 monovalent influenza vaccines be separated by 28 or more days (4 weeks). However, trials of the inactivated 2009 H1N1 vaccines have often used a 21 day interval. Administering the two doses of a 2009 H1N1 monovalent inactivated influenza vaccine at least 21 days apart is safe and acceptable. Therefore, if the second dose of an inactivated 2009 H1N1 monovalent vaccine is separated from the first dose by at least 21 days, the second dose can be considered valid. If the interval separating the doses is less than 21 days, the second dose should be repeated 28 or more days after the invalid (second) dose (≥ 21 days is acceptable for this interval also).³

Can a child who requires 2 doses of a 2009 H1N1 monovalent influenza vaccine and who received the first dose with an inactivated 2009 H1N1 monovalent vaccine complete the series with the 2009 H1N1 monovalent LAIV, or vice versa?

There are limited data describing the immune response to mixed schedules. Therefore, when feasible, the same type of vaccine (live attenuated or inactivated) should be used in a two-dose schedule. Mixed schedules however, are preferable to not completing the series. A 28 day interval between doses is recommended, but 21 days is acceptable. If vaccines are separated by 1-20 days, repeat the invalid (second) dose 28 days (21 days acceptable) from the invalid second dose.³

Pregnant Women

How many vaccine doses will a pregnant woman need to get?

The U.S. Food and Drug Administration (FDA) has approved the use of one dose of vaccine for full protection for persons 10 years and older. Therefore, a pregnant woman is recommended to get one dose of the 2009 H1N1 monovalent vaccine.²

Can the 2009 H1N1 monovalent flu vaccine be given at any time during pregnancy?

Seasonal flu vaccine is recommended for all pregnant women at any time during pregnancy, and has not been shown to cause harm to a pregnant woman or her baby. The Advisory Committee on Immunization Practices also recommends that 2009 H1N1 monovalent flu vaccine be given to all pregnant women at any time during pregnancy.⁴

Can pregnant women receive the nasal spray vaccine?

The nasal spray vaccine is not licensed for use by pregnant

women. Pregnant women should not receive nasal spray vaccine for either seasonal flu or 2009 H1N1 flu. After delivery, women can receive the nasal spray vaccine, even if they are breastfeeding.⁴

What if a pregnant woman receives the live attenuated influenza vaccine?

Live attenuated influenza vaccines (seasonal or H1N1 LAIV) have not been studied in pregnant women and LAIV is not recommended for pregnant women. The inactivated influenza vaccines (seasonal and 2009 monovalent H1N1) are recommended for pregnant women. However, if a pregnant woman receives LAIV, for example, before she knows she is pregnant, she would not be expected to have any additional risks, compared with women who are not pregnant. The influenza vaccine virus replicates in the nose where body temperature is lower and has never been shown to replicate in other parts of the body or be passed to the unborn baby.

There are not any special measures to be taken if a pregnant woman has received live vaccine, i.e., revaccination with inactivated vaccine, taking antivirals, or enhanced testing. She should have pregnancy monitoring and testing as clinically indicated.

CDC and FDA are requesting that these instances of using LAIV in pregnant women be reported to the Vaccine Adverse Event Reporting System (VAERS). This will allow us to track these instances, even if there is no adverse event following the incident.⁴

For planned pregnancies, how long should a woman wait after receiving nasal spray flu vaccines before becoming pregnant?

There are no studies of live attenuated influenza vaccine among women who are pregnant or who are planning to become pregnant. However, the vaccine virus is cold-adapted and replicates in the nasopharyngeal tissues rather than at core body temperature. Consequently, infection of a fetus with live attenuated influenza virus is very unlikely. It is not necessary to defer pregnancy for a specific interval following receipt of live attenuated influenza vaccine.²

Can pregnant women be in contact with someone who has gotten the nasal spray vaccine (LAIV)?

Yes. A pregnant woman can be in close contact with someone who has gotten the nasal spray flu vaccine (LAIV). A pregnant woman can also administer (give) a nasal spray vaccine (LAIV). Because the viruses in the nasal spray vaccine are attenuated or weakened, vaccine viruses are unlikely to cause any illness symptoms, even if an unvaccinated person inadvertently gets vaccine viruses in their nose. The nasal spray vaccine against seasonal influenza viruses has been used in millions of school children and healthy adults since it was licensed, and there have been no reports of pregnant women

becoming ill after exposure to their vaccinated children or other family members.

While it's OK for her contacts to get the nasal spray vaccine, this vaccine should not be given to pregnant women. While LAIV is not known to be a safety risk for pregnant women, there have not been studies of LAIV among pregnant women to assess safety and effectiveness for use in this group. LAIV can be given to women after they have delivered, even if they are nursing.

CDC recommends that pregnant women get both the 2009 H1N1 flu shot and the seasonal flu shot. Flu shots are made with a killed virus, and have not been shown to cause harm to pregnant women or their babies.¹

If a pregnant woman delivers her baby before receiving her seasonal flu shot or her 2009 H1N1 flu shot, should she still receive them?

Yes. In addition to protecting her from infection, the vaccine may also help protect her young infant. Flu vaccines are recommended only for infants 6 months or older. It is recommended that everyone who lives with or provides care for an infant less than 6 months old receive both the seasonal flu vaccine and the 2009 H1N1 monovalent flu vaccine.⁴

Can a woman who is breastfeeding receive the vaccine?

Yes. Both seasonal flu and 2009 H1N1 monovalent influenza vaccines should be given to breastfeeding mothers. Breastfeeding is fully compatible with flu vaccination, and preventing maternal infection provides secondary protection to the infant. Maternal vaccination is especially important for infants less than 6 months old, who are ineligible for vaccination. In addition, transfer of vaccination-related antibodies by breastfeeding further reduces the infant's chances of getting sick with the flu. While pregnant women should just receive the inactivated injectable form of influenza vaccine, nursing mothers can receive either the injectable or nasal spray form.⁴

Is the 2009 H1N1 monovalent flu vaccine safe for pregnant women?

Flu vaccines have not been shown to cause harm to a pregnant woman or her baby. The seasonal flu shot has been recommended for pregnant women for many years. The 2009 H1N1 monovalent flu vaccine will be made using the same processes as the seasonal flu vaccine, and clinical trials of H1N1 monovalent vaccine safety in non-pregnant children and adults found results similar to those seen in studies of seasonal flu vaccine. Studies that test the 2009 H1N1 monovalent flu vaccine in pregnant women began in September. For more information, see: <http://www3.niaid.nih.gov/news/QA/vteuH1N1qa.htm>.⁴

Does the 2009 H1N1 monovalent flu vaccine have preservative in it?

Multi-dose vials of flu vaccine contain the preservative thimerosal to prevent bacterial growth. There is no evidence that thimerosal is harmful to a pregnant woman or a fetus. However, because some women are concerned about exposure to preservatives during pregnancy, manufacturers are producing preservative-free seasonal flu vaccine and 2009 H1N1 monovalent flu vaccine in single dose syringes. CDC recommends that pregnant women receive flu vaccine with or without thimerosal.⁴

Does the 2009 H1N1 monovalent flu vaccine have an adjuvant or squalene in it?

Adjuvants are agents that are sometimes added to a vaccine to increase its effectiveness. There are no adjuvants (such as squalene) in either the 2009 H1N1 monovalent or seasonal flu vaccines used in the United States.⁴

Vaccinating Persons Who Have Had Influenza-Like Illness

Will the 2009 H1N1 vaccine be recommended for patients who had influenza-like illness since spring 2009?

All people in a recommended vaccination target group who did not have 2009 H1N1 virus infection confirmed by real-time reverse transcriptase-polymerase chain reaction (rRT-PCR) test should be vaccinated with the 2009 H1N1 vaccine. People who had an illness confirmed by rRT-PCR to be 2009 H1N1 virus earlier in 2009 can be considered to be immune and do not need to be vaccinated this year. However, most people with respiratory illnesses since this spring have not had testing with the rRT-PCR test, which is the only test that can confirm infection specifically with the 2009 H1N1 virus. Tests such as rapid antigen detection assays and diagnoses based on symptoms alone without rRT-PCR testing, cannot specifically determine if a person has 2009 H1N1 influenza. Although people who were not tested, but who became ill within 1-4 days after close contact with a person with lab confirmed 2009 H1N1 influenza might have been infected with 2009 H1N1, they cannot be certain since many pathogens can cause respiratory illness. These people should get the 2009 H1N1 vaccine as recommended for their age and risk group.

People who were infected with the 2009 H1N1 virus and who are not severely immune compromised will likely have immunity to subsequent infection with 2009 H1N1 virus. However, vaccination of a person with some existing immunity to the 2009 H1N1 virus will not be harmful, and patients who are uncertain about how they were diagnosed should get the 2009 H1N1 vaccine. In addition, people recommended for seasonal vaccine should get a seasonal vaccine because infection with the 2009 H1N1 virus does not provide protection against

seasonal influenza viruses.²

Simultaneous and Sequential Administration of 2009 H1N1 Vaccines and Other Vaccines

Can 2009 H1N1 vaccine be administered at the same visit as other vaccines?

Inactivated 2009 H1N1 vaccine can be administered at the same visit as any other vaccine, including pneumococcal polysaccharide vaccine. Live 2009 H1N1 vaccine can be administered at the same visit as any other live or inactivated vaccine **EXCEPT** seasonal live attenuated influenza vaccine.²

Can seasonal influenza vaccine and 2009 H1N1 vaccine be given at the same visit?

Both seasonal and 2009 H1N1 vaccines are available as inactivated and live attenuated (LAIV) formulations.

The simultaneous and sequential administration of seasonal and 2009 H1N1 inactivated vaccines is currently being studied. However, existing recommendations are that two inactivated vaccines can be administered at any time before, after, or at the same visit as each other (General Recommendations on Immunization, *MMWR* 2006;55[RR-15]).

Existing recommendations also state that an inactivated and live vaccine may be administered at any time before, after or at the same visit as each other. Consequently, providers can administer seasonal and 2009 H1N1 inactivated vaccines, seasonal inactivated vaccine and 2009 H1N1 LAIV, or seasonal LAIV and inactivated 2009 H1N1 at the same visit, or at any time before or after each other.

Live attenuated seasonal and live 2009 H1N1 vaccines should **NOT** be administered at the same visit until further studies are done.²

What is the minimum interval between doses of seasonal LAIV and 2009 H1N1 monovalent LAIV?

There are no data on sequential administration of seasonal and 2009 H1N1 monovalent LAIV. The ACIP recommends a minimum interval of 28 days (4 weeks) between use of a seasonal LAIV and a 2009 H1N1 monovalent LAIV because these are considered to be 2 different vaccines. The ACIP recommendations were developed based on data from studies using attenuated injectable live virus vaccines such as the measles, mumps and rubella vaccine. Trials of 2009 H1N1 live attenuated vaccines have used a 28 day interval between doses and therefore, 28 days is the recommended interval between 2 doses of LAIV (seasonal and H1N1 monovalent LAIV). However, based on previous studies of LAIV replication and immune response, as little as 14 days (2 weeks) might be sufficient to allow for an appropriate immune response to both vaccines. Therefore, an interval between the two types of LAIV of 2 weeks or more may be acceptable, although an interval

of 28 days is preferred.³

If seasonal LAIV and 2009 H1N1 monovalent LAIV are not administered on the same day, but are separated by less than 14 days (2 weeks), do either or both doses need to be repeated, and if so, when?

Seasonal LAIV and 2009 H1N1 monovalent LAIV should not be administered at the same visit, and should be separated by at least 28 days (14 days acceptable based on previous studies of attenuated influenza vaccine virus replication and immune response). If accidentally given at the same visit, neither dose needs to be repeated. If given 1-13 days apart, the second dose should be repeated 28 days (14 days acceptable) from the invalid (second) dose.³

If seasonal LAIV and 2009 H1N1 monovalent LAIV are inadvertently given at the same visit, do either or both doses need to be repeated, and if so, when?

Seasonal LAIV and 2009 H1N1 monovalent LAIV should not be administered at the same visit. While use of the 2 types of LAIV at the same visit could result in reduced immunogenicity for one vaccine, according to some experts, there are no data describing what happens with the vaccine response following simultaneous administration of LAIV vaccines. However, if both types of LAIV are inadvertently administered at the same visit neither vaccine, needs to be repeated.³

Adverse Reactions

What are the possible side effects of the 2009 H1N1 monovalent flu vaccine?

The side effects from 2009 H1N1 monovalent flu vaccine are expected to be similar to those from seasonal flu vaccines. The most common side effects following vaccination are expected to be mild, such as soreness, redness, tenderness, or swelling where the shot was given. Some people might experience headache, muscle aches, fever, fatigue, and nausea. If these problems occur, they usually begin soon after the shot is given and may last as long as 1-2 days. Fainting may occur shortly after receiving any injection and has uncommonly been reported after the flu shot. Like any medicines, vaccines can cause serious problems like severe allergic reactions. However, life-threatening allergic reactions to vaccines are very rare.

Pregnant women are not known to have an increased risk of side effects from the flu vaccine.

Anyone who has a severe (life-threatening) allergy to eggs or to any other substance in the vaccine should not get the vaccine. Providers should ask patients whether they have any severe allergies or if they have ever had a severe allergic reaction following flu vaccination.⁴

Is the 2009 H1N1 flu vaccine expected to be

associated with Guillain-Barre Syndrome (GBS)?

During the 1976 Swine Flu vaccination program in the U.S., using a vaccine virus very different than the 2009 H1N1 virus, the 1976 vaccine was associated with cases of a severe paralytic illness called Guillain-Barre Syndrome (GBS). Approximately 1 additional case of GBS per 100,000 persons vaccinated occurred with the 1976 swine flu vaccine. Most studies done on seasonal flu vaccines after the 1976 vaccine showed no increased risk of GBS. However, two studies did demonstrate a small risk of approximately 1 additional case of GBS per 1 million persons vaccinated.

GBS occurs at a rate of 10-20 cases per 1 million adults, per year, regardless of vaccination. Substantial evidence exists that multiple infectious illnesses, most notably *Campylobacter jejuni* gastrointestinal infections and upper respiratory tract infections, including respiratory illness caused by influenza, are associated with GBS.

In general, seasonal flu vaccine has not been found to increase the risk for GBS. If a risk exists, it is low (i.e., approximately one additional case per 1 million persons vaccinated). The potential benefits of flu vaccination in preventing serious illness, hospitalization, and death substantially outweigh this estimate of risk for flu vaccine-associated GBS. Persons who have previously had GBS should not receive influenza vaccine.⁴

What can providers do if there is a clinical adverse event following vaccine administration?

The Vaccine Adverse Event Reporting System (VAERS) is a US vaccine safety surveillance system, co-managed by CDC and FDA.

Clinically significant adverse events that follow vaccination should be reported to VAERS. Reports may be filed securely online at <http://vaers.hhs.gov/>, by mail, or by fax. Report forms are available online or can be obtained by calling 1-800-822-7967 to request reporting forms or other assistance.⁴

Sources:

1. CDC. *Questions & Answers: 2009 H1N1 Nasal Spray Vaccine*, October 7, 2009. http://www.cdc.gov/h1n1flu/vaccination/nasalspray_qa.htm
2. CDC. *H1N1 Clinicians Questions and Answers*, October 23, 2009. http://www.cdc.gov/h1n1flu/vaccination/clinicians_qa.htm
3. CDC. *Frequently asked questions on use of influenza A(H1N1) 2009 monovalent vaccines (2009 H1N1 monovalent influenza vaccines): Practical considerations for immunization programs and providers*, November 10, 2009. http://www.cdc.gov/H1N1flu/vaccination/top10_faq.htm
4. CDC. *2009 H1N1 Influenza Vaccine and Pregnant Women: Information for Healthcare Providers*, November 2, 2009. http://www.cdc.gov/h1n1flu/vaccination/providers_qa.htm