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Using Live, Attenuated Influenza Vaccine for Prevention and Control of Influenza

Supplemental Recommendations of the Advisory Committee on Immunization Practices (ACIP)

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Using Live, Attenuated Influenza Vaccine for Prevention and Control of Influenza

Supplemental Recommendations of the Advisory Committee on Immunization Practices (ACIP)

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Summary

This report summarizes recommendations by the Advisory Committee on Immunization Practices (ACIP) for using intranasally administered, trivalent, cold-adapted, live, attenuated influenza vaccine (LAIV), which was approved for use in the United States on June 17, 2003 (FluMist™, produced by MedImmune, Inc., Gaithersburg, Maryland). LAIV is currently approved for use among healthy persons (i.e., those not at high risk for complications from influenza infection) aged 5–49 years. This report includes information regarding 1) vaccine composition and mechanisms of action; 2) comparison between LAIV and trivalent inactivated influenza vaccine; 3) effectiveness and safety of LAIV; 4) transmission and stability of LAIV viruses; 5) recommendations and contraindications for using LAIV; and 6) dosage and administration of LAIV. This report supplements the 2003 ACIP recommendations regarding prevention and control of influenza (CDC. Prevention and Control of Influenza: Recommendations of the Advisory Committee on Immunization Practices [ACIP]. MMWR 2003;52[No. RR-8]:1–36.)

Introduction

Each year, influenza virus infections cause substantial morbidity and mortality in the United States (*1*). Prevention of influenza relies primarily on vaccination. Until recently, only inactivated influenza vaccine administered by injection was available for use in the United States. Inactivated influenza vaccine is approved for persons aged ≥6 months, both with and without chronic medical conditions. In 2003, an intranasal, trivalent, cold-adapted, live, attenuated vaccine (LAIV) was newly approved for use among healthy persons aged 5–49 years. LAIV adds an option for vaccinating healthy persons aged 5–49 years who either want to avoid influenza or who have close contact with persons at high risk for experiencing serious complications from influenza infection.

The material is this report originated in the National Center for Infectious Diseases, James M. Hughes, M.D., Director, and the Division of Viral and Rickettsial Diseases, James LeDuc, Ph.D., Director; and the National Immunization Program, Walter A. Orenstein, M.D., Director, and Epidemiology and Surveillance Division, Melinda Wharton, M.D., Director.

Description and Action Mechanisms of LAIV

LAIVs are in use in Russia and have been in development since the 1960s in the United States, where they have been evaluated as mono-, bi-, and trivalent formulations (*2–6*). The newly licensed LAIV is produced by MedImmune, Inc., (Gaithersburg, Maryland; http://www.medimmune.com) and marketed under the name FluMist™. It is a live, trivalent, intranasally administered vaccine that is

- attenuated, producing mild or no signs or symptoms related to influenza virus infection;
- temperature-sensitive, a property that limits the replication of the vaccine viruses at 38°C–39°C, and thus restricts LAIV viruses from replicating efficiently in human lower airways; and
- cold-adapted, replicating efficiently at 25°C, a temperature that is permissive for replication of LAIV viruses, but restrictive for replication of different wild-type viruses.

In animal studies, LAIV viruses replicate in the mucosa of the nasopharynx, inducing protective immunity against

viruses included in the vaccine, but replicate inefficiently in the lower airways or lungs. Identical to inactivated influenza vaccine, LAIV contains strains representative of each of the three influenza viruses recommended by the U.S. Public Health Service (*1*). For the 2003–04 influenza season, both inactivated influenza vaccine and LAIV contain A/New Caledonia/20/99-like (H1N1), A/Panama/2007/99-like (H3N2), and B/Hong Kong/330/2001-like viruses.

The first step in developing an LAIV was the derivation of two stably attenuated master donor viruses (MDV), one for type A and one for type B influenza viruses. The two MDVs each acquired the cold-adapted, temperature-sensitive, attenuated phenotypes through serial passage in viral culture conducted at progressively lower temperatures. The vaccine viruses in LAIV are reassortant viruses containing genes from these MDVs that confer attenuation, temperature sensitivity, and cold adaptation and genes from the recommended contemporary wild-type influenza viruses, encoding the surface antigens hemagglutinin (HA) and neuraminidase (NA). Thus, MDVs provide the stably attenuated vehicles for presenting influenza HA and NA antigens, to which the protective antibody response is directed, to the immune system. The reassortant vaccine viruses are grown in embryonated hens' eggs. After the vaccine is formulated and inserted into individual sprayers for nasal administration, the vaccine must be stored at –15°C or colder.

The immunogenicity of the approved LAIV has been assessed in multiple studies (*7–15*), which included approximately 100 children aged 5–17 years, and approximately 300 adults aged 18–49 years. LAIV virus strains replicate primarily in nasopharyngeal epithelial cells. The protective mechanisms induced by vaccination with LAIV are not completely understood but appear to involve both serum and nasal secretory antibodies. No single laboratory measurement closely correlates with protective immunity induced by LAIV.

Comparison of LAIV with Inactivated Influenza Vaccine

Major Similarities

LAIV and inactivated influenza vaccine contain strains of influenza viruses that are antigenically equivalent to the annually recommended strains: one influenza A (H3N2) virus, one A (H1N1) virus, and one B virus. Each year, one or more virus strains might be changed on the basis of global surveillance for influenza viruses and the emergence and spread of new strains. Viruses for both vaccines are grown in eggs. Both vaccines are administered annually to provide optimal protection against influenza infection. This report includes a more detailed comparison of LAIV with inactivated influenza vaccine (Tables 1 and 2).

Major Differences

Inactivated influenza vaccine contains killed viruses, whereas LAIV contains attenuated viruses still capable of replication. LAIV is administered intranasally by sprayer, whereas inactivated influenza vaccine is administered intramuscularly by injection. LAIV is more expensive than inactivated influenza vaccine. LAIV is approved for use only among healthy persons aged 5–49 years; inactivated influenza vaccine is approved for use among persons aged ≥6 months, including those who are healthy and those with chronic medical conditions. This report includes a more detailed comparison of LAIV with inactivated influenza vaccine (Tables 1 and 2).

Efficacy and Effectiveness of LAIV

Efficacy Among Healthy Children

A randomized, double-blind, placebo-controlled trial among 1,602 healthy children initially aged 15–71 months assessed the efficacy of the trivalent LAIV against culture-confirmed influenza during two seasons* (*8,9*). This trial included subsets of 238 healthy children (163 vaccinees and 75 placebo recipients) aged 60–71 months who received two doses and 74 children (54 vaccinees and 20 placebo recipients) aged 60–71 months who received a single dose during season one, and a subset of 544 children (375 vaccinees and 169 placebo recipients) aged 60–84 months during season two. Children who continued from season one to season two remained in the same study group. In season one, when vaccine and circulating virus strains were well-matched, efficacy was 93% for all participants, regardless of age, among subjects receiving 2 doses of LAIV. Efficacy was 87% in the 60–71-month subset for those who received 2 doses, and was 91% in the subset for those who received 1 or 2 doses. In season two, when the A (H3N2) component was not well-matched between vaccine and circulating virus strains, efficacy was 86% overall and 87% among those aged 60–84 months. The vaccine was 92% efficacious in preventing culture-confirmed influenza during the two-season study. Other results included a 27% reduction in febrile otitis media and a 28% reduction in otitis media with concomitant antibiotic use. Receipt of LAIV also resulted in decreased fever and otitis media among vaccine recipients who experienced influenza.

* Influenza seasons usually occur October—May.

TABLE 1. Live, attenuated influenza vaccine (LAIV) compared with inactivated influenza vaccine

Characteristic	LAIV	Inactivated influenza vaccine
Route of administration	Intranasal spray	Intramuscular injection
Type of vaccine	Live virus	Killed virus
Number of included virus strains	3 (2 influenza A, 1 influenza B)	Same as LAIV
Vaccine virus strains updated	Annually	Same as LAIV
Frequency of administration	Annually	Same as LAIV
Can be administered to children and adults at high risk* for complications resulting from influenza infection	No	Yes
Can be administered to family members or close contacts of immunosuppressed persons	Inactivated influenza vaccine preferred	Yes†
Can be administered to family members or close contacts of persons at high risk but who are immunocompetent	Yes	Yes
Can be simultaneously administered with other vaccines	Yes§	Yes¶
If not simultaneously administered, can be administered within 4 weeks of another live vaccine	Prudent to space 4 weeks apart	Yes
If not simultaneously administered, can be administered within 4 weeks of an inactivated vaccine	Yes	Yes

* Populations at high risk from complications of influenza infection include persons aged ≥65 years; residents of nursing homes and other facilities that house persons with chronic medical conditions; adults and children with chronic disorders of the pulmonary or cardiovascular systems; adults and children with chronic metabolic diseases (including diabetes mellitus), renal dysfunction, hemoglobinopathies, or immunnosuppression; children and adolescents receiving long-term aspirin therapy (at risk for developing Reye syndrome after wild-type influenza infection); and women who will be in the second or third trimester of pregnancy during influenza season.
† Immunosuppressed persons include, but are not limited to, those persons with human immunodeficiency virus, malignancy, or those receiving immunosuppressive therapies.
§ No data are available regarding effect on safety or efficacy.
¶ Inactivated influenza vaccine coadministration with pneumococcal polysaccharide vaccine has been evaluated systematically only among adults.

TABLE 2. Recommended vaccines for different age groups

Vaccine	Age groups			
	6 mos–3 yrs	4 yrs	5–49 yrs	≥50 yrs
FluMist™ (MedImmune, Inc.)			X	
Fluvirin™ (Evans Vaccines, Ltd.)		X	X	X
Fluzone® (Aventis Pasteur, Inc.)	X*	X	X	X

* Children aged 6–35 months should receive 0.25 mL/dose. Children aged >35 months should receive 0.50 mL/dose.

Effectiveness and Efficacy Among Healthy Adults

A randomized, double-blind, placebo-controlled trial among 4,561 healthy working adults aged 18–64 years assessed multiple endpoints, including reductions in illness, absenteeism, health-care visits, and medication use during peak and total influenza outbreak periods (*16*). The study was conducted during the 1997–98 influenza season, when the vaccine and circulating A (H3N2) strains were not well-matched. The study did not include laboratory virus testing of cases. During peak outbreak periods, no difference was identified between LAIV and placebo recipients experiencing any febrile episodes. However, vaccination was associated with reductions in severe febrile illnesses of 19% and febrile upper respiratory tract illnesses of 24%. Vaccination also was associated with fewer days of illness, fewer days of work lost, fewer days with health-care provider visits, and reduced use of prescription antibiotics and over-the-counter medications.

Among the subset of 3,637 healthy adults aged 18–49 years, LAIV recipients (n = 2,411) had 26% fewer febrile upper respiratory illness episodes; 27% fewer lost work days as a result of febrile upper respiratory illness; and 18%–37% fewer days of health-care provider visits caused by febrile illness, compared with placebo recipients (n = 1,226). Days of antibiotic use were reduced by 41%–45% in this age subset.

Another randomized, double-blind, placebo-controlled challenge study among 92 healthy adults (LAIV, n = 29; placebo, n = 31; inactivated influenza vaccine, n = 32) aged 18–41 years assessed the efficacy of both LAIV and trivalent inactivated vaccine (*15*). The overall efficacy of LAIV and inactivated influenza vaccine in preventing laboratory documented influenza from all three influenza strains combined was 85% and 71%, respectively, on the basis of experimental challenge by viruses to which study participants were susceptible before vaccination. The difference between the two vaccines was not statistically significant.

Person-to-Person Transmission of Vaccine Viruses

Because LAIV contains live influenza viruses, a potential exists for transmission of these viruses from vaccinees to other persons. Vaccinated immunocompetent children can shed vaccine viruses for ≤3 weeks (*6*). One unpublished study in a child care center setting assessed transmissibility of vaccine viruses from 98 vaccinated to 99 unvaccinated subjects, all aged 8–36 months. Eighty percent of vaccine recipients shed ≥1 virus strain, with a mean of 7.6 days duration (*17*). One influenza type B isolate was recovered from a placebo recipient and was confirmed to be vaccine-type virus. The estimated probability of acquiring vaccine virus after close contact with a single LAIV recipient was 0.58%–2.4%. The type B isolate retained the cold-adapted, temperature-sensitive, attenuated phenotype, and it possessed the same genetic sequence as a virus shed from a vaccine recipient in the same children's play group.

Stability of Vaccine Viruses

In clinical trials, viruses shed by vaccine recipients have been phenotypically stable. In one study, nasal and throat swab specimens were collected from 17 study participants for 2 weeks after vaccine receipt (*18*). Virus isolates were analyzed by multiple genetic techniques. All isolates retained the LAIV genotype after replication in the human host, and all retained the cold-adapted and temperature-sensitive phenotypes.

Recommendations for Influenza Vaccination

Recommendations for inactivated influenza vaccination have targeted specific groups for annual immunization, including persons aged ≥6 months who are at high risk for complications from influenza because of age or presence of certain medical conditions, persons who are in close contact with those at

high risk, persons aged 50–64 years, and close contacts of infants aged 0–6 months (*1*). Vaccination with inactivated influenza vaccine is also encouraged when feasible for children aged 6–23 months and their close contacts and caregivers. In addition, physicians should administer inactivated influenza vaccine to any person who wishes to reduce the likelihood of becoming ill with influenza. Recommendations for use of inactivated influenza vaccine are located at http://www.cdc.gov/mmwr/PDF/rr/rr5208.pdf.

Recommendations for Using Live, Attenuated Influenza Vaccine

LAIV is an option for vaccination of healthy persons aged 5–49 years, including persons in close contact with groups at high risk and those wanting to avoid influenza (Tables 1 and 2). Possible advantages of LAIV include its potential to induce a broad mucosal and systemic immune response, its ease of administration, and the acceptability of an intranasal rather than intramuscular route of administration (*1*).

Persons Who Should Not Be Vaccinated with LAIV

The following populations should not be vaccinated with LAIV:

- persons aged <5 years or those aged ≥50 years;[†]
- persons with asthma, reactive airways disease or other chronic disorders of the pulmonary or cardiovascular systems; persons with other underlying medical conditions, including such metabolic diseases as diabetes, renal dysfunction, and hemoglobinopathies; or persons with known or suspected immunodeficiency diseases or who are receiving immunosuppressive therapies;[†]
- children or adolescents receiving aspirin or other salicylates (because of the association of Reye syndrome with wild-type influenza infection);[†]
- persons with a history of Guillain-Barré syndrome;
- pregnant women;[†] or
- persons with a history of hypersensitivity, including anaphylaxis, to any of the components of LAIV or to eggs.

Close Contacts of Persons at High Risk for Complications from Influenza

Close contacts of persons at high risk for complications from influenza should receive influenza vaccine to reduce transmission of wild-type influenza viruses to persons at high risk. No data are available assessing the risk for transmission of LAIV from vaccine recipients to immunosuppressed contacts. In the absence of such data, use of inactivated influenza vaccine is preferred for vaccinating household members, health-care workers, and others who have close contact with immunosuppressed persons because of the theoretical risk that a live, attenuated vaccine virus could be transmitted to the immunosuppressed person and cause disease. Otherwise, no preference is given to either inactivated influenza vaccine or LAIV for vaccination of healthy persons aged 5–49 years in close contact with all other groups at high risk.

Timing of LAIV Administration

Administration of LAIV is not subject to tiered timing recommendations because it is not approved for use among populations at high risk. The optimal time to vaccinate is usually in October and November, but providers can begin vaccinating with LAIV as soon as vaccine supplies are available. Children aged 5–8 years who have never received influenza vaccine should receive LAIV for the first time in October or earlier because they need a second dose 6–10 weeks after the initial dose.

Dosage, Administration, and Storage

LAIV Dosage

LAIV is intended for intranasal administration only and should not be administered by the intramuscular, intradermal, or intravenous route. LAIV must be stored at –15°C or colder. LAIV should not be stored in a frost-free freezer (because the temperature might cycle above –15°C), unless a manufacturer-supplied freezer box is used. LAIV must be thawed before administration. This can be accomplished by holding an individual sprayer in the palm of the hand until thawed, with subsequent immediate administration. Alternatively, the vaccine can be thawed in a refrigerator and stored at 2°C–8°C for ≤24 hours before use. Vaccine should not be refrozen after thawing. LAIV is supplied in a prefilled single-use sprayer containing 0.5 mL of vaccine. Approximately 0.25 mL (i.e., half of the total sprayer contents) is sprayed into the first nostril while the recipient is in the upright position. An attached dose-divider clip is removed from the sprayer to administer the second half of the dose into the other nostril. If the vaccine recipient sneezes after administration, the dose should not be repeated.

LAIV should be administered annually according to the following schedule:

- Children aged 5–8 years previously unvaccinated at any time with either LAIV or inactivated influenza vaccine should receive 2 doses[§] of LAIV separated by 6–10 weeks.

[†] These persons should receive inactivated influenza vaccine.

[§] One dose equals 0.5 mL, divided equally between each nostril.

- Children aged 5–8 years previously vaccinated at any time with either LAIV or inactivated influenza vaccine should receive 1 dose of LAIV. They do not require a second dose.
- Persons aged 9–49 years should receive 1 dose of LAIV.

LAIV can be administered to persons with minor acute illnesses (e.g., diarrhea or mild upper respiratory tract infection with or without fever). However, if clinical judgment indicates nasal congestion is present that might impede delivery of the vaccine to the nasopharyngeal mucosa, deferral of administration should be considered until resolution of the illness.

Whether concurrent administration of LAIV with other vaccines affects the safety or efficacy of either LAIV or the simultaneously administered vaccine is unknown. In the absence of specific data indicating interference, following the ACIP general recommendations for immunization is prudent (*19*). Inactivated vaccines do not interfere with the immune response to other inactivated vaccines or to live vaccines. An inactivated vaccine can be administered either simultaneously or at any time before or after LAIV. Two live vaccines not administered on the same day should be administered ≥4 weeks apart when possible.

LAIV Administration and Use of Influenza Antiviral Medications

The effect on safety and efficacy of LAIV coadministration with influenza antiviral medications has not been studied. However, because influenza antivirals reduce replication of influenza viruses, LAIV should not be administered until 48 hours after cessation of influenza antiviral therapy, and influenza antiviral medications should not be administered for 2 weeks after receipt of LAIV.

LAIV Storage

LAIV must be stored at –15°C or colder. LAIV should not be stored in a frost-free freezer because the temperature might cycle above –15°C, unless a manufacturer-supplied freezer box or other strategy is used. LAIV may be thawed in a refrigerator and stored at 2°C–8°C for ≤24 hours before use. It should not be refrozen after thawing. Additional information is available at Wyeth Product Quality (1-800-411-0086) or at http://www.FluMist.com.

Side Effects and Adverse Reactions

Twenty prelicensure clinical trials assessed the safety of the approved LAIV. In these combined studies, approximately 28,000 doses of the vaccine were administered to >20,000 subjects. A subset of these trials were randomized, placebo-controlled studies in which >4,000 healthy children aged 5–17 years and >2,000 healthy adults aged 18–49 years were vaccinated. The incidence of adverse events possibly complicating influenza (e.g., pneumonia, bronchitis, bronchiolitis, or central nervous system events) was not statistically different among LAIV and placebo recipients aged 5–49 years.

Children

Signs and symptoms reported more often among vaccine recipients than placebo recipients included runny nose or nasal congestion (20%–75%), headache (2%–46%), fever (0%–26%), and vomiting (3%–13%), abdominal pain (2%), and myalgias (0%–21%) (*7,12,14,20–22*). These symptoms were associated more often with the first dose and were self-limited. In a subset of healthy children aged 60–71 months from one clinical trial (*8,9*), certain signs and symptoms were reported more often among LAIV recipients after the first dose (n = 214) than placebo recipients (n = 95) (e.g., runny nose, 48.1% versus 44.2%; headache, 17.8% versus 11.6%; vomiting, 4.7% versus 3.2%; myalgias, 6.1% versus 4.2%), but these differences were not statistically significant. 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 among children aged <60 months (see Recommendations for Using Live, Attenuated Influenza Vaccine).

Adults

Among adults, runny nose or nasal congestion (28%–78%), headache (16%–44%), and sore throat (15%–27%) have been reported more often among vaccine recipients than placebo recipients (*16,23,24*). In one clinical trial (*16*), among a subset of healthy adults aged 18–49 years, signs and symptoms reported more frequently among LAIV recipients (n = 2,548) than placebo recipients (n = 1,290) within 7 days after each dose included cough (13.9% versus 10.8%); runny nose (44.5% versus 27.1%); sore throat (27.8% versus 17.1%); chills (8.6% versus 6.0%); and tiredness/weakness (25.7% versus 21.6%).

Safety Among Groups at High Risk from Influenza-Related Morbidity

Until additional data are acquired, persons at high risk for experiencing complications from influenza infection (e.g., immunocompromised patients; patients with asthma, cystic fibrosis, or chronic obstructive pulmonary disease; or persons aged ≥65 years) should not be vaccinated with LAIV. Protection from influenza in these groups should be accomplished

by using inactivated influenza vaccine (see Recommendations for Using Live, Attenuated Influenza Vaccine).

Serious Adverse Events

Serious adverse events among healthy children aged 5–17 years or healthy adults aged 18–49 years occurred at a rate of <1%. Surveillance should continue for adverse events that might not have been detected in previous studies.

References

1. CDC. Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2003;52(No. RR-08):1–36.
2. Kendal AP, Maassab HF, Alexandrova GI, Ghendon YZ. Development of cold-adapted recombinant live, attenuated influenza A vaccines in the U.S.A. and U.S.S.R. Antiviral Res 1981;1:339–65.
3. Maassab HF, DeBorde DC. Development and characterization of cold-adapted viruses for use as live virus vaccines. Vaccine 1985;3:355–69.
4. Murphy BR. Use of live attenuated cold-adapted influenza A reassortant virus vaccines in infants, children, young adults, and elderly adults. Infect Dis Clin Pract 1993;2:174–81.
5. Potter CW. Attenuated influenza virus vaccines. Rev Med Virol 1994;4:279–92.
6. Clements ML, Stephens I. New and improved vaccines against influenza. In: Levine MM, Woodrow GC, Kasper JB, et al., eds. New generation vaccines. New York: Marcel Dekker, Inc 1997:645–70.
7. King JC, Lagos R, Bernstein DI, et al. Safety and immunogenicity of low and high doses of trivalent live cold-adapted influenza vaccine administered intranasally as drops or spray to healthy children. J Infect Dis 1998;177:1394–7.
8. Belshe RB, Mendelman PM, Treanor J, et al. Efficacy of live attenuated, cold-adapted, trivalent, intranasal influenzavirus vaccine in children. N Engl J Med 1998;338:1405–12.
9. Belshe RB, Gruber WC, Mendelman PM, et al. Efficacy of vaccination with live attenuated, cold-adapted, trivalent, intranasal influenza virus vaccine against a variant (A/Sydney) not contained in the vaccine. J Peds 2000;136:168–75.
10. Belshe RB, Gruber WC, Mendelman PM, et al. Correlates of immune protection induced by live, attenuated, cold-adapted, trivalent, intranasal influenza virus vaccine. J Infect Dis 2000;181:1133–7.
11. Boyce TG, Gruber WC, Coleman-Dockery SD, et al. Mucosal immune response to trivalent live attenuated intranasal influenza vaccine in children. Vaccine 2000;18:82–8.
12. Zangwill KM, Droge J, Mendelman P, et al. Prospective, randomized, placebo-controlled evaluation of the safety and immunogenicity of three lots of intranasal trivalent influenza vaccine among young children. Pediatr Infect Dis J 2001;20:740–6.
13. Bernstein DI, Yan L, Treanor J, et al. Effect of yearly vaccinations with live, attenuated, cold-adapted, trivalent, intranasal influenza vaccines on antibody responses in children. Pediatr Infect Dis J 2003;22:28–34.
14. Nolan T, Lee M-S, Cordova JM, et al. Safety and immunogenicity of a live-attenuated influenza vaccine blended and filled at two manufacturing facilities. Vaccine 2003;21:1224–31.

15. Treanor JJ, Kotloff K, Betts RF, et al. Evaluation of trivalent, live, cold-adapted (CAIV-T) and inactivated (TIV) influenza vaccines in prevention of virus infection and illness following challenge of adults with wild-type influenza A (H1N1), A (H3N2), and B viruses. Vaccine 2000;18:899–906.
16. Nichol KL, Mendelman PM, Mallon KP, et al. Effectiveness of live, attenuated intranasal influenza virus vaccine in healthy, working adults: a randomized controlled trial. JAMA 1999;281:137–144.
17. Vesikari T, et al. Randomized, double-blind, placebo-controlled trial of the safety, transmissibility and phenotypic stability of a live, attenuated, cold-adapted influenza virus vaccine (CAIV-T) in children attending day care [Abstract G-450]. Presented at the 41st Annual Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), Chicago, IL, 2001.
18. Cha TA, Kao K, Zhao J, Fast PE, Mendelman PM, Arvin A. Genotypic stability of cold-adapted influenza virus vaccine in an efficacy clinical trial. J Clin Micro 2000;38:839–45.
19. CDC. General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP) and the American Academy of Family Physicians (AAFP). MMWR 2002;51(No. RR-2):1–35.
20. King JC, Fast PE, Zangwill KM, et al. Safety, vaccine virus shedding and immunogenicity of trivalent, cold-adapted, live attenuated influenza vaccine administered to human immunodeficiency virus-infected and noninfected children. Pediatr Infect Dis J 2001;20:1124–31.
21. Redding G, Walker RE, Hessel C, et al. Safety and tolerability of cold-adapted influenza virus vaccine in children and adolescents with asthma. Pediatr Infect Dis J 2002;21:44–8.
22. Piedra PA, Yan L, Kotloff K, et al. Safety of the trivalent, cold-adapted influenza vaccine in preschool-aged children. Pediatrics 2002;110:662–72.
23. Jackson LA, Holmes SJ, Mendelman PM, Huggins L, Cho I, Rhorer J. Safety of a trivalent live attenuated intranasal influenza vaccine, FluMist™, administered in addition to parenteral trivalent inactivated influenza vaccine to seniors with chronic medical conditions. Vaccine 1999;17:1905–9.
24. King JC, Treanor J, Fast PE, et al. Comparison of the safety, vaccine virus shedding and immunogenicity of influenza virus vaccine, trivalent, types A and B, live cold-adapted, administered to human immunodeficiency virus (HIV)-infected and non-HIV-infected adults. J Infect Dis 2000;181:725–8.

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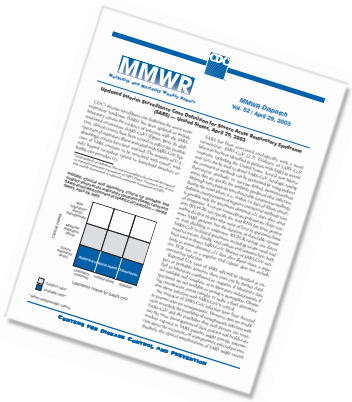
up-to-the-minute: *adj*

1 : extending up to the immediate present, including the very latest information; see also *MMWR*.



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