

Strategies for Use of a Limited Influenza Vaccine Supply

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THE DRASTICALLY DECREASED SUPPLY OF INACTIVATED influenza vaccine for the 2004-2005 US influenza season presents a unique challenge for health care institutions. At the core of this challenge is the dual responsibility that health care institutions have to protect patients as well as the health professionals who are integral to the functioning of the institution. Many major hospitals and long-term care facilities have reduced or no supplies of inactivated influenza vaccine and have limited guidance about how to obtain additional vaccine or whether to expect redistribution from the remaining supply. Consequently, issues have arisen ranging from the appropriate allocation of vaccine to the role of the intranasal live, attenuated influenza vaccine (LAIV) within a health care institution. These issues pose an interesting juxtaposition of science, public policy, politics, law, and ethics. This article will briefly review available literature that may assist institutions in making the difficult decisions associated with an influenza vaccine shortage.

Vaccination of Health Professionals

Nosocomial transmission of influenza has been increasingly recognized as a cause of significant morbidity and cost.¹ Vaccination of health professionals has been recommended to reduce the risk of influenza transmission to patients. In a study conducted in geriatric long-term care facilities during the 1994-1995 influenza season, vaccination of clinicians and other health care workers who have direct patient contact reduced patient mortality from 17% to 10%.² In contrast, vaccination of patients at the same facility did not affect mortality.

Vaccination of healthy working adults also minimizes absenteeism and maintains an adequate workforce.³ In a ran-

domized study with 359 person-winters of serologic surveillance, vaccinated health professionals were less likely to develop serologic evidence of influenza (1.7% vs 13.4% of unvaccinated controls) and had fewer days of absence from work (9.9/100 in the vaccination group vs 21.1/100 in the control group).⁴

Defining High-Risk Chronic Medical Conditions

In the face of the current shortage of influenza vaccine, the revised Centers for Disease Control and Prevention recommendations for which individuals should preferentially receive influenza vaccine should be used (BOX 1).⁵ In addition, as of January 3, 2005, the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices has recommended that in areas where public health authorities determine that there is adequate influenza vaccine supply, adults aged 50-64 and close contacts of individuals in high risk groups are also eligible for vaccination.⁶ Determining which children and adults meet most of these criteria is straightforward. However, defining persons with underlying chronic medical conditions can present a challenge because different degrees of risk of influenza complications are associated with various chronic medical conditions, and some are likely not associated with increased risk. Individuals with certain chronic medical conditions are at highest risk for influenza complications. These suggestions are meant to guide clinicians who have a limited vaccine supply; there may be other conditions that health professionals judge to confer influenza risk.

Individuals Who Are Unlikely to Have an Adequate Immunologic Response to Influenza Vaccine

Studies of the use of inactivated vaccine in certain immunosuppressed patients have demonstrated diminished or

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Box 1. Priority Populations for Influenza Vaccination and Underlying Medical Conditions at High Risk for Influenza Complications

Characteristics of Prioritized Populations

Aged 6-23 months
 Aged 65 years or older
 Pregnant
 Residents of nursing homes and long-term care facilities
 Aged 6 months to 18 years receiving chronic aspirin therapy
 Health workers and professionals involved in direct patient care
 Out-of-home caregivers and household contacts of individuals aged 6 months or younger
 Aged 2 to 64 years with underlying chronic medical conditions

Underlying Chronic Medical Conditions at Particularly High Risk for Complications From Influenza

Acute leukemia
 Chronic leukemia
 Dialysis dependence
 End-stage liver disease
 Heart failure (ejection fraction < 40%)
 Hematopoietic stem cell transplant*
 Hemodynamically significant congenital heart disease
 Human immunodeficiency virus (HIV)*
 Type 1 diabetes mellitus
 Moderate to severe underlying lung disease
 Reactive airway disease requiring daily therapy
 Rheumatologic, hematologic, or inflammatory bowel disease requiring immunosuppression
 Sickle cell anemia
 Solid organ malignancy currently undergoing therapy
 Solid organ transplant*

*Patients receiving hematopoietic stem cell transplant within less than 6 months, solid organ transplant within less than 3 months, or HIV with CD4 cell counts $\leq 100/\mu\text{L}$ are unlikely to have an adequate immunologic response to influenza vaccine.

absent immune responses to vaccination. Specifically, patients who have had hematopoietic stem cell transplant within 6 months, have human immunodeficiency virus infection (HIV) with CD4 counts less than 100 to 200 cells/ μL , and have had solid organ transplant and are receiving aggressive immunosuppressive regimens in the first 3 months following transplantation are unlikely to benefit from vaccination.⁷ Alternative methods of prevention and prophylaxis may prove more effective.

Other Strategies to Extend Injectable Influenza Vaccine Supply

In a study evaluating the efficacy of administering half doses of inactivated, injectable vaccine in the 2000-2001 season,⁸ young healthy patients had appropriate immunologic response to the reduced dose, but the clinical efficacy was not studied. Similarly, in 2 recent studies that examined intradermal administration of reduced vaccine doses,^{9,10} vaccinated participants demonstrated an appropriate immunologic response, but clinical efficacy was not evaluated. Thus, although these strategies are promising, there are not enough data to recommend them at this point.

Another approach for extending injectable influenza vaccine supply is to use syringes with minimal dead space. When regular syringes are used, a small amount of vaccine is left in the dead space of the syringe after the injection. However, the use of syringes that have been designed to minimize this dead space can yield up to 2 additional doses of vaccine from each 5-mL vial of influenza vaccine.¹¹

Role of Intranasal LAIV in the Health Care Setting

Some institutions have received LAIV and will use it for health professionals in lieu of inactivated vaccine, and thus, preserve inactivated vaccine for patients at highest risk for influenza complications. Two major issues regarding the use of LAIV exist—the current US Food and Drug Administration labeling of the product and the administration of a live virus in health care settings. The live vaccine is US Food and Drug Administration approved only for healthy individuals aged 5 through 49 years; however, many healthy clinicians are older than 49 years of age. Fortunately, a growing number of studies indicate that LAIV is effective in such persons. In the study that supported LAIV licensure, LAIV was equally effective in adults younger than 50 years of age and adults aged 50 to 64 years in reducing episodes of influenza-like illness.¹² Although days of work missed due to influenza-like illness were not significantly decreased in the younger cohort, days absent from work were significantly reduced by 19.9% when the older cohort was included. In addition, serious adverse events were not noted in vaccine recipients between 50 and 64 years or in a second study of elderly LAIV recipients aged 65 or more years with chronic cardiovascular disease, pulmonary disease, or diabetes.¹³ LAIV also appears to be safe in HIV-infected adults and children with CD4 counts of more than 200 cells/ μL .^{14,15}

These data support the efficacy and safety of LAIV in healthy adults older than 49 years, especially those aged 50 through 65 years. Given that many health professionals would otherwise receive no vaccine during this influenza season, its use in healthy persons older than 49 years appears reasonable as a public health intervention despite the lack of a US Food and Drug Administration indication in this group.

There is concern that health professionals will shed the vaccine virus from their nasopharynx, placing their patients and colleagues at risk for secondary influenza infection. This concern is likely overestimated, since several events must occur for a person recently vaccinated with LAIV to effectively transmit virus and for that virus to result in a clinical infection: (1) the vaccine recipient must shed the attenuated vaccine virus, (2) the amount of virus shed must be of sufficient quantity to result in secondary acquisition, (3) once acquired, the attenuated virus must lose its temperature-sensitive phenotype to allow replication in the lower airways, and (4) the attenuated virus must revert to wild type and produce disease.

Although children are known to have prolonged nasopharyngeal shedding after LAIV vaccination, shedding in adults occurs less frequently, at a lower level, and for a shorter duration. In a study of healthy adults aged 18 to 49 years, nasopharyngeal shedding was detected in 50% of participants at day 3 postvaccination, but in only 1 of 18 participants on day 7.¹⁶ HIV-infected patients who receive LAIV also have minimal shedding.¹⁴ Furthermore, in adults who shed virus, the quantity of virus shed, expressed as log₁₀ 50% tissue culture infectious dose (TCID₅₀), is lower than the LAIV dose required to infect an adult (10² TCID₅₀/mL vs 10⁵-10⁷ TCID₅₀/mL).^{17,18} Indeed, there have been no instances of symptomatic transmission of the vaccine virus reported in adults. The only documented case of person-to-person transmission of the vaccine virus occurred when one child transmitted vaccine virus to another in a daycare setting where there was presumably close contact and a higher level of shedding.¹⁹

In addition, the attenuated virus in the LAIV is a temperature-sensitive mutant that has marked restriction of replication at temperatures above 37°C to 39°C, which dramatically precludes its ability to replicate systemically or in the lower respiratory tract.¹⁷ The attenuated virus has been found to remain genotypically stable after replication in the human host.²⁰ Given that the attenuated virus has not been shown to lose its temperature sensitivity or revert to wild type, the likelihood that vaccination with attenuated virus would lead to clinical influenza in a secondary contact appears exceedingly unlikely.

Due to the reduced rate of shedding in adults after LAIV vaccination and the low rate of secondary transmission, the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices²¹ makes no recommendation for furlough of health professionals after vaccination with the exception of individuals who care for severely immunosuppressed persons (eg, patients with hematopoietic stem cell transplants) during the time that the patients are in a protective environment. Given the lack of clinical data regarding the safety of the LAIV in highly immunosuppressed patients with hematopoietic stem cell transplant, patients with acute leukemia, and premature infants, it may be preferable to avoid administration of LAIV

Box 2. Health Professionals Who Could Receive Live, Attenuated Influenza Vaccine (LAIV) Beyond the Current Guidelines and Those Who Should Not Receive LAIV

Characteristics of Professionals Who Could Receive LAIV

Breastfeeding

Aged 50 to 65 years

Chronic illnesses that have not required hospitalization within 1 year such as hypertension, well-controlled diabetes, and chronic renal insufficiency

Workers with immunocompromised patients, except patients receiving care on special units (hematopoietic stem cell transplant, acute leukemia, and neonatal intensive care units)

Characteristics of Professionals Who Should Not Receive LAIV

Currently with febrile illness*

Currently receiving influenza antivirals

History of reactive airways disease requiring daily therapy or other chronic lung disease

History of chronic illnesses requiring hospitalization within 1 year

History of serious allergy to eggs

History of other live virus vaccines in the past 4 weeks

History of Guillain-Barré syndrome in the 6 weeks after a prior influenza vaccination

Individuals who directly care for patients who are severely immunocompromised and hospitalized on special units (hematopoietic stem cell transplant, acute leukemia, and neonatal intensive care units)

Pregnant

*Should defer vaccination until acute illness resolved.

to health professionals whose primary responsibilities are the care of these patients.

Because of the need to use an efficacious vaccine in health professionals and to preserve the limited supply of inactivated vaccine for patients who cannot receive LAIV, the use of LAIV should be considered for other groups of health professionals not specified in the current guidelines (BOX 2). Health professionals who should not receive LAIV also are listed in Box 2.

Nonvaccine Methods to Prevent Influenza

During this 2004-2005 influenza season prevention of influenza transmission is especially important. Respiratory hygiene including wearing standard surgical masks if entering a health care environment with respiratory symptoms, cough etiquette, meticulous hand hygiene, and implemen-

tation of droplet precautions (standard precautions, private room for patients, and donning a standard surgical mask when working within 3 feet of a patient) for individuals presenting with respiratory symptoms and who are febrile are essential in limiting the spread of influenza in health care settings.²² Symptomatic, febrile employees must not be allowed to work, and restriction of hospital visitors may become necessary when respiratory viruses are actively circulating in the community. Administration of antiviral medications for 6 to 8 weeks has been used for prophylaxis of influenza in outbreaks involving health care institutions and for postexposure prophylaxis.²¹

Conclusion

The available evidence supports our recommendations to relax the criteria for administration of LAIV in the setting of the current vaccine shortage. These guidelines should help protect health professionals from transmitting disease, while maintaining the function of health care institutions and providing maximum protection for patients. In addition, our suggestions to make the criteria for the use of inactivated, injectable vaccine more stringent will hopefully assist in directing access to inactivated vaccine to individuals with the highest risk of complications due to influenza and to others who are most likely to benefit.

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