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eInfluenza Review

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Prevention and Control of Influenza in the Healthcare Setting

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In this issue...

The threat of pandemic influenza and potentially virulent strains of avian origin is forcing infection control and public health professionals to review currently recommended strategies to prevent transmission of influenza virus in healthcare settings. This focus is particularly important in settings that serve patients at increased risk of influenza complications, i.e. where medical care requires close contact or the use of procedures that facilitate transmission of the virus, and where individuals may not recognize they are infected and thus contribute to viral transmission among patients, visitors, and healthcare workers. Interestingly, little new data have emerged about influenza transmission in healthcare settings or the efficacy of commonly used strategies. However, a body of evidence from the SARS epidemic can provide us with clues about these potential risks.

In this issue, to guide practitioners in developing strategies for those who are at the highest risk of exposure, transmission, and complications, we focus on the efficacy of vaccination, types of vaccination, and the use of personal protective equipment (PPE).

THIS ISSUE

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At the conclusion of this activity, participants should be able to:

- Describe evidence-based procedures healthcare workers can use to prevent transmission of influenza;
- Identify potential strategies to prioritize influenza vaccine among patients and healthcare workers;
- Explain how the influenza virus is transmitted and various situational factors that can impact transmission.

COMMENTARY

Four key issues are relevant to influenza prevention and control efforts in healthcare settings. The first is the question of how the virus is transmitted. Experts agree that influenza virus is transmitted through large droplets which are generally transmitted 3 to 6 feet. In addition, influenza virus is known to survive on hard and porous surfaces for hours, a fact that supports the role of the environment and direct contact as a source of infection among humans. More recently, however, investigators have been reviewing epidemiologic and experimental data that support virus transmission via small particles and the airborne route. Tellier's 2006 report for the CDC, reviewed herein, provides important new data that can impact decisions for the types of protection proposed.

The second issue involves preventing transmission of the virus, and is especially important in the context of a virulent virus where vaccine and/or anti-influenza drugs may not be available. While we all agree that influenza vaccination is one of the primary mechanisms of prevention, we must be prepared not to have vaccine for 4 to 6 months and when available to have it in limited quantities. The 2005 JAMA article by Cosgrove et al provides guidance for practitioners on how to most effectively distribute a limited vaccine supply so that those who are likely to respond to it and those who are at greatest risk of complications from influenza infection receive it, as well as prioritizing those who will not respond to receiving antiviral agents. Adding further to our understanding is a 2006 report from the BMJ by Hayward et al on a controlled clinical trial evaluating how vaccination of healthcare workers affects patient mortality, the rate of influenza-like illness, and the use of healthcare resources.

The third issue, also focused on preventing transmission, relates to respiratory protection. Practitioners need to understand the most current data regarding respirators, so that should (or when) a pandemic influenza event occurs, they can best protect healthcare workers who will be key in the diagnosis, care, and management of influenza cases. It is this understanding that will promote the best use of limited resources and the adoption of public health recommendations. Balazy's 2006 series of experiments, using manikins to evaluate the efficacy of two different types of N95 masks and two different types of surgical masks in preventing penetration of aerosolized MS2 virus, provides some surprising (and concerning) results.

Finally, there is the difficult issue of healthcare worker compliance with prevention and control recommendations. Moore provides an extensive review of the literature that looks at the organizational and personal characteristics that promote

compliance with precautions. Although much of the data is drawn from the SARS epidemics, its relevance to influenza is obvious.

Preparation for seasonal and pandemic influenza requires an understanding of the disease and its epidemiology, as well as an ability to implement key prevention and control strategies. The role of hand hygiene within the home and healthcare setting cannot be overemphasized in prevention of any respiratory disease. Strategies to prevent transmission such as respiratory etiquette programs will be critical in our prevention efforts. The data presented herein will provide key background to allow practitioners to go beyond the traditional prevention strategies to minimize transmission and provide optimum patient care.

AEROSOL TRANSMISSION OF INFLUENZA A VIRUS

Tellier, R. **Review of Aerosol Transmission of Influenza A Virus**. Emerging Infect Dis. 2006 Nov;12(11).

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Traditionally, large droplet transmission has been thought to be the primary mode of spreading influenza A. Increasingly, however, contact with aerosols and contaminated secretions and fomites are being recognized as significant modes of influenza transmission. Tellier reviews the available evidence, through both experimental influenza infection and epidemiologic studies, that support the hypothesis that aerosol transmission of influenza may play a significant role in the spread of the virus. In addition, the author highlights the implications that aerosol transmission of influenza has with regards to infection control, and specifically discusses the type of personal protective equipment that should be used by healthcare workers caring for patients with influenza, especially in a pandemic setting.

An aerosol can be defined as a suspension of solid and/or liquid particles in gas, typically <5µm, that remains airborne for a prolonged period of time. Coughing, sneezing, and even laughing generates a large number of pathogen-containing aerosols that have the potential to cause infection in a human host. Some of the strongest laboratory evidence linking the role of aerosols to transmission of influenza infection results from an elegant series of studies performed by Alford et al in the 1960s[1]. Alford exposed a group of human volunteers to carefully titrated aerosolized influenza virus suspensions and then monitored the study subjects for either serologic conversion or recovery of virus from throat swabs taken daily. The investigators were able to show that not only did subjects exposed to aerosolized influenza particles develop clinical signs of infection, but that the 50% human infectious dose for the aerosolized influenza was significantly less than that observed when subjects were inoculated with intranasal drops (a proxy for large droplet transmission).

Additional epidemiologic observations support the hypothesis that aerosols are a source of transmission for influenza A. Moser et al reported on an influenza outbreak among 54 people who were aboard a commercial airliner with a nonfunctional ventilation system[2]. 72% of the passengers developed clinical signs/symptoms and/or serologic evidence of influenza infection within 3 days of the implicated flight. Additionally, at the Livermore Veterans Administration Hospital during the 1957-58 influenza pandemic[3], the seroconversion rate for influenza A was 19% for patients on a typical ward, as compared to only 2% on a ward with ceiling-mounted UV lighting (a technology that would kill viruses that are airborne). Staffing, illness, and all other factors were similar between the two wards. Interestingly, UV irradiation is very effective at killing viruses in aerosols but ineffective at surface decontamination or for large droplets. Both the Livermore and the airplane outbreaks strongly suggest aerosolization of influenza A virus leads to transmission among humans.

Tellier, after reviewing the available evidence for aerosol transmission of influenza, suggests that the use of surgical masks to protect healthcare workers caring for patients with influenza, particularly in a pandemic setting where a vaccine and prior immunity may not play a role in attenuating the disease, may

not be sufficient. N95 or other respirators are more effective at preventing transmission from aerosolized viruses and as such, could be potentially lifesaving in the event of an influenza pandemic.

Although the debate continues with regards to the nature of transmission of influenza from person to person, Tellier's review provides considerable experimental and epidemiologic evidence that aerosols likely play a significant role in the transmission of the influenza A virus. Given this evidence and the risk of transmission in healthcare settings, personal protective gear that includes highly filtered respirators (N95 or PAPRs) should be used by healthcare workers when caring for patients with highly virulent strains of influenza or where vaccine is delayed or not available. While not specifically discussed, gowns and gloves decrease the risk of contamination from environmental sources and should remain central components of infection control efforts to prevent influenza.

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METHODS OF MAXIMIZING A LIMITED INFLUENZA VACCINE SUPPLY

Cosgrove, SE, Fishman, NO, Talbot, TR, et al. **Strategies for use of a limited influenza vaccine supply**. JAMA. 2005;293(2):229-232.

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Vaccination continues to be the primary prevention method for influenza, a virus that infects 10-20% of the U.S. population yearly. The severe shortage of influenza vaccine during the winter of 2004-2005 and the ever-present threat of H5N1 or pandemic influenza has brought the issue of vaccine supply and its distribution to the forefront of the medical, public health, legal, and ethical arenas. Cosgrove et al recognized the immediacy of these issues, and reviewed the existing literature on influenza, influenza vaccine, and response to vaccine, in order to determine the most effective approaches for maximizing the distribution of the vaccine supply that is available.

The authors propose a tiered approach to vaccine distribution that includes those individuals that are exposed to infected patients (healthcare workers), those who commonly transmit infection to patients who are at high risk of influenza complications (healthcare workers and caregivers), and those that are at risk of complications but likely to respond to vaccine (patients with some ability to develop immunity). The authors' primary recommendations include: 1) the appropriate use of available influenza vaccine, including strategies to prolong the supply of injectable vaccine and effectively include intranasal live attenuated influenza vaccine (LAIV) into distribution plans, and 2) proposals about the use of non-vaccine methods to prevent influenza among persons who may not or can not respond to vaccine.

The importance of preferentially vaccinating those persons at extremes of age, those who are residents of long-term care facilities, or those with chronic medical conditions that place them at highest risk of the complications of influenza, seems obvious. It is important to note, however that due to impaired immunity, these individuals may not respond as efficiently as other members of the population to vaccination. A number of studies[1,2] have shown that patients who have recently received a bone marrow or solid organ transplant, or who have HIV with a CD4 count of less than 100, have markedly diminished immune responses to vaccination. In these circumstances, vaccination of the health care worker and patient contacts (children, family members) is required to more fully protect the patient.

Cosgrove et al also address the controversy over the appropriate use of LAIV. Given the lack of documented cases (in adults) of symptomatic transmission of the vaccine virus and the reduced rate of viral shedding, the authors propose that the use of LAIV could be extended to otherwise healthy individuals aged 50-65 (the vaccine is not currently FDA-labeled for persons over age 49), those with stable chronic illnesses (i.e. hypertension, well-controlled diabetes), and healthcare personnel who work with immunosuppressed patients (with the exception of those that mainly care for the most highly immunosuppressed groups such as neonates or patients with bone marrow transplants or acute leukemia). Infection control measures such as hand hygiene, use of droplet precautions (including wearing a surgical mask, gown and gloves when working within 3 feet of a patient with known or suspected influenza), and furlough of febrile employees remain crucial to the prevention of influenza transmission.

Summarizing Cosgrove's findings: despite the fact that the influenza vaccine is an indispensable health resource, the structure and organization of the current vaccine manufacturing system has led to recent distribution delays and vaccine shortages. In this setting of a limited vaccine supply, the expanded use of LAIV would allow increased vaccination of important groups who would otherwise go unvaccinated and are potential sources of significant nosocomial transmission. Among these groups, healthcare workers should be vaccinated[3], and are generally good candidates for LAIV. Those patients at highest risk of morbidity and mortality from influenza who cannot take LAIV should preferentially receive the injectable vaccine.

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BARRIERS TO HEALTHCARE WORKERS' ADHERENCE TO INFECTION CONTROL GUIDELINES

Moore, D, Gamage, B, et al. **Protecting healthcare workers from SARS and other respiratory pathogens: Organizational and individual factors that affect adherence to infection control guidelines**. AJIC. 2005;33(2): 88-96.

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The well-documented 2002-2003 nosocomial outbreaks of SARS in Canada, China, Hong Kong, Vietnam, and Singapore served as a wakeup call with regards to infection control practices among healthcare professionals throughout the world. The willingness and/or ability of healthcare workers to adhere to infection control practices, protocols, and guidelines varies widely from institution to institution and individual to individual. Behavioral scientists suggest that all individuals must have the knowledge, understanding, and the appropriate attitudes to comply with institutional (or national/federal) recommendations, and that effective behaviors need to be facilitated by providing supplies, engineering solutions, and reinforcing good practices. Moore et al reviewed 168 publications over the past 15 years to determine organizational and individual factors, beyond masks and standard procedures, which protect health care workers from acquiring or transmitting respiratory infectious diseases such as SARS or influenza while at work.

The authors identified a number of organizational factors that contribute in varying degrees to healthcare worker compliance with infection control practices. Perhaps most importantly, they found that a favorable institutional safety climate (i.e. worker perceptions about the importance of safety in their institution and the institution's level of commitment to safety) correlated with knowledge of and

compliance with standard precautions, and resulted in a decrease in blood and bodily fluid exposures[1,2]. Moore's review summarizes several available studies that show how feedback to workers about how their adherence to precautions improves compliance with infection control practices and procedures[3], and reinforces the importance of effective communication, training, and feedback in improving adherence to infection control policies. However (and unfortunately), the authors also found the long-term effectiveness of educational and feedback programs to be limited.

Additionally, factors attributed to the individual healthcare worker were reviewed. Increased knowledge (acquired both through training programs and through personal experience) and lower risk-taking tendencies were found to be associated with improved compliance. Not surprisingly, perceived barriers (i.e. interference with performing tasks, decreased ability to communicate while wearing masks, feeling overworked, lack of supplies, and lack of time with patients) decrease healthcare worker compliance with infection control practices[4].

In summary, Moore's extensive review of the available literature provides important insight into the barriers to healthcare worker compliance with infection control policies and practices. While the availability of personal protective equipment and standardized procedures are important components of an infection control prevention and control program, organizations that have the best compliance have well-managed training, feedback of compliance data, and an organizational-wide climate that promotes safety. The authors also point out the relative paucity of data in this area, especially with regards to respiratory pathogens, and the need for future research.

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VACCINATION OF HEALTHCARE WORKERS

Hayward, AC, Harling, R, et al. **Effectiveness of an influenza vaccine programme for care home staff to prevent death, morbidity and health service use among residents: cluster randomized controlled trial**. BMJ. 2006; 333: 1241. Epub 2006 Dec 1.

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Nosocomial transmission of influenza was described in the 1970s and is increasingly acknowledged as a cause of substantial morbidity and mortality. A number of studies over the past several years have documented the importance of vaccinating healthcare workers and have shown that this practice decreases not only mortality among patients but also worker absenteeism and illness[1,2]. The findings of the available studies, however, have been limited by small sample sizes[3]. Most recently, Hayward et al performed a large, cluster randomized, controlled clinical trial evaluating whether vaccination of healthcare workers affects patient outcomes, including mortality and the rate of influenza-like illness, as well as the use of healthcare resources.

During the winters of 2003-2004 and 2004-2005, the investigators randomized 44 long-term care facilities (involving 1703 staff members and 2604 residents) to either an intervention arm where healthcare workers were offered and

encouraged to take the influenza vaccine or a control arm where healthcare workers were not offered the vaccine. Control and intervention arms were matched for size of facility, percentage of high-dependency residents, and baseline mortality of residents. In both the control and intervention arms, home residents were routinely offered vaccination.

Influenza vaccine coverage in full-time staff was 48.2% in 2003-4 and 43.2% in 2004-5 among personnel at intervention hospitals, versus 5.9% in 2003-4 and 3.5% in 2004-5 in the control hospital personnel. In 2003-4, intervention hospitals had significantly lower all cause mortality (11.2 deaths per 100 residents) as compared to control homes (15.3 deaths per 100 residents, weighted rate difference per 100 residents per period -5.0, 95% confidence interval -7.0 to -2.0, p=0.002). Similarly, residents in the intervention care homes as compared to control facilities had significantly decreased rates of influenza-like illness as well as general practitioner consultations and admissions to a hospital for influenza-like illnesses. Using these statistics, the authors predict that in order to prevent one care home resident death, 8 staff members would need to be vaccinated, and to prevent one case of influenza-like illness, 5 staff members would need to be vaccinated. No significant differences in influenza-like illness death rates were noted between the two groups in any other time period. Interestingly, in periods with no influenza activity and in 2004-5 (a year in which national influenza infection rates were considerably lower than average and approximately half of the rate seen in 2003-4), no significant differences were seen between the intervention and control arms in any of the outcomes of interest.

According to the NHIS, in 2003 only 40% (approximately) of healthcare workers in the United States received an influenza vaccine[4], despite longstanding recommendations for routine vaccination in this group by health authorities in many countries. Hayward's recently published data reinforces findings from two previously published studies[1,2], showing that vaccination of healthcare workers not only improves outcomes for the workers themselves, but can also significantly reduce rates of all cause mortality and the use of influenza-related healthcare resources in the patients. In addition, the increasing benefit of healthcare worker vaccination seen in the year with higher rates of influenza suggests that in the event of pandemic influenza, vaccination of health care workers will be even more essential.

Sources for Additional Information
The 2006 CDC's HICPAC evidenced-based recommendations for influenza prevention in healthcare settings can be accessed at:
www.cdc.gov/MMWR/preview/mmwrhtml/rr5502a1.htm

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EFFECTIVENESS OF N95 AND SURGICAL MASKS IN PREVENTING PENETRATION OF VIRAL PARTICLES

Balazy A, Toivola M, Adhikari A, Sivasubramani SK, Roponen T, and Grinshpun SA. **Do N95 respirators provide 95% protection level against airborne viruses, and how adequate are surgical masks?** Am J Infect Control. 2006;34:51-7.

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While appropriate cough etiquette, good hand hygiene and use of personal

protective equipment consisting of gowns, gloves and masks are essential components of influenza prevention efforts, the appropriate type of mask to use, especially in a setting of pandemic influenza, remains controversial. Currently a number of institutions recommend use of a surgical mask for seasonal influenza. Balazy et al. performed an elegant series of experiments using manikins to evaluate the efficacy of two different types of N95 masks (one with a high fit-factor value and one with a lower fit-factor value) and two different types of surgical masks in preventing penetration of aerosolized MS2 virus (virus particles ranging in size from 10 to 600 nm). Of note, fit factor value is defined by OSHA as a quantitative estimate of the fit of a particular respirator to a specific individual, and typically estimates the ratio of the concentration of a substance in ambient air to its concentration inside the respirator when worn. Balazy's study used manikins with the mask of interest sealed to the manikin's face by silicon sealant to prevent any leaks around the mask that could affect the outcome; they then evaluated the penetration of virus particles through the N95 mask at both low and high flow rates.

Viruses are some of the smallest known agents, often ranging in size from 20 to 300 nm. Typically, N95 masks are certified if the penetration of an aerosol of 300 nm-sized sodium chloride particles is less than 5%. The investigators found that the higher fit-factor value N95 respirator met industry standards of less than 5% penetration even when challenged with the smaller MS2 viral particles. However, the lower fit-factor value N95 mask did not; at a high inhalation flow rate, the mean penetration of MS2 was 5.6%. In comparison to the N95 masks, the surgical masks, as could be expected, showed significantly increased penetration, with values as high as 20.5% for one mask type and 84.5% for the other. Interestingly. both surgical masks were manufactured by the same company, yet demonstrated very different rates of particle penetration.

This study has several implications for infection prevention and control to limit transmission of influenza. Firstly, the authors demonstrated that some but not all N95 masks available in the healthcare setting meet the industry standard of providing 95% protection. In other words, not all respirators met standards when challenged with the smaller sized viral particles. Secondly, and perhaps more significantly, surgical masks provide much less protection against aerosolized viral particles. Given the increasing data that aerosols may be a significant mode of transmission for influenza, this observation is particularly relevant to healthcare settings where it is likely patients who are symptomatic and more infectious will receive care. Additionally, procedures such as intubation, nebulization of medication (and other aerosol generating procedures) occur with increasing frequency in healthcare settings; healthcare workers protected only by surgical masks are likely to be more vulnerable to unintended/unwanted inhalation.

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At the conclusion of this activity, participants should be able to:

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