Outbreaks of Influenza A and B in a Highly Immunized Nursing Home Population

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BACKGROUND. Large outbreaks of influenza A and B may occur in nursing homes despite high resident vaccination rates, even when the vaccine strain is matched to the circulating strain. This study reports the occurrence of separate influenza A and B outbreaks in a nursing home where more than 85% of residents were vaccinated.

METHODS. Prospective surveillance was used to identify symptomatic residents in a rural Wisconsin nursing home with 680 residents. Viral cultures were obtained from all consenting residents identified with new respiratory symptoms even in the absence of temperature elevation. A "case" refers to a resident with a respiratory illness and an influenza isolate.

RESULTS. During the 1992-93 season, 86% of 670 total residents were vaccinated, 104 (15.5%) were cases with influenza B. During the 1993-94 season, 89% of 690 total residents were vaccinated, 68 (9.8%) were cases with influenza A. The antigenic matches between vaccine and epidemic strains were characterized as "identical or minimal difference" by the Centers for Disease Control and Prevention.

CONCLUSIONS. There is still a need to protect residents from infectious secretions and for contingency plans to permit the rapid use of antiviral agents. Future efforts are needed to develop vaccines that provide greater protection and to improve staff vaccination rates.

KEY WORDS. Influenza vaccine; nursing homes; nursing home staff [non-MeSH]; amantadine; rimantadine.
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In 1987, a Centers for Disease Control and Prevention (CDC) publication, "Managing an Influenza Vaccination Program in the Nursing Home," stated that "herd immunity is likely to be achieved when at least 80% of residents in a home have been vaccinated." This publication also stressed the importance of immunizing health care personnel.[1] Clinicians may believe that outbreaks will not occur in highly immunized nursing home residents, especially during seasons with a good match between the vaccine and circulating strains. However, such influenza A outbreaks have been reported. Arden and associates[2] reported five nursing home outbreaks defined by clinical illness in which 80% or more of residents were vaccinated. In separate reports, Degelau, Houck, and Findlater and their colleagues[3-5] reported laboratory-confirmed outbreaks in nursing homes with resident vaccination rates between 93% and 95%. In each outbreak, 16% of residents had respiratory illness with temperatures ≥37.5°C to 38°C (ie, 91 clinical cases). However, only 18 cases were confirmed by culture or serology in all of these outbreaks combined. Other respiratory viruses, such as respiratory syncytial virus may be co-circulating, and can clinically mimic influenza infection.[6] In all of the previous reports, other respiratory illnesses could account for clinical cases.[2-5]

In our study, we describe separate outbreaks of influenza A and B in a nursing home with residents' vaccination rates greater than 80%. All data were collected prospectively with an aggressive surveillance system. Cultures were obtained with a low clinical threshold on individuals with respiratory symptoms of new onset. We describe 68

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residents with influenza A and 104 with influenza B confirmed by viral culture during seasons in which the circulating and vaccine strains were well matched.

METHODS

The Wisconsin Veterans Home is a skilled nursing facility for veterans and their spouses administered by the State of Wisconsin. The average census was 670 in 1992-93, and 690 in 1993-94. Table 1 lists demographic information. The facility has four residential buildings and an activity building.

Beginning in the last week of October, vaccination was strongly encouraged for all residents and staff. In 1992-93, the strains of virus included in the vaccine were A/Texas/36/91-like (H1N1), A/Beijing/353/89-like (H3N2), B/Panama/45/90-like. In 1993-94, the strains of virus included in the vaccine were A/Texas/36/91-like (H1N1), A/Beijing/32/92-like (H3N2), B/Panama/45/90-like. Vaccination for residents and staff was encouraged by announcements over the public address system, as well as by memos from the medical director and nursing supervisors. Staff vaccination was encouraged to protect residents from a potentially lethal infection, as well as staff and their families from a "miserable" infection. Vaccination was offered to staff during all shifts in all buildings. Subsequently, vaccinations were offered to newly admitted residents and new employees and re-offered to those who had refused. The decision-makers for incapacitated residents were asked to give consent for annual influenza vaccinations at the time of admission. (Setia and associates have shown that requiring annual consent is associated with lower rates of vaccination.[7])

A subset of residents was enrolled in a National Institute of Health–sponsored study designed to provide data on the optimal duration of amantadine prophylaxis. The study was approved by the University of Wisconsin Human Subjects Committee and the Wisconsin Veterans Home Ethics Committee. Informed consent was obtained from 377 residents in 1992-93, and 411 in 1993-94. Participants were visited twice weekly by a study nurse to identify new respiratory symptoms. Nursing staff who provided routine care also prepared daily reports of new respiratory symptoms for *all* residents. These reports were reviewed by study nurses.

Respiratory illness was defined as any new sign or symptom including cough, sore throat, and runny nose. Even afebrile residents with minor respiratory symptoms were cultured. A nasopharyngeal and throat swab (2 separate swabs) were obtained from all consenting residents whether amantadine prophylaxis study subjects or not. Swabs were obtained rather than nasal washes because of easier collection and processing, and to diminish aspiration risk in a frail elderly population. Swabs were placed in transport media (veal broth with gentamicin, penicillin, streptomycin, and amphotericin), cooled to 4°C within 1 hour, transported cold (4°C to 8°C) to the Wisconsin State Laboratory of Hygiene, and inoculated into cell culture (Madin, Darby, canine kidney, and monkey kidney) for respiratory virus within 30 hours of collection. Only individuals whose cultured illness yielded an influenza isolate were considered "cases." Treatment for those with presumed influenza infections was provided on a case-by-case basis by their personal physician. Amantadine was recommended for 5 days for residents identified with a new respiratory illness detected within 48 hours of onset.

When influenza A had been cultured

TABLE 1

Description of Nursing Home Residents at Midpoint of Influenza Outbreaks

	Outbreak Years	
	1992-93 (n = 670)	1993-94 (n = 690)
Male residents, %	78	80
Age, years (±SD)	76 (±10)	76 (±10)
Annual mortality, %*	20	18
Title XIX levels of care		
Skilled nursing facility, %	56	56
Intermediate care facility, 1-4, %	44	44

* Annual mortality means 1993 for the 1992-93 season, and 1994 for the 1993-94 season

in the facility and 10% of the residents on a floor developed respiratory illness within a 7-day period, amantadine chemoprophylaxis was initiated on that floor per protocol on approval by the medical director. Amantadine chemoprophylaxis was dosed at 100 mg per day with downward adjustment if the calculated creatinine clearance (Cockcroft-Gault)[8] was less than 30 cc per minute. The amantadine prophylaxis study compared short-duration therapy (minimum 14 days *and* 7 days following the last reported onset of a case in the building) with long-duration therapy (minimum 21 days *and* 7 days following the last reported onset of a case in the four-building facility). Those residents who were not participating in the study were treated using the same protocol as short-duration prophylaxis (ie, minimum 14 days).

During influenza outbreaks, recommendations were made to limit influenza transmission. Residents with respiratory illness were asked to remain in their rooms, and wear masks if they left their room. These actions were strongly encouraged, but could not be mandated, and compliance was not tracked. Only those residents who were asymptomatic were permitted to attend therapies and appointments. Staff caring for symptomatic residents were encouraged to wear masks and wash hands frequently. Notices were placed on building entrances requesting that visitors with respiratory symptoms postpone their visit. Staff were encouraged to take sick leave if they were symptomatic with a respiratory illness and to make special efforts to maintain a barrier between their respiratory secretions and residents or the environment, such as wearing masks and hand-washing.

RESULTS

We report two separate influenza outbreaks (1992-93 and 1993-94) (Table 2). During the 1992-93 season, prospective surveillance was in place from November 18 through April 16. During this 5-month period, 321 residents who demonstrated new onset of respiratory symptoms were cultured; only 12 residents refused culture.

Influenza B was isolated from 104 cultures (32% of all cultures and 15.5% of all residents) between 12/19/92 and 3/07/93 (86 days). During this influenza B outbreak, a number of other respiratory viruses were also isolated: 2 rhinoviruses, 1 parainfluenza type 3, 1 adenovirus, 1 respiratory syncytial virus, and 16 herpes simplex virus type 1. Compared with a vaccination rate of 86% in all residents, 85% of cases had received vaccine. However, only 56% of nursing staff had been vaccinated. Forty-two percent of cases had an oral temperature ≥100°F when the culture was obtained. Six residents with positive cultures (6%) died within 30 days of the culture; 5 had been vaccinated. These deaths occurred in individuals with malnutrition, severe COPD, aspiration, acute urinary retention, asbestosis, or a recent hip fracture.

Total as well as pneumonia/influenza mortality was calculated from the date of the first influenza isolate until 30 days after the last one. Fifty residents died over the 116-day period, or 0.68 deaths per 1000 resident-days. Nineteen residents died of pneumonia/influenza, or 0.26 deaths per 1000 resident-days. The total and pneumonia/influenza mortality rate during noninfluenza epidemic days in 1992 through 1994 (866 days) was 0.48 and 0.13 deaths per 1000 resident-days, respectively. The differences in total and pneumonia/influenza mortality were not significant when compared with the

TABLE 2

Comparison of Outbreak Years for Influenza in a Nursing Home Population

Variables	Outbreak Years 1993-94 (n = 670)	Outbreak Years 1992-93 (n = 690)
Influenza type	B	A
Residents vaccinated, %	86	89
Nursing staff vaccinated, %	56	46
Dates of prospective surveillance	11/18/92—04/16/93	11/15/93—03/18/94
Total number of residents cultured	321	302
Number of positive cultures	104	68
Duration of outbreak, days	86	51

nonepidemic period by continuity adjusted χ^2 ($P = .18$, $P = .14$, respectively).

During the 1993-94 influenza season, prospective surveillance was in place from November 15, 1993, through March 18, 1994. Three hundred two residents were cultured; only 15 residents refused culture. Influenza A was isolated from 68 cultures (22.5% of all cultures and 9.8% of all residents) obtained between December 1, 1993, and January 20, 1994 (51 days). During the period when influenza A was being isolated, the following viruses were also isolated: 3 rhinoviruses, 1 parainfluenza type 1, and 7 herpes simplex viruses type 1. Compared with a vaccination rate of 89% in all residents, 90% of cases had received influenza vaccine. Only 46% of nursing staff had been vaccinated. Twenty-five percent of cases had an oral temperature ≥100°F at the time of culture. Nine of 14 nursing units were treated with amantadine prophylaxis. None of the residents with culture-proven influenza A died within the 30 days after the culture.

Total mortality in the institution was calculated between the date of the first influenza isolate until 30 days following the last influenza isolate. Thirty-eight residents died over an 81-day period or 0.68 deaths per 1000 resident-days. Thirteen residents died from pneumonia/influenza or 0.23 deaths per 1000 resident-days. These rates were not significantly different when compared with the nonepidemic period ($P = .24$, $P = .65$, respectively).

In 1992-93, both the vaccine strain and the epidemic strain isolated at the Wisconsin Veterans Home were determined to be B/Panama/45/90-like. In 1993-94, the vaccine strain and the epidemic strain isolated at the home were A/Beijing/32/92-like (H3N2). The antigenic match between vaccine and epidemic strain was characterized by the CDC as "identical or minimal difference" during both outbreak years. This determination is based on similar hemagglutination-inhibition titers (less than a fourfold difference) between the two viruses when challenged with reference antisera.[9]

DISCUSSION

We have demonstrated that large outbreaks of influenza A and B may occur in a nursing home where 85% of residents are vaccinated and an influenza prevention program is in place. These outbreaks occurred despite a close match between the vaccine strain and the circulating strain. In comparison to others, we carried out prospective surveillance for clinical symptoms, and cultures were performed even on those who were afebrile with mild respiratory symptoms. Nevertheless, it is unlikely that we identified all infected residents, as some symptomatic residents refused culture and demented residents may not complain of symptoms. Individuals who were hospitalized with respiratory symptoms of short duration may have been unavailable for culture. Finally, serologic evidence of infection has been noted in the absence of symptomatic infection.[10,11]

Both outbreaks were associated with nonsignificant increases in pneumonia and influenza mortality (0.26 and 0.23 vs 0.13 deaths per 1000 resident-days). Excess mortality from pneumonia and influenza is well described during influenza A outbreaks on a national scale. There is a 20% to 30% seasonal variation in expected deaths due to "pneumonia and influenza" independent of influenza "epidemics." Our simple comparisons of mortality during outbreak and non-outbreak periods did not include such a correction. Our observation and another study also describe influenza B as a cause of serious illness.[12] The 6% case mortality rate described during the 1992-93 influenza outbreak underscores that influenza B prevention should not be taken lightly.

There are many reasons high resident vaccination rates could fail to produce "herd" immunity. The natural antigenic drift of influenza may reduce the match between the circulating strain and the vaccine.[11,13,14] However, this was not the situation in our nursing home population. It is well known that some elderly patients fail to mount a "protective" response to vaccination,[15] and as such, may not contribute to "herd" immunity. Although vaccination may not prevent illness in nursing home residents, it can reduce the severity of illness and complications (ie, pneumonia, hospitalizations, and death)[16,17,18] It has also been observed that staff illness often precedes resident illness, suggesting that staff is a source of influenza in the nursing home.[13,14,19] Since dependent residents and staff are in close contact during basic care, it seems reasonable that the induction of herd immunity may depend on the combined protective immune status of residents and staff. The immune response of staff to vaccination would be expected to be more vigorous than that of residents, and therefore, make a more reliable contribution toward

achieving "herd" immunity. Attaining high staff vaccination rates, however, is difficult. Coles et al[13] reported that only 18% of staff and 84% of residents received vaccine following a survey of 349 New York State nursing homes. Nonetheless, efforts to increase staff vaccination appear highly worthwhile. A controlled study in long-term care hospitals has recently shown that staff vaccination programs were associated with reduced mortality in residents and reduced "proportions of patients developing suspected viral illness or influenza-like illness."[20]

Influenza vaccination of nursing home staff (who are a likely source of initial cases) is encouraged, but not required. The Occupational Safety and Health Agency allows employers to require tuberculin testing to protect staff. Perhaps nursing homes could be allowed to require staff vaccination to protect residents.[21] Such a step should be cost-effective and would be expected to limit the discomfort of staff influenza illness and the expense of staff sick leave.[22] Without such a regulation, major efforts are required to educate staff (see Methods) and to offer convenient times for vaccination during all shifts. Staff attitudes interfering with vaccination need to be studied and addressed. To avoid outbreaks, we strongly believe facilities should pursue high vaccination rates in both residents and staff[20]

Beyond increasing staff immunizations, our 1992 to 1994 influenza control program could be improved with procedures designed to "isolate" infectious secretions produced by staff, visitors, and residents. The CDC recommends droplet precautions for those who care for patients with influenza (ie, wearing masks within 3 feet of infected patients and asking infected patients to wear a mask if they leave their room).[23] Optimal protocols for utilizing amantadine/rimantadine need to be identified, including size of the outbreak unit and precise criteria for beginning and ending prophylaxis. We recommend that outbreaks be confirmed by culture since other viruses may be clinically indistinguishable. In addition, Degalau and colleagues[5] have suggested the special importance of isolating amantadine-treated residents with influenza infection to avoid the transmission of amantadine-resistant virus.[5]

The failure of vaccine to prevent infection does not mean vaccination of residents is useless. Larger studies in nursing home residents have demonstrated reduced attack rates following vaccination.[2,24] A prospective placebo-controlled study of 1938 community elderly has shown that vaccination reduces the rate of serologically diagnosed infection by 50%.[10] Other studies in nursing homes have demonstrated vaccine protection from more severe disease as evidenced by reduced rates of pneumonia, hospitalization, or death.[5,16,17,18,24,25] Gross and colleagues[26] performed a meta-analysis on the efficacy of influenza vaccine in elderly persons. The analysis was based on 20 observational studies, all except one consisting of institutionalized elderly. In most instances, the controls were patients who refused vaccination. The pooled estimates of vaccine efficacy were: 56% for preventing respiratory illness, 53% for preventing pneumonia, 50% for preventing hospitalization, and 68% for preventing death.[26] We expect that vaccinated residents who become infected will have less severe disease than those who are not vaccinated. Vaccine remains effective in reducing both morbidity and mortality, especially when circulating strains and vaccine are well matched.

Our report of 68 nursing home residents with laboratory-confirmed influenza A adds considerable data to previous reports (18 laboratory-confirmed cases) documenting influenza A outbreaks in highly immunized nursing homes when vaccine and circulating strains were well matched[3-5] We have also extended this observation to influenza B (104 influenza isolates). It is important that caregivers not have a false sense of security in the face of high resident vaccination rates. There is still a need for surveillance, limiting resident exposure to infected secretions from visitors and staff, isolation of infected residents, adaptation of activities, as well as amantadine/rimantadine treatment and prophylaxis after outbreaks have been identified. Programs to fully immunize nursing home staff and more effective vaccines will be required to reliably establish "herd" immunity.[20,27]

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