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ORIGINAL ARTICLE

## Does Influenza Vaccination Improve Pediatric Asthma Outcomes?

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**Objective.** Controversy exists regarding the effectiveness of influenza vaccination in preventing influenza-related asthma exacerbations in the pediatric population. While yearly influenza immunization is widely recommended for children with asthma, there is currently little evidence to support this practice. Several studies have demonstrated no measurable benefit in asthma outcomes. This study sought to determine whether influenza vaccination status is associated with indicators of asthma morbidity within the military pediatric population. **Methods.** A survey was conducted of patients 3 to 18 years of age with a diagnosis of asthma enrolled in the pediatric clinics of Brooke Army Medical Center, Fort Sam Houston, Texas, and Wilford Hall Medical Center, Lackland Air Force Base, Texas. Management practices and outcomes for 80 children were evaluated. Data were analyzed using the statistical package SPSS version 12 (SPSS Inc., Chicago). Univariate analyses were performed to identify associations between influenza vaccination, selected demographic variables and asthma exacerbation defined by oral steroid prescription, hospital visits, and unscheduled clinic or emergency department visits for asthma symptoms. Logistic regression analyses were conducted to detect possible confounding variables. **Results.** In the univariate analyses, current influenza vaccination status was associated with a significant reduction of oral steroid use in the 12 months before the survey. This relationship was appreciated to a lesser extent with emergency department or unscheduled clinic visits in the last 12 months. No significant differences were found regarding the distribution of influenza vaccination status across selected demographic variables. In the multivariate analyses, current influenza vaccination status was independently associated with significantly decreased odds of using oral steroids in the previous 12 months. There was no evidence of confounding or effect modification. **Conclusions.** This study suggests influenza vaccination is associated with fewer asthma exacerbations. After controlling for several potential confounding variables, administration of influenza vaccine was associated with a protective effect against indicators of asthma exacerbations. Our results indicate that children with asthma in the military beneficiary population may benefit from annual influenza vaccination.

**Keywords** asthma, influenza, pediatrics, immunizations, military

### INTRODUCTION

Asthma is the most common chronic disease of childhood, affecting over 9 million children 18 years of age and below at some point in their lives (1, 2). It is the third leading cause of hospitalizations in the pediatric population less than 15 years of age and accounts for 3.2 billion dollars in treatment costs annually. Acute pediatric asthma exacerbations lead to nearly 14 million missed school days per year and result in a significant amount of lost time at work by parents (3).

It is well known that upper respiratory tract infections, including influenza, can exacerbate asthma in children. Based on this association, several organizations currently advocate the use of annual influenza vaccination for asthmatic children. The American Academy of Pediatrics (AAP) and the American Academy of Allergy, Asthma and Immunology (AAAAI) both recommend annual influenza vaccination for all children with a diagnosis of asthma (4, 5). Additionally, the National Asthma Education and Prevention Program

(NAEPP) supports yearly influenza vaccination as a key measure in reducing the burden of asthma attacks in the pediatric population (6).

Despite the impact of influenza infection on the pediatric asthma population, controversy exists regarding the efficacy of influenza vaccination on reducing asthma exacerbations. While previous studies have suggested annual influenza vaccinations to be protective against acute pediatric asthma exacerbations (7, 8), recent studies have found that influenza vaccination does not prevent pediatric asthma attacks (9, 10). Recent reviews of the literature suggest that there is insufficient evidence supporting the use of influenza vaccination as a means of protecting against asthma exacerbations in children (11, 12).

Based on current literature, it is apparent that a paucity of information exists regarding the effectiveness of influenza vaccinations on preventing asthma exacerbations in children. The identification of an association between influenza vaccination and reduced childhood asthma exacerbations could provide improved outcomes and quality of life in children with asthma. In the Military Health System (MHS), status asthmaticus is the most common diagnosis among childhood hospitalizations and a common reason for outpatient and unscheduled emergency department (ED) visits. While the direct costs of frequent health care encounters are apparent, there are substantial indirect costs associated with pediatric asthma. Having a child with asthma results in lost productivity of parents owing to sick visits, hospitalizations, and

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missed school days. In the military population, the designation of asthma as a chronic disease can limit parents of children with asthma from certain duty assignments. Thus, confirmation of a protective association between influenza vaccination and pediatric asthma outcomes would provide supporting evidence for the current public health recommendations for this intervention and potentially reduce both direct and indirect costs of asthma exacerbations.

The MHS provides equal access to care for eligible enrollees regardless of socioeconomic status. Care delivered within Military Treatment Facilities (MTFs), including hospitalizations, outpatient visits, and medications, are free of charge. This model provides a unique opportunity for the evaluation of health outcomes. This study sought to determine whether influenza vaccination status is associated with indicators of asthma morbidity within the military pediatric population.

### METHODS

The Survey of Pediatric Asthma in the Military (SPAM) is a computer-based, provider-administered survey designed to collect information on asthma severity, asthma control, health-related quality of life, prescribed medications, medication adherence, and environmental factors. In addition, the survey collects military-specific information on study participants. The target population in this study was children between the ages of 3 to 18 years, with a physician-confirmed diagnosis of asthma, referred to the pediatric pulmonary clinics of participating MTFs for consultation, asthma education, or pulmonary function testing. This survey was administered to the parents of children with asthma at the pediatric pulmonary clinics of Brooke Army Medical Center, Fort Sam Houston, Texas, and Wilford Hall Medical Center, Lackland Air Force Base, Texas. The study was approved as an exempt protocol by the Brooke Army Medical Center Institutional Review Board (IRB), and families' agreements to be surveyed implied consent for participating in the study. No compensation was given for participation. Survey responses were transmitted and stored to a central secure database server without identifying information. Management practices as defined as prescription and use of inhaled corticosteroids, influenza vaccination status, existence of an asthma action plan, history of formal asthma education, and outcomes as defined as prescribed oral steroids in last 12 months, hospitalizations, and unscheduled clinic or Emergency Department (ED) visits for treatment of asthma symptoms for 80 children were evaluated. The analysis focused on current vaccination status during the 2003–2004 influenza season and subsequent asthma exacerbations. Univariate analyses (SPSS, version 13, SPSS inc, Chicago) were performed to identify associations between current influenza vaccination status and asthma outcomes defined as oral steroid prescription, hospitalizations, or unscheduled clinic or Emergency Department visits for asthma symptoms. A separate logistic regression analysis was conducted to detect an association between influenza vaccination and asthma outcomes while controlling for multiple covariates.

### RESULTS

In the univariate analyses, current influenza vaccination status was associated with a significant reduction of oral

TABLE 1.—Influenza vaccination and selected covariates, pilot data, n = 80.

| Independent variable                          | Received vaccination<br>(n = 49)<br>Number (%) | No vaccination<br>(n = 31)<br>Number (%) | Chi Square<br>p value |
|-----------------------------------------------|------------------------------------------------|------------------------------------------|-----------------------|
| Race                                          |                                                |                                          |                       |
| White                                         | 16 (32)                                        | 10 (29)                                  | 0.97                  |
| Non-white                                     | 33 (67)                                        | 21 (70)                                  |                       |
| Gender                                        |                                                |                                          |                       |
| Male                                          | 24 (49)                                        | 20 (65)                                  | 0.62                  |
| Female                                        | 25 (51)                                        | 11 (35)                                  |                       |
| Has asthma action plan                        | 28 (57)                                        | 20 (68)                                  |                       |
| Received formal asthma education              | 28 (55)                                        | 20 (68)                                  |                       |
| Military housing                              | 13 (27)                                        | 5 (16)                                   | 0.99                  |
| Prescribed oral steroid                       | 24 (49)                                        | 23 (75)                                  | 0.03                  |
| Hospitalized in last 12 months                | 8 (16)                                         | 4 (13)                                   | 0.68                  |
| Unscheduled ED or clinic Visit last 12 months | 27 (55)                                        | 19 (61)                                  | 0.59                  |
| Prescribed inhaled corticosteroid             | 42 (86)                                        | 27 (87)                                  | 0.25                  |
| Exceptional Family Member program (EFMP)      | 10 (20)                                        | 7 (23)                                   |                       |
| Has continuity physician                      | 42 (86)                                        | 25 (81)                                  | 0.35                  |
| Active duty family member                     | 34 (69)                                        | 20 (65)                                  |                       |
| Has pets (dog or cat)                         | 32 (65)                                        | 18 (58)                                  |                       |

steroid use in the 12 months before the survey (Table 1). This relationship was appreciated to a lesser extent with ED or unscheduled clinic visits in the previous 12 months. No significant differences were found in the univariate analyses regarding influenza vaccination and selected covariates. In the multivariate analysis, current influenza vaccination status was independently associated with significantly decreased odds of oral steroid usage in the previous 12 months (Table 2). There was no evidence of confounding or effect modification.

### DISCUSSION

Asthma is a common childhood disease that has a significant impact on quality of life in the pediatric population. Recent data have shown that when compared to all asthmatics, children between the ages of 5 and 17 years were at highest risk for having an exacerbation (13). During asthma exacerbations, children are more likely to be hospitalized, miss school time, and are at higher risk for mortality. The current literature clearly indicates viral upper respiratory tract infections, including influenza, trigger asthma exacerbations in children (14), yet there are few studies associating influenza vaccination with a reduction in pediatric asthma outcomes. Some studies suggest that no evidence exists to warrant routine influenza vaccination of asthmatic children. This study found that current influenza vaccination status is associated with reduced prescriptions of oral steroids. Additionally, the relationship between influenza vaccination and reduced unscheduled office visits and ED visits was found to approach significance. Even after controlling for several potential confounding variables, administration of influenza vaccine was still associated with a protective effect against the outcomes of interest. This finding is significant because it provides new evidence supporting the current public health recommendations for routine influenza vaccination of asthmatic children. It is therefore possible that improved adherence to these recommendations by healthcare providers and patients may improve the quality of life of asthmatic children and reduce the economic burden of asthma.

TABLE 2.—Effect of influenza vaccination on asthma exacerbation, pilot data, n = 80.

| Independent variable                         | Odds of prescribed oral steroid in last 12 months OR (95% CI) | Odds of being hospitalized in last 12 months OR (95% CI) | Odds of ED or unscheduled clinic visit in last 12 months OR (95% CI) |
|----------------------------------------------|---------------------------------------------------------------|----------------------------------------------------------|----------------------------------------------------------------------|
| Race                                         |                                                               |                                                          |                                                                      |
| African-American                             | 1.16 (0.37–3.60)                                              | 3.73 (0.66–21.08)                                        | 1.07 (0.34–3.37)                                                     |
| Hispanic                                     | 2.00 (0.60–6.63)                                              | 2.01 (0.32–12.70)                                        | 0.72 (0.23–2.25)                                                     |
| Gender, male                                 | 1.70 (0.60–4.84)                                              | 0.48 (0.12–1.94)                                         | 2.41 (0.86–6.78)                                                     |
| Received influenza vaccine in last 12 months | 0.29 (0.10–0.84)                                              | 1.39 (0.340–5.67)                                        | 0.54 (0.20–1.50)                                                     |
| On-post housing                              | 1.56 (0.49–5.02)                                              | 0.59 (0.11–3.10)                                         | 1.61 (0.51–5.02)                                                     |
| Prescribed inhaled corticosteroid            | 2.15 (0.48–9.61)                                              | 1.48 (0.15–15.09)                                        | 2.55 (0.58–11.30)                                                    |

Several facets unique to the MHS were strengths of this study. In our population of interest, access to outpatient and immunization clinics and EDs were provided free of charge. Multiple MHS facilities were in close proximity to all families with children diagnosed with asthma, reducing geographical access concerns. In addition, active-duty parents are allowed time from work to bring children in for health visits if they are ill. These factors allowed us to substantially reduce access barriers commonly seen in the civilian population. Also, the use of a computer-based, nurse-administered survey instrument facilitated data collection. By surveying all participants with a single program, data were collected in a standardized way, and the risk of mishandled, lost, or misinterpreted responses was minimized. Military pediatricians in San Antonio comprise a relatively small, closely collaborating group. Quality assurance audits have consistently demonstrated similar asthma management practice styles among military pediatricians, limiting large variability in asthma care. Because the analysis focused on a single vaccination season, variability due to different strains of influenza or effectiveness of the inactivated vaccine from year to year was eliminated.

There were also limitations to this study. Because information was collected retrospectively, data were dependent on the accuracy of recollections from parents. This introduced an element of recall bias to our results. Owing to the cross-sectional nature of our study design, there was no prospective follow-up with our subjects. In addition, our relatively small sample size may have had insufficient power to detect other relationships between influenza vaccination and other outcomes of interest. It is possible that influenza vaccination status may be merely a surrogate marker for children and families who are highly adherent to their asthma medical regimen. Measures of cause and effect were not collected in this study. It is possible that a portion of asthma exacerbations were attributable to causes other than influenza infection. More detailed studies would be necessary to further understand these relationships.

This study focused on outcomes of children with asthma during the 2003–2004 influenza season. By concentrating our efforts into a single season, we were able to eliminate the variability seen year-to-year in the effectiveness of any year's vaccine and the prevalent viral strain for that season. As this study was survey based, it did not seek to confirm the diagnosis of any particular strain of influenza in children who had asthma exacerbations. We acknowledge that children who had asthma exacerbations may have had other precipitating triggers, such as other viral infections. We also acknowledge that if the same study were conducted in a year

when the vaccine was less effective against the strain of influenza prevalent in the community, the results may have been quite different.

Because some number of both vaccinated and unvaccinated children may have had factors other than influenza as a cause for their exacerbation, these children could reasonably be expected to be afforded no protection by the vaccine and require hospitalization. Additionally, it should be noted that in such a heterogeneous disease, many other factors, such as individual immune response to infection, level of asthma severity, and level of symptom control, could influence children with a respiratory tract infection to develop a severe exacerbation leading to hospitalization. Therefore, it is possible that children who received the vaccine were afforded some level of protection, but not enough to prevent a hospitalization if the child had enough factors present to lead to a severe exacerbation. Finally, due to the small number of children in our sample population, it is also possible that there is a significant protective effect of the influenza vaccine regarding the hospitalization outcome, but our study did not have enough power to detect it.

In conclusion, our study suggests that a protective association exists between influenza vaccinations and asthma exacerbations in the pediatric population. Our results indicate that children with asthma in the military beneficiary population may benefit from annual influenza vaccination. Because of the controversy regarding this issue, the findings in this study emphasize the need for further evaluation of the relationship between influenza vaccination and pediatric asthma exacerbations through the use of a large prospective study that tests all children with asthma exacerbations for influenza infection during the winter months.

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