Respiratory Tract Viral Infections in Inner-City Asthmatic Adults

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Background: Respiratory tract viral infections (RTVIs) have been identified frequently in association with asthma exacerbations in children, but few studies have shown similar rates of viral infections in adults with asthma. Further studies using newer diagnostic techniques to evaluate the frequency of RTVIs in adults with acute exacerbations of asthma need to be performed.

Methods: Twenty-nine asthmatic adults were recruited from the pulmonary clinic of an urban county hospital and were followed up in a longitudinal cohort study for signs and symptoms of asthma and RTVI. One hundred twenty-two asthmatic adults presenting to the emergency department (ED) of the same hospital with acute symptoms of asthma underwent evaluation for RTVI in a cross-sectional prevalence study. In both studies, respiratory secretions and paired serum samples were collected from subjects with acute wheezing episodes and evaluated using virus culture, serologic testing, and reverse transcription–polymerase chain reaction (RT-PCR).

Results: In the longitudinal cohort study, 138 respiratory illnesses, of which 87 were asthma exacerbations, were evaluated; 41% of all illnesses and 44% of asthma exacerbations were associated with an RTVI. In the ED study, 148 asthma exacerbations were evaluated; 55% were associated with an RTVI. An RTVI was identified in 21 (50%) of 42 of the subjects hospitalized in the ED study. Picornaviruses (rhinoviruses), coronaviruses, and influenza viruses were the most commonly identified causes of RTVI. Forty-six (60%) of the 77 picornavirus infections and 22 (71%) of the 31 coronavirus infections were identified only using RT-PCR.

Conclusions: Asthmatic exacerbations in adults are frequently associated with an RTVI. Identification of such infections often requires newer diagnostic methods, such as virus-specific RT-PCR. The high frequency of RTVIs identified in association with asthmatic exacerbations in adults from the inner city suggests that strategies for the prevention of RTVI should be targeted toward this population.

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ASTHMA IS a common disease, affecting 14 to 15 million Americans.[1] Recent epidemiological studies of asthmatic patients report morbidity and mortality to be increasing.[2,3] Certain subpopulations, such as racial and ethnic minorities who are poor and live in the inner city, appear to be at the highest risk for hospitalization and mortality.[4,5] The economic burden associated with asthma also is great. In 1990, there were estimated to be more than 450 000 hospital admissions for asthma-related illnesses and approximately $6.2 billion spent for total health care costs.[6]

Although the cause of asthma remains unknown, the association between respiratory tract viral infections (RTVIs) and exacerbations of asthma has been acknowledged for more than 25 years.[7-9] Respiratory tract viruses have been identified in up to 80% of children with wheezing episodes and asthma exacerbations.[9-11] The most commonly identified viruses have been rhinoviruses, coronaviruses, and parainfluenza viruses. Studies in adults with asthma have documented RTVIs less commonly, with the frequency of asthma exacerbations associated with RTVI ranging from 0% to 44% in 3 recent studies.[12-14]

We conducted 2 studies evaluating the role of RTVIs in exacerbations of asthma in adults who used an urban public hospital for their medical care. In 1 study, adults with asthma were followed up longitudinally during 2 fall and winter seasons and underwent testing for viral infection for each reported asthma exacerbation. An additional study evaluated acute exacerbations of asthma in adults coming to the emergency department (ED) of the same urban public hospital. The role of RTVIs in the morbidity of these adults with asthma is described.

SUBJECTS, MATERIALS, AND METHODS

STUDY GROUPS

Longitudinal Cohort Study

Asthmatic adults were recruited for a longitudinal cohort study (December 6, 1991-May 3, 1994). Asthma was defined by a history of multiple episodes of wheezing and documented by at least a 15% improvement in forced expiratory volume in 1 second following bronchodilator therapy or positive results of a methacholine chloride challenge test.[15] Study subjects were recruited from patients at an urban public hospital pulmonary clinic (Ben Taub General Hospital, Houston, Tex). Subjects with a greater than 5 pack-years smoking history and those receiving daily systemic steroid therapy were excluded from participation.

ED Study

A convenience sample of adults presenting to the ED of Ben Taub General Hospital for acute care of an asthma exacerbation was recruited for this cross-sectional prevalence survey (October 9, 1992-March 22, 1994). Asthma was defined by a history of multiple episodes of wheezing. Adults with known chronic obstructive lung disease or a history of cigarette smoking (>5 pack-years) were excluded from participation.

Written informed consent was obtained from all subjects. These studies were approved by the Institutional Review Board of Baylor College of Medicine, Houston, Tex.

PROCEDURES

Longitudinal Study

A brief medical history was obtained and a physical examination was performed at enrollment. Baseline information included current and past use of medications, history of cigarette smoking, and complete influenza virus and pneumococcal vaccination history. Spirometric studies were performed with and without bronchodilators. Any subject who could not perform spirometry was excluded. At the time of the initial visit and in the fall of each year during the study, each subject was offered free inactivated influenza virus vaccine. Although the administration of influenza virus vaccine would be expected to lower the frequency with which influenza virus infections occurred, vaccine was offered because of ethical reasons (ie, vaccine is indicated for subjects with chronic lung disease).

Blood was collected for viral serologic tests, and nasopharyngeal secretions were obtained for virus culture and reverse transcription–polymerase chain reaction (RT-PCR) assays. In brief, 5 mL of lactated Ringer solution was instilled into each nostril, and secretions were collected in a cup as described previously.[16] The nasal wash sample was added to viral transport media (veal infusion broth), combined with a pharyngeal swab specimen, and placed at 4°C for transport to the viral diagnostic laboratory.

Follow-up visits for all subjects were scheduled in September, December, and April of each year. During these visits, the brief history and physical examination were repeated. Blood for serologic studies and nasopharyngeal samples for virus culture were obtained as described.

Subjects were instructed to contact an investigator when they experienced acute changes in pulmonary symptoms, so that potential respiratory tract illnesses could be evaluated further. In addition, each subject was contacted by telephone or by return postcard every 2 weeks. When an illness occurred, the subject was seen as soon as possible. During each illness visit, signs and symptoms of RTVI were sought, and a pertinent, focused physical examination was performed. Nasopharyngeal specimens were obtained for virus cultures as already described. Blood for serologic studies was obtained if it had not been collected in the previous 4 weeks. A convalescent serum sample was collected 2 to 4 weeks after the illness.

ED Study

A brief medical history was obtained and a physical examination was performed at enrollment. Nasopharyngeal specimens were obtained for virus cultures as already described. Blood for serologic studies was obtained at enrollment and 2 to 4 weeks later. Decisions about treatment and the need for hospitalization were made by nonstudy physicians.

ILLNESS DEFINITIONS

Upper respiratory tract illnesses (URTIs) were defined by the presence of symptoms of acute rhinitis and/or pharyn-

RESULTS

DEMOGRAPHICS

The demographic characteristics of the subjects of both studies are described in **Table 1**. Thirty-six subjects were enrolled in the longitudinal cohort study, and 29 continued in the study past the initial (enrollment) visit and were eligible for evaluation. The mean and median durations of follow-up were 19.5 and 22.4 months, respectively (range, 2.5-28.5 months). The documented influenza virus vaccination rates were 64% (7/11), 78% (21/27), and 64% (14/22), respectively, for the 3 influenza seasons from December 1, 1991, to April 30, 1994. The ED study was conducted from October 9, 1992, until March 22, 1994. Fifty-seven percent of the subjects approached from October 9, 1992, to May 31, 1993, for participation in the study were enrolled; the principal reasons for nonparticipation were inability to confirm the diagnosis of asthma and unwillingness to participate. One hundred twenty-two participants were enrolled. The mean age was similar to that of participants in the longitudinal study, but a significantly larger percentage of black subjects participated in the ED study ($P = .03$).

RESPIRATORY TRACT VIRAL INFECTIONS

In the longitudinal study, picornaviruses and parainfluenza viruses were the most common causes of RTVI (**Table 2**). Of the 17 culture-positive picornavirus infections, 12 were rhinoviruses, 2 were enteroviruses, and 3 were not further identified. Seven picornavirus and 6

gitis (ie, sore throat, rhinorrhea, or sneezing). Lower respiratory tract illnesses were defined by increased cough and sputum production or increased wheezing. An exacerbation of asthma was defined by an increase in wheezing and/or dyspnea.

VIRUS CULTURES

Specimens were inoculated (usually within 12 hours) onto the following 4 different cell culture tubes: human diploid lung fibroblasts (WI-38), Madin-Darby canine kidney cells, human tracheal carcinoma cells (HEp-2), and monkey kidney cells (LLC-MK2) (BioWhittaker, Walkersville, Md). The cell culture tubes were incubated on a roller drum at 33°C. Standard detection and identification methods for respiratory tract viruses were used.[17] Rhinoviruses were distinguished from enteroviruses using acid lability or RT-PCR,[18] and some type A influenza viruses were subtyped using RT-PCR.[19]

SEROLOGIC TESTS

Serum samples were stored at –20°C until tested. Hemagglutination inhibition and microneutralization tests were used to measure antibodies against influenza virus types A and B using strains representative of those circulating in the community.[20] Microneutralization tests were used to measure antibodies to parainfluenza viruses 1, 2, and 3; coronavirus 229E; and respiratory syncytial viruses (RSV) using previously published techniques.[21-23] A serologic rise was defined as a 6-fold or greater rise in antibody titer between acute and convalescent serum samples or a 4-fold (influenza virus only) or greater antibody rise in hemagglutination-inhibition and microneutralization tests. Enzyme-linked immunosorbent assay antibody tests for coronavirus OC43 were used as described previously.[23]

REVERSE TRANSCRIPTION–POLYMERASE CHAIN REACTION

Viral nucleic acids were extracted from respiratory secretions using RNAzol (Biotecx, Houston) as previously described.[12,18,24] Primers used for amplification were as follows: complementary DNA (cDNA) synthesis (R1) 5′-ACGGACACCCAAAGTA-3′, upstream primer (R2) 5′-AGCACTTCTGTTTCCC-3′ for picornavirus[25]; cDNA synthesis (FAM1) 5′-CAGAGACTTGAAGATGTCTTTGC-3′, upstream primer (FAM2) 5′-GCTCTGTCCATGTTATTTG (GA)AT-3′ for influenza virus type A[26,27]; and cDNA synthesis (CVP3) 5′-IIAAATTGCTIITCTTGTTCTGGC-3′ (I indicates inosine), downstream primer (CVP4) 5′-CCAAAATTCTGATTAGGGCCTCTC-3′ for coronavirus OC43.[28] Complementary DNA was synthesized for 1 hour at 43°C in a reaction mix containing 10-mmol/L tromethamine hydrochloride (pH, 8.3), 50-mmol/L potassium chloride, 1.5-mmol/L magnesium chloride, 3.3-µmol/L cDNA synthesis primer, 667-µmol/L deoxynucleoside triphosphates, 20 U of RNase inhibitor (RNasin; Promega Corporation, Madison, Wis), and 5 U of avian myeloblastosis virus reverse transcriptase (Life Sciences, Inc, St Petersburg, Fla). The PCR amplification was performed in a solution containing 10-mmol/L tromethamine hydrochloride (pH, 8.3), 50-mmol/L potassium chloride, 1.5-mmol/L magnesium chloride, 1-µmol/L each of the cDNA synthesis and upstream primers, 200-µmol/L deoxynucleoside triphosphates, and 5 U of *Taq* polymerase (Perkin-Elmer Corporation, Norwalk, Conn) using a thermal cycler (PTC-100, MJ Research, Inc, Cambridge, Mass). After an initial 4-minute heat denaturation at 94°C, 40 cycles of heat denaturation at 94°C for 1 minute, primer annealing at 49°C (picornavirus), 55°C (influenza virus type A), or 58°C (coronavirus) for 1 minute 30 seconds, and primer extension at 72°C for 1 minute were followed by a final primer extension step at 72°C. Amplified products were 394, 212, and 186 base pairs in length for picornavirus, influenza virus type A, and coronavirus OC43, respectively. Positive results were confirmed by slot-blot hybridization using the following digoxigenin-labeled oligonucleotides[27]: 5′-TCCTCCGGCCCCTGAATG-3′ (R4) for picornavirus; 5′-TCCTGTCACCTCTGACTAAGGGGATTTTG-3′ (AH2) for influenza A virus; and 5′-AAGCAIAITGCCAAAIAAGTCAGICAGAAAATTTT-3′ (CVPP) for coronavirus OC43.

STATISTICAL ANALYSIS

Discrete variables were compared using χ^2 test or Fisher exact test. Parametric data were analyzed using Student *t* test.

coronavirus OC43 infections were identified using RT-PCR assay only. Fourteen of the 16 parainfluenza virus infections were detected using serologic testing only. Subjects had received influenza virus vaccine during the same respiratory virus season in 9 of the 12 instances in which an influenza virus infection was identified. A dual respiratory viral infection was detected in the following 3 patients: 1 patient with coronavirus OC43 and a picornavirus, 1 with a rhinovirus and parainfluenza virus, and 1 with coronavirus OC43 and parainfluenza virus. None of these patients went to the ED or was hospitalized.

The following 10 asymptomatic infections were identified during the longitudinal study (method of identification is given in parentheses): 4 parainfluenza virus infections (serologic testing), 1 coronavirus OC43 infection (serologic testing), 1 RSV infection (serologic testing), 1 influenza virus type A/H3N2 infection (culture), 1 adenovirus infection (culture), 1 rhinovirus infection (culture and RT-PCR), and 1 cytomegalovirus infection (culture). Virus cultures were more likely to yield positive results when the subject was symptomatic than asymptomatic (26/137 [19%] vs 4/143 [3%], respectively; $P<.001$, χ^2). Thirty-seven culture-negative respiratory samples obtained during follow-up visits when no illness was present also yielded negative results for picornaviruses and coronaviruses when assayed using RT-PCR.

Picornavirus and coronavirus infections were the most common RTVIs identified in the ED study. Ninety-two (62%) of the illness episodes were evaluable using serologic testing. Thirty-nine (74%) of 53 picornavirus and 16 (76%) of 21 coronavirus infections were identified using RT-PCR only. Of the 14 culture-positive picornavirus infections, 10 infections were rhinoviruses,

Table 1. Demographics of Asthmatic Adults With Respiratory Tract Viral Infections and Illnesses*

	Longitudinal Study	Emergency Department Study
Number	29	122
Age, mean (SD), y	37.8 (9.1)	38.5 (13.9)
Age range, y	19-50	17-77
Sex, M/F	6:23	37:85
Race, No. of subjects		
White	10	18
Hispanic	12	44
Black	7	56
Asian	0	4
Length of follow-up, mean (SD), mo	19.5 (7.4)	. . .

**Study groups are described in the "Study Groups" subsection of the "Materials and Methods" section. Ellipses indicate not applicable.*

Table 2. Virus-Associated Illnesses in Asthmatic Adults*

Respiratory Viruses	Longitudinal Study	Emergency Department Study
Picornavirus†	24 (7)	53 (39)
Coronavirus	10 (6)	21 (16)
Influenza viruses type A and B	11	12 (0)
Parainfluenza viruses 1-3	16	0
Respiratory syncytial virus	0	4
Adenovirus	1	1
Cytomegalovirus	0	3

**Study groups are described in the "Study Group" subsection of the "Materials and Methods" section. Data are given as number of cases. Numbers in parentheses indicate number of infections documented using reverse transcription–polymerase chain reaction.*

†Majority of these are rhinoviruses.

3 infections were enteroviruses, and 1 infection was not further identified. More than 1 associated respiratory tract viral pathogen was identified in 11 illnesses (13%); 3 of these resulted in hospitalization.

RESPIRATORY ILLNESSES

Of 138 respiratory illnesses in the longitudinal study, 137 were evaluated at an illness visit (**Table 3**). Of these, 41% of the illnesses and 44% of the asthma exacerbations were associated with a documented RTVI. Viral infections were documented more frequently from November through April than from May through October (39/79 [49%] vs 18/59 [30%], respectively; $P = .03$, χ^2). Symptoms of a URTI plus asthma exacerbation were seen in 52%, a URTI alone in 36%, an asthma exacerbation alone in 11%, and bronchitis alone in 1%. An RTVI was as likely to be identified with a URTI illness (19/50 URTIs only and 32/72 URTIs with asthma exacerbations) as with an asthma exacerbation (6/15) alone. Eleven ED visits resulted in 3 hospitalizations. An RTVI was documented in 6 ED visits (3 picornaviruses, 1 influenza virus type A, 1 parainfluenza virus 2, and 1 parainfluenza virus 3) and in 1 hospitalization (rhinovirus).

Table 3. Use of Medical Care by Asthmatic Adults*

	Longitudinal Study	Emergency Department Study
Illnesses associated with RTVI/total acute respiratory illnesses	57/138 (41)	82/148 (55)
ED visits associated with RTVI/total ED visits for asthma	6/11 (55)	82/148 (55)
Hospitalizations associated with an RTVI/total hospitalizations	1/3 (33)	21/42 (50)

**Study groups are described in the "Study Groups" subsection of the "Materials and Methods" section. RTVI indicates respiratory tract viral infection; ED, emergency department. Data are given as number (percentage) of total cases.*

There were 148 illness visits in the ED study (Table 3). An RTVI was identified in 82 visits (55%). The number of illness visits per month ranged from 1 (April 1993) to 22 (February 1993), and the number of RTVIs identified per month ranged from 0 (August 1993) to 11 (October 1993). One hundred thirteen subjects (76%) had URTI symptoms; 67 (59%) of 113 subjects had an associated RTVI, compared with 15 (43%) of 35 subjects without URTI symptoms ($P = .09$). Forty-two (28%) of the illnesses resulted in hospitalization; 21 patients (50%) had a documented RTVI (11 picornavirus, 6 coronavirus OC43, 6 influenza virus type A, 1 RSV, and 1 cytomegalovirus; 2 patients had a dual and 1 patient a triple virus infection). Hospitalizations associated with RTVI were seen throughout the study, including the summer months (June and July 1993). The duration of hospitalization for illnesses (mean ± SD) associated with an RTVI was similar to that of illnesses not associated with an RTVI (4.9 ± 2.7 vs 4.0 ± 2.0 days; $P = .23$). No deaths occurred in any of the hospitalized patients.

COMMENT

In our 2 studies, RTVIs were identified frequently in association with asthma exacerbations in adults. An RTVI was documented in 44% of exacerbations in a small cohort of patients with asthma who were followed up longitudinally and in 55% of those undergoing evaluation in an acute-care setting (ED). Picornaviruses, coronaviruses, and influenza viruses were the most commonly identified viruses, with parainfluenza viruses and RSV being recognized less frequently. Most of the picornaviruses characterized were rhinoviruses, and it is likely that most of the uncharacterized picornaviruses also were rhinoviruses.[10] Asthma exacerbations associated with RTVIs were identified throughout the year, but the presence of an RTVI did not increase the likelihood or the duration of hospitalization for an asthma exacerbation.

One previous study also found a similar frequency of RTVIs associated with worsening asthma in adults (**Table 4**).[29-33] Nicholson et al[12] reported RTVIs in

Table 4. Respiratory Tract Viral Infections and Illnesses in Asthmatic Adults*

Reference (Year[s] Study Performed)	Design	Duration, mo	No. of Subjects	Documented RTVI in Asthma Exacerbations, No./Total (%)	Most Common RTVIs	Diagnostic Methods
Huhti et al[29] (1970)	Cross-sectional prevalence, inpatient	12	63	24/142 (17)	Influenza, RSV, parainfluenza	CF Ab only
Minor et al[30] (1972-1973)	Longitudinal incidence, outpatient	8	8	NS	NS	Cell culture, HAI and Nt Ab, no coronavirus
Clarke[31] (1973-1974)	Longitudinal incidence, outpatient	18	51	12/111 (11)	Rhinovirus, influenza	Cell culture, CF Ab, no coronavirus
Hudgel et al[32] (1977-1978)	Longitudinal incidence, outpatient	8-19	19	8/76 (11)	Influenza, rhinovirus, parainfluenza	Cell culture, CF and HAI Ab
Beasley et al[33] (1984)	Longitudinal incidence, outpatient	12	31	18/178 (10)	RSV, rhinovirus, parainfluenza	Cell culture, CF and HAI Ab, no coronavirus
Nicholson et al[12] (1990-1992)	Longitudinal incidence, outpatient	18	138	27/61 (44)	Rhinovirus, coronavirus, parainfluenza	Cell culture, CF and EIA Ab, RT-PCR
Sokhandan et al[13] (1990-1991)	Cross-sectional prevalence, ED	6	35	0/35 (0)	None	Cell culture, CF Ab, no coronavirus
Teichtahl et al[14] (1993-1994)	Cross-sectional prevalence, inpatient	12	79	23/79 (29)	Influenza, rhinovirus, adenovirus	Cell culture, CF Ab for influenza only
Present study (1991-1994)	Longitudinal incidence, outpatient	20	29	38/87 (44)	Rhinovirus, parainfluenza, influenza	Cell culture, HAI and Nt and EIA Ab, RT-PCR
Present study (1992-1994)	Cross-sectional prevalence, ED	18	122	82/148 (55)	Rhinovirus, coronavirus, influenza	Cell culture, HAI and Nt and EIA Ab, RT-PCR

**RTVI indicates respiratory tract viral infection; RSV, respiratory syncytial virus; CF, complement fixation; Ab, antibody; NS, not specified; HAI, hemagglutination inhibition; Nt, neutralization; EIA, enzyme immunoassay; RT-PCR, reverse transcription–polymerase chain reaction; and ED, emergency department.*

association with 44% of asthma exacerbations and upper respiratory tract symptoms in 80% of asthma exacerbations, with viruses identified in 57% of the subjects with symptomatic colds. The results from Nicholson et al[12] and those of our studies contrast sharply with those of other investigators (Table 4).[13,14,29-33] The most likely explanation for these disparate findings is the different methods used for the identification of RTVI. The studies with lower rates of RTVI associated with asthma exacerbations used less-sensitive serologic methods (complement fixation), did not test for some important respiratory viruses (eg, coronavirus), and/or did not use RT-PCR assays to identify rhinovirus infections. Eighty-two percent of the rhinoviruses in the study of Nicholson et al[12] and 29% and 73% of the picornavirus infections in our 2 studies were identified only using RT-PCR. Similar increases in frequencies of viral infection have been seen when RT-PCR has been used as a diagnostic tool in studies of asthma exacerbations of children.[10,11]

There was a marked difference in the identification of parainfluenza virus infections between our studies. The reason for this difference is unexplained. Most of the parainfluenza infections were identified using serologic methods. These are likely to represent true infections, because the definition of an infection was limited to 6-fold or greater increases in serum antibody titer (vs the traditional ≥4-fold increase). The performance characteristics of the serologic assay predict that there is a greater than 97% likelihood that, for the number of serum samples tested, no more than 2 serologic rises were false-positive results. Parainfluenza virus infections have been commonly demonstrated in several longitudinal studies of RTVI in adults with asthma,[12,32,33] but they have been identified less commonly in studies of patients seen in the hospital or ED.[13,14] It is possible that parainfluenza virus infections lead to wheezing severe enough to cause a patient to seek medical care less frequently than rhinovirus and coronavirus infections. Further study of this question is needed.

Wheezing and increased bronchial reactivity in adults also have been documented after experimental and natural RTVIs.[9] The mechanisms responsible for these observations have not yet been determined, although considerable effort is being made to delineate these factors.[34,35] The human rhinovirus challenge model has been used to demonstrate that, following rhinovirus infection, there is increased bronchial reactivity in response to histamine or methacholine[36-39] and to allergen,[37,38] the likelihood of a late asthmatic response following allergen exposure increases,[37,38] lymphocytic infiltration of the bronchial submucosa increases transiently,[40] and the induction of several inflammatory mediators, including interleukin 8 and bradykinin, are increased.[39,41] The induction of virus-specific immunoglobulin E, direct damage to respiratory tract epithelium, down-regulation of β-adrenergic function, induction of other cytokines and chemokines, and activation of cellular immune responses are other proposed mechanisms by which respiratory tract viruses may contribute to increased bronchial reactivity.[34,35,42]

Several studies have shown that RTVIs are not invariably associated with airway obstruction in adults with asthma.[12,43,44] One third of the symptomatic RTVIs in our longitudinal study were not associated with worsening of lower respiratory tract symptoms. Both host- and virus-related factors appear to contribute to the different clinical manifestations associated with RTVI in subjects with asthma.[34] These factors remain to be defined.

The morbidity and mortality associated with asthma have been increasing since the late 1970s.[2,3] Residents of the inner city are at increased risk for asthma-related hos-

pitalization and mortality.[2,45] Potential reasons for the increased risk in this population include increased exposure to allergens such as mites and cockroaches,[46,47] decreased access to or underuse of medical care,[48,49] poor air quality,[50,51] psychosocial problems,[52,53] exposure to cigarette smoke,[54,55] and crowding.[4] Race and ethnicity appear to be a less significant risk factor than socioeconomic status.[4,56] Although this study does not evaluate the contribution of any of the aforementioned factors to the morbidity associated with asthma, it demonstrates that RTVIs are commonly associated with asthma exacerbations in adults from the inner city. Thus, another potential target for the control of asthma is the prevention of RTVIs with vaccines or antiviral agents. Because there is no group for comparison, the occurrence of influenza virus infections in vaccinated individuals does not indicate that influenza virus vaccination was ineffective; however, it does suggest that there is room for improvement in currently licensed influenza virus vaccines.

We performed 2 clinical studies that found RTVIs to be frequently associated with asthma exacerbations in adults receiving medical care at an urban hospital. Although the longitudinal cohort study was small, the results obtained are similar to those of Nicholson et al[12] and to the results seen in several pediatric studies.[9-11] The use of new diagnostic technology (ie, RT-PCR) greatly increased the identification of RTVIs. Although picornaviruses identified using RT-PCR were not separated into genera, most of these were likely to have been rhinoviruses.[10] Because we did not look for other infections (ie, those caused by *Mycoplasma pneumoniae* and *Chlamydia pneumoniae*) that have been associated with asthma exacerbations in the past,[7,29,57] the relative importance of respiratory tract infections as potential precipitants of asthma exacerbations may have been underestimated. The high frequency of RTVIs identified in association with asthma exacerbations suggests that strategies for the prevention of RTVIs should be targeted toward the population with asthma.

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