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Atopy and Upper and Lower Airway Disease Among Former World Trade Center Workers and Volunteers

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Learning Objectives

- Demonstrate familiarity with the respiratory symptoms and pulmonary function abnormalities documented in workers at the World Trade Center site, including previously reported risk factors.
- Discuss the evaluation and findings of the workers seen at the WTC Health Effects Treatment Program, focusing on the prevalence of atopy and its relationship to respiratory diagnoses.
- Summarize the authors' conclusions regarding the involvement of atopy in the development of WTC-related upper and lower airway disease.

Abstract

Objective: *A large number of workers seemed to have developed upper and lower airway disease (UAD and LAD, respectively) in relation to their occupational exposures at the World Trade Center (WTC) disaster site. This study examined atopy as a risk factor for presumably WTC-related UAD and LAD.* ***Methods:*** *Atopy was examined in 136 former WTC workers and volunteers by radioallergosorbent test, skin prick testing, or both. Overall prevalence of atopy was estimated, and bivariate and multivariate logistic regression analyses were conducted to examine associations of atopy with WTC-related UAD and LAD.* ***Results:*** *Atopy was prevalent in 54.4% of these WTC workers. Atopy was associated with higher symptom severity scores for both WTC-related UAD and LAD. Atopy was a predictor of WTC-related UAD but not LAD. Early arrival at the WTC site, and pre-2001 asthma diagnosis were predictors of LAD.* ***Conclusion:*** *The prevalence of atopy in this population is similar to what has been described for the general U.S. population. Atopy seemed to be a risk factor for presumably WTC-related UAD but not for LAD.* (J Occup Environ Med. *2009;51:992–995*)

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The attack to the World Trade Center (WTC) in New York City on September 11, 2001, and the subsequent 9.5-month long massive effort to rescue, recover, and restore services to the area, exposed a large number of workers to many occupational toxicants and stressors, which remain to be fully characterized. Although sampling and analyses of the WTC dust were delayed and limited, it is widely accepted that it was hazardous, containing a large amount of respirable particles, a high concentration of polyaromatic hydrocarbons, and, most notably, a very alkaline pH (9.5 to 11).[1,2]

Early screening surveys of firefighters,[3,4] police officers,[5] and other workers[6] suggested a consistent pattern of self-reported and persistent upper and lower airway symptoms and pulmonary functional abnormalities. We previously reported the major disease types observed in this population and characterized the clinical presentation of their upper airway disease (UAD) and lower airway disease (LAD).[7]

Important risk factors for occupational UAD and LAD include exposure, smoking history, and atopy.[8,9] In our previous studies, we examined the role of the first two.[7] The aim of this study was to examine atopy as a risk factor for presumably WTC-related UAD and LAD.

Methods

Patients were evaluated at the WTC Health Effects Treatment Program (WTC HETP) at Mount Sinai Medical Center in New York City.

The WTC HETP was a clinical program established in January of 2003 to diagnose and treat the adverse health effects observed in former rescue, recovery, and service restoration workers and volunteers at the WTC disaster site, the Staten Island landfill, and the barges that transported debris between those two sites. Eligibility to receive clinical services also required presence at the WTC site during the fall of 2001.[6] The Mount Sinai School of Medicine Institutional Review Board approved this review, exempting it from the requirement for informed consent.

A total of 136 patients were included in this study because they had undergone a complete allergy evaluation (discussed below). Patients were evaluated at the WTC HETP from January 14, 2003 to January 24, 2005. The majority of the patients (71%) was seen before January 6, 2004, and was part of our previously reported series of 554 patients.[7]

Before presenting to the WTC HETP, all patients had already undergone basic testing at screening programs, or at the request of their primary care physicians. This basic testing consisted of blood tests (cell counts, chemistry, and liver function panels), urine analysis, spirometry, and chest radiograph. Presence of potential WTC-related symptoms or laboratory abnormalities prompted a referral to the WTC HETP for further clinical evaluation. Philanthropic funding allowed the WTC HETP to provide all diagnostic and treatment services to all segments of its patient population for the conditions reported herein. The diagnostic evaluation has been described previously.[7] Physicians' diagnoses were based on clinical symptoms, physical findings, supportive diagnostic test data, or response to specific treatment. A diagnosis of UAD required the presence of at least three symptoms of rhinitis,[10] persistent for more than 8 weeks and unrelated to an infection, with or without associated symptoms of sinusitis, pharyngitis, or laryngitis (clinical investigation algorithms are available from the authors). Upper airway endoscopic abnormalities were qualitatively and quantitatively assessed[11] by a single otolaryngologist (M.R.S.). A diagnosis of LAD required the presence of symptoms of dyspnea associated with cough or wheezing, and the exclusion of infectious diseases. Additional diagnostic testing and criteria were described previously.[7] Airway symptom severity was assessed by using a previously described rhinosinusitis (RS) and asthma (A) symptom score,[12] as well as the combined overall score (RSA).

Atopy (the main variable of interest) was evaluated by means of radioallergosorbent test (RAST, 127 patients), skin prick testing (SPT, 45 patients), or both (36 patients).[13] For a limited time during this study, allergy testing was offered to all patients, irrespective of their disease status. The immunocapture technique was used for RAST, with a panel of 17 common allergens, including house dust mites, tree pollens, grasses, weeds, ragweeds, cat and dog dander, *Aspergillus*, and Alternaria. Evidence of sensitization to at least one aeroallergen by either or both techniques was required to classify a patient as atopic.

Ethnic and cultural background was established by self-identification as White, African-American, or Latino. A patient was considered a lifetime nonsmoker if (s)he had smoked less than 20 packs of cigarettes (or 12 oz. of tobacco) in a lifetime, or less than 1 cigarette/d (or 1 cigar/wk) for 1 year. A minimum of 12 months was required to deem a patient a former smoker.[14] For analytical purposes, smokers were divided between lifetime nonsmokers and ever smokers. We used arrival at the WTC site within the first 48 hours of the attack ("early arrival") as an occupational exposure-related predictor.[7]

Statistical Analyses

To determine whether the study sample was representative of our previously reported (and larger) study population,[7] binomial testing was used to compare proportions of categorical characteristics like sex, language spoken, major occupational groups, lack of health insurance, and clinical diagnoses of UAD and LAD. The *t* test was used to compare age. None of those variables was significantly different, and the sample was considered representative of the WTC HETP patient population as described previously.

The χ^2 and the Mann-Whitney tests were used to determine significant differences between patients with and without atopy on categorical and continuous variables, respectively. Logistic regression[15] was used to evaluate atopy as a risk factor for UAD and LAD, adjusting for other potential risk factors. Because UAD and LAD are probably interrelated pathophysiologically,[16] patients without any diagnosed airway disease ($n = 18$) where used as controls for the logistic regression analyses.

All statistical analyses were performed using SPSS software.[17] Two-tailed statistical significance testing with a P level less than 0.05 was used throughout.

Results

Table 1 summarizes the demographic and occupational characteristics of our study population and their major disease categories. Atopy was found in 74/136 (54.4%) of the patients.

Table 2 shows that although atopic subjects were not more likely to have been diagnosed with a WTC-related lower and UAD, they had significantly higher RSA (as well as RS and A) scores, and serum IgE levels. Ethnic background was not associated with atopic status, but immigrants were less likely to be atopic (22/62 vs 39/74, $P = 0.044$).

Multivariate logistic regression analyses (Table 3) identified early arrival at the WTC site and a previous diagnosis of asthma (but not atopy) as risk factors for a diagnosis of

TABLE 1
Demographic and Clinical Characteristics of Former WTC Workers in this Study (n = 136)

Characteristic	Number (%)
Sex: male	100 (73.5)
Age, yr (mean ± SD)	45.7 ± 8.1
Racial/cultural background	
Latino	75 (55.1)
White	50 (36.8)
African-American	11 (8.1)
Occupation	
Laborers	63 (46.3)
Firefighters	14 (10.3)
Police officers	5 (3.7)
Other (26 occupations)	54 (19.0)
Health uninsured	47 (34.6)
Never smokers	85 (62.5)
Clinical diagnoses	
UAD	110 (80.9)
LAD	56 (41.2)
Gastroesophageal reflux disease	76 (55.9)
Psychiatric disease	62 (45.6)
Musculoskeletal diseases	35 (25.7)
Atopic status	
Atopic	74 (54.4)

TABLE 2
Comparisons Between the Atopic and the Nonatopic Group

Variable	Atopic Group	Nonatopic Group	*P*
Age (yr), mean, SD	45.2 ± 8.5	46.4 ± 7.6	0.38
Ethnic/cultural background			0.59
White	30/50	20/50	
Latino	38/75	37/75	
African-American	6/11	5/11	
RSA score, mean, SD	34.7 ± 20	26 ± 19	0.02
Total IgE (IU/mL), mean, SD	223 ± 352	73 ± 137	0.002
Eosinophil count (per μl), mean, SD	203 ± 257	164 ± 161	0.31
LAD diagnoses	33/74	23/62	0.38
UAD diagnoses	63/74	47/62	0.17

TABLE 3
Logistic Multivariate Regression Models for UAD and LAD

	UAD		LAD	
	OR	*P*	OR	*P*
Age	1.01	0.80	1.07	0.12
Sex				
Female	1.00			
Male	1.53	0.49	0.99	0.20
Caucasian	1.00			
African-American	1.72	0.66	1.98	0.61
Latino	1.51	0.62	0.72	0.71
Nonatopic	1.00			
Atopic	3.04	0.048	2.99	0.13
Lifetime non-smokers	1.00			
Ever smoker	2.48	0.17	3.09	0.26
Late arrival	1.00			
Early arrival*	2.23	0.27	7.78	0.03
No previous asthma	1.00			
Previous asthma	0.82	0.76	5.41	0.03

*Arrival at the WTC site within the first 48 hours of the terrorist attack.

WTC-related LAD. In contrast, only atopy was significantly associated with a WTC-related UAD diagnosis.

Discussion

Atopy was present in 54.4% of this sample of symptomatic WTC workers. Bivariate analyses suggested that atopy was associated with higher symptom severity scores for both WTC-related UAD and LAD. Multivariate logistic regression analyses identified atopy as a predictor of WTC-related UAD but not LAD, after adjusting for age, sex, smoking status, early arrival at the WTC site, and having had a previously diagnosed asthma before September 11, 2001. With respect to LAD, however, the analyses confirmed our previous finding that early arrival at the WTC disaster site (within 48 hours of the attack) was a risk factor[7] and revealed that a history of a preexistent asthma (but not atopy) was also a risk factor.

It is generally accepted that dust and particulate exposures at the WTC disaster site had an nonspecific irritant nature, related to its high alkalinity, and the presence of a variety of low-molecular weight combustion products.[1,2] Atopy, a genetically determined characteristic, has appeared as an inconsistent risk factor in its association with occupational rhinitis,[9] and generally has not been associated with irritant-induced occupational asthma.[8] Our study suggests an association with UAD, but not with LAD in the WTC-exposed population.

A strength of this study relates to the study population, which is representative of the widest possible spectrum of occupations present at the WTC disaster site, and their associated exposure risk factors. Another strength is that clinical evaluations allowed a high level of detail in the characterization of the patients' exposures, competing risk factors, and their diagnoses, which has not been reported by surveillance data based studies thus far. Limitations of this study include the fact that WTC-dust exposed but completely asymptomatic workers were likely to be underrepresented in the study sample. On the other hand, that did not impede the exploration of the risk factors of interest, because there was enough variability in exposure and disease outcomes to allow the comparisons presented. Our analyses assume that atopy is a genetically determined trait in most individuals that preceded the development of WTC-related airway disease. Although that assumption still appears correct, there is at least some evidence from in vitro studies suggesting that polyaromatic hydrocarbons (which were in high concentration at the WTC site[2]) may initiate and enhance allergic airway disease.[18] Finally, although all patients with UAD had rhinitis, not all patients with LAD met diagnostic criteria for asthma. We can only presume a similar irritant-induced mechanism for the different WTC-related asthma and other LAD types.

With the above considerations in mind, the prevalence of atopy in this population is essentially identical to what has been reported (54.3%) in a national health survey in the United States,[19] suggesting that atopic indi-

viduals are not overrepresented in our sample of symptomatic workers, and our patient population in general. It also suggests, but does not prove, a predominantly irritant-induced effect in the causation of LAD. Atopy, on the other hand, seemed to be associated with WTC-related UAD, and also appeared to be associated with increased symptom severity for both types of airway disease.

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