

Reflux Symptoms and Disorders and Pulmonary Disease in Former World Trade Center Rescue and Recovery Workers and Volunteers

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Background: Gastroesophageal reflux disease is one of the most prevalent conditions among former World Trade Center (WTC) rescue and recovery workers. The reason for this proposed association with an inhalation injury is unclear. In this study, we clinically characterized the reflux disorders in former WTC workers, and we investigated their association with pulmonary function abnormalities and with clinical diagnoses of other WTC-related diseases. **Methods:** Forty-two former WTC workers underwent the following testing: symptom inventories, physical examination, spirometry, esophagogastroduodenoscopy, and 24-hour pH monitoring studies for the evaluation of chronic reflux-like symptoms. Patients were classified into two groups based on clinical evaluation: group 1 (reflux patients) including definitive reflux disorders (gastroesophageal reflux, nonerosive reflux, nonacid reflux, and laryngopharyngeal reflux diseases) and group 2 (no-reflux patients) patients without clinically significant reflux disease, including functional heartburn, and hypersensitive esophagus disorder. **Results:** The reflux and no-reflux patients had significantly different Johnson-DeMeester scores and esophageal acid exposure times. Patients with reflux disorders were more likely to have reduced forced vital capacity ($\chi^2 = 5.49, P = 0.031$) and also more likely to have been diagnosed with a lower airway disease ($\chi^2 = 7.14, P = 0.008$). We found no significant association between reflux and psychiatric disorders ($\chi^2 = 0.02, P = 0.89$), levels of exposure at the WTC site, or incidence of dry cough, or other upper airway disorders. **Conclusions:** A spectrum of reflux symptoms and disorders are present in WTC responders. Our data suggest that the presence of reflux disease is related to that of pulmonary function abnormality suggestive of air trapping and a diagnosis of a lower respiratory disease. (J Occup Environ Med. 2008;50:1351-1354)

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Gastroesophageal reflux disease (GERD) is one of the most frequently reported conditions among former World Trade Center (WTC) rescue and recovery workers (57.6%).¹ Our data on this patient population indicate that reflux disease is the only major disease category (together with lower airway disease) for which early (ie, within the first 48 hours) arrival at the WTC disaster site appears to be a risk factor¹ (a similar association has been recently reported for posttraumatic stress disorder²). The reason for this proposed association with a toxicant inhalation injury is unclear. A recent report by Ghanei et al,³ described features suggestive of GERD in a long-term follow-up study of inhalation injury victims. GERD has been associated with psychological conditions,^{4,5} and with lung functional abnormalities and diseases,⁶⁻⁸ both of which are highly prevalent among the former WTC workers.¹

In this study, we characterized clinically the reflux disorders in former WTC workers, and investigated their association with pulmonary functional abnormalities and with clinical diagnoses of other major WTC-related disease categories (namely, lower and upper airway, as well as psychiatric disease).

Materials and Methods

Patient Population

Patients were evaluated at the WTC Health Effects Treatment Program, a clinical unit established in January 2003 and dedicated exclu-

TABLE 1
Criteria for Each Reflux Disorder, and Group (for Analytical Purposes)

Diagnosis	pHmetry*	EGD	SAP/SI	Group
GERD	Abnormal	Abnormal	Either	(Definite) reflux
Nonerosive reflux disease (NERD)	Abnormal	Normal	Either	(Definite) reflux
Nonacid reflux disease (NARD)	Normal	Abnormal	Either	(Definite) reflux
Laryngopharyngeal reflux disease (LPR)	Abnormal	Normal	Either	(Definite) reflux
Hypersensitive esophagus syndrome (HSE)	Normal	Normal	Correlated	(Definite) reflux
No reflux	Normal	Normal	Normal	No reflux

EGD indicates esophagogastroduodenoscopy; SAP, symptom association probability; SI, symptom index.

*Abnormal pHmetry,¹¹ except for LPR.¹²

sively to the provision of diagnostic and treatment services to former WTC rescue and recovery workers and volunteers.¹ The eligibility criteria were described previously.⁹ The Mount Sinai School of Medicine Institutional Review Board approved this review, exempting it from the requirement for informed consent.

Clinical Evaluation

Physicians' diagnoses for upper and lower airway disease, GERD, and psychiatric diseases were based on clinical symptoms, general, and WTC-related occupational history, supportive diagnostic test data, and/or response to specific treatment, and have been described in detail previously.¹ Forty-two former WTC workers were selected sequentially to undergo esophagogastroduodenoscopy and 24-hour pH monitoring studies (pHmetries, off medications) for the evaluation of persistent reflux-like symptoms. pHmetries were performed by the BRAVO capsule¹⁰ ($n = 28$), or the wire method¹¹ ($n = 14$). The results of those studies and symptom correlation scores (either symptom association probability or symptom index) allowed a classification of the reflux disorder into a specific subtype and then two groups, as described in Table 1.

A pHmetry was considered abnormal if the esophageal acid exposure time exceeded 4% of the monitoring period and the Johnson-DeMeester score exceeded 22.¹¹ A symptom correlation score (symptom association probability or symptom index) exceeding 95% was considered indicative of a correlation between

esophageal acid exposure and symptoms (heartburn, chest pain, and cough) during pHmetry. Esophagogastroduodenoscopy abnormalities (deemed indicative of acid reflux disease) included esophageal erosions or Barrett's esophagus. A diagnosis of (isolated) laryngopharyngeal reflux disease required evidence of at least 15 episodes of reflux and 1.1% of acid exposure time detected in the proximal pH channel,¹² with normal distal pH channel acid exposure results.

Analytical Procedures

Patients were classified into two groups based on their diagnoses, and as suggested by others.¹³ The first group (reflux patients) included definitive reflux disorders (gastroesophageal reflux, nonerosive reflux, nonacid reflux, and laryngopharyngeal reflux diseases). The second group (no-reflux patients) included patients with functional heartburn and hypersensitive esophagus disorder, and normal studies.

The three most frequent psychiatric diagnoses in these patients were chronic posttraumatic stress disorder ($n = 19$), major depressive disorder ($n = 5$), agoraphobia with panic disorder ($n = 3$), and anxiety disorders ($n = 3$). Since these diseases often coexisted, any combination of them was grouped as psychiatric diagnoses ($n = 22$) for analytical purposes.

Statistical analyses were performed using Statistical Package for the Social Sciences, Statistical Products and Service Solutions (SPSS,

Inc, Chicago, IL) software.¹⁴ The χ^2 test (or the Fisher exact test when appropriate) and the Mann-Whitney tests were used to determine significant differences between two groups on categorical and continuous variables, respectively.¹⁵ Two-tailed statistical significance testing with a P level < 0.05 were used throughout.

Results

Clinical and demographic characteristics are summarized in Table 2.

TABLE 2
Clinical Characteristics of Former WTC Workers in This Study ($n = 42$)

Characteristic	n (%)
Male sex	31 (73.8%)
Age, yr	49.1; SD 7.7
English speaking	19 (45.2%)
Occupation	
Laborers	23 (54.8%)
Firefighters	8 (19.0%)
Health care	3 (7.1%)
Other (eight , occupations)	8 (19.0%)
Volunteers	5 (11.9%)
Union members	29 (69.0%)
Health uninsured	17 (40.5%)
Present at WTC first 48 hr	20 (46.5%)
WTC exposure duration, wk	17.4; SD 12.7
Smoking status	
Lifetime nonsmokers	25 (59.5%)
Former smokers	13 (31.0%)
Present smokers	4 (9.5%)
Symptoms	
Heartburn >once weekly	42 (100.0%)
Dry cough	30 (71.4%)
Exertional dyspnea	29 (69.0%)
Upper airway disease	31 (73.8%)
Lower airway disease	17 (40.5%)
Psychiatric disease	19 (45.2%)

These characteristics were similar to what we previously reported for a much larger ($n = 554$) group of patients.¹

Table 3 summarizes the results of the gastroenterological evaluation of the patients, according to the criteria described in Table 1.

As seen on Table 4, the reflux had significantly higher Johnson-DeMeester scores and esophageal acid exposure times compared with the no-reflux patients. Patient with reflux disorders were more likely to have reduced forced vital capacity (FVC) and also more likely to have been diagnosed with a lower airway disease. In contrast, we found no significant association between reflux and psychiatric or upper airway disorders, exposure duration at the WTC site, or prevalence of dry cough.

Conclusions

A spectrum of reflux disorders is present in WTC responders. To our knowledge, the association between inhalation injury and reflux disease had not been described until the recent report from Ghanei et al^{3,16} and our own.¹ The reason for this association is unclear. Since respiratory disease and psychological diseases are both very prevalent among the WTC responders,¹ one can hypothesize that reflux disease is associated with either one of those types of conditions. Reflux symptoms have been documented more frequently in individuals with psychological diseases,^{4,5} and experimental data have linked stress responses to esophageal mucosal abnormalities.^{17,18} Acid aspiration and the triggering of esophago-, esophago-pharyngeal-, or esophago-laryngeal-bronchial reflexes^{19,20} have been invoked as possible mechanisms mediating the close relationship between reflux disease and pulmonary symptoms and diseases. On the other hand, the association between reflux and respiratory symptoms appears to be independent from excessive body weight, a risk factor for both.^{21,22}

TABLE 3
Diagnostic Categories and Their Frequency

Diagnoses	Frequency		Group
GERD	9 (21.4%)	27 (64.2%)	Reflux
NERD	9 (21.4%)	27 (64.2%)	Reflux
NARD	7 (16.7%)	27 (64.2%)	Reflux
LPR	2 (4.8%)	27 (64.2%)	Reflux
HSE	9 (21.4%)	15 (35.8%)	No reflux
No reflux	6 (14.3%)	15 (35.8%)	No reflux

TABLE 4
Comparisons Between the Reflux and the No-Reflux Group

Variable	Reflux group	No Reflux group	P
Johnson-DeMeester score	34.1; SD 27.8	8.6; SD 5.9	0.002
Acid exposure time (min)	98.4; SD 89.4	20.3; SD 20.3	0.002
Abnormal spirometry	14/27	3/15	0.044
Reduced FVC	11/27	1/15	0.031
LAD diagnoses	15/27	2/15	0.008
UAD diagnoses	22/27	9/15	0.126
Psychiatric diagnoses	15/27	8/15	0.890
Dry cough	20/27	10/15	0.726
Exertional dyspnea	20/27	9/15	0.273

Reduced FVC is the most frequent functional abnormality in this patient population,¹ which probably reflects most often gas trapping, perhaps at the bronchiolar level.²³ Our data suggest that the presence of reflux disease in this patient population is related to a significant degree to that of pulmonary function abnormality such as reduced FVC (and presumably air trapping), and also to carrying a diagnosis of a WTC-related lower airway disease. Reflux disease, on the other hand, appeared unrelated to psychiatric disease. The association suggested by our data would seem to leave a balance of unexplained cases of reflux disease where lung disease and/or function abnormalities have not been identified thus far and, in fact, reflux appears consistently more prevalent than lung disease among these workers.¹

Further studies with larger samples should examine the correlation of psychiatric symptoms (as opposed to diagnoses) and specific subtypes of respiratory diagnoses and functional abnormalities with specific subtypes of reflux diseases. Such

larger studies aimed at exploring the proposed association between reflux disorders and toxic inhalation injuries will also have to include methodologies to clearly differentiate reflux syndromes as we did in our study. Finally, and in view of the intensity of the reported symptoms, the significant impact on quality of life, and the interactions with comorbidities, our study underscores the importance of comprehensive detailed clinical observation and multidisciplinary diagnosis and treatment of victims of toxicant inhalations.

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References

- de la Hoz RE, Shohet MR, Chasan R, et al. Occupational toxicant inhalation injury: the World Trade Center (WTC) experience. *Int Arch Occup Environ Health*. 2008;81:479–485.

2. Perrin MA, DiGrande L, Wheeler K, Thorpe L, Farfel M, Brackbill R. Differences in PTSD prevalence and associated risk factors among World Trade Center disaster rescue and recovery workers. *Am J Psychiatry*. 2007;164:1385–1394.
3. Ghanei M, Khedmat H, Mardi F, Hosseini A. Distal esophagitis in patients with mustard-gas induced chronic cough. *Dis Esophagus*. 2006;19:285–288.
4. Avidan B, Sonnenberg A, Giblovich H, Sontag SJ. Reflux symptoms are associated with psychiatric disease. *Aliment Pharmacol Ther*. 2001;15:1907–1912.
5. Baker LH, Lieberman D, Oehlke M. Psychological distress in patients with gastroesophageal reflux disease. *Am J Gastroenterol*. 1995;90:1797–1803.
6. Ruigómez A, García Rodríguez LA, Wallander M-A, Johansson S, Thomas M, Price D. Gastroesophageal reflux disease and asthma—a longitudinal study in U.K. general practice. *Chest*. 2005;128:85–93.
7. Kempainen RR, Savik K, Whelan TP, Dunitz JM, Herrington CS, Billings JL. High prevalence of proximal and distal gastroesophageal reflux disease in advanced COPD. *Chest*. 2007;131:1666–1671.
8. Schachter LM, Dixon J, Pierce RJ, O'Brien P. Severe gastroesophageal reflux is associated with reduced carbon monoxide diffusing capacity. *Chest*. 2003;123:1932–1938.
9. Centers for Disease Control and Prevention. Physical health status of World Trade Center rescue and recovery workers and volunteers—New York City, July, 2002–August, 2004. *MMWR*. 2005; 53:807–812.
10. Ahlawat SK, Novak DJ, Williams DC, Maher KA, Barton F, Benjamin SB. Day-to-day variability in acid reflux patterns using the BRAVO pH monitoring system. *J Clin Gastroenterol*. 2006; 40:20–24.
11. Johnson LF, Demeester TR. Twenty-four-hour pH monitoring of the distal esophagus. A quantitative measure of gastroesophageal reflux. *Am J Gastroenterol*. 1974;62:325–332.
12. Richardson BE, Heywood BM, Sims S, Stoner J, Leopold DA. Laryngopharyngeal reflux: trends in diagnostic interpretation criteria. *Dysphagia*. 2007;19: 248–255.
13. Frazzoni M, Manno M, De Micheli E, Savarino V. Pathophysiological characteristics of the various forms of gastro-oesophageal reflux disease: spectrum disease or distinct phenotypic presentations? *Dig Liver Dis*. 2006;38:643–648.
14. SPSS Inc. *SPSS for Windows ver. 12.0*. Chicago: SPSS Inc; 2003.
15. Zar JH. *Biostatistical Analysis*. Upper Saddle River, NJ: Prentice Hall; 1996:1–662.
16. Ghanei M, Hosseini AR, Arabbaferani Z, Shahkarami E. Evaluation of chronic cough in chemical chronic bronchitis patients. *Environ Toxicol Pharmacol*. 2005; 20:6–10.
17. Farre R, De Vos R, Geboes K, et al. Critical role of stress in increased oesophageal mucosa permeability and dilated intercellular spaces. *Gut*. 2007;56: 1191–1197.
18. Söderholm JD. Stress-related changes in oesophageal permeability: filling the gaps of GORD? *Gut*. 2007;56:1177–1180.
19. Tomonaga T, Awad ZT, Filipi CJ, et al. Symptom predictability of reflux-induced respiratory disease. *Dig Dis Sci*. 2002;47: 9–14.
20. Lang IM, Haworth ST, Medda BK, Roerig DL, Forster HV, Shaker R. Airway responses to esophageal acidification. *Am J Physiol Regul Integr Comp Physiol*. 2008; 294:R211–R219.
21. Hancox R, Poulton R, Taylor DR, et al. Associations between respiratory symptoms, lung function and gastro-oesophageal reflux symptoms in a population-based birth cohort. *Respir Res*. 2006;7:142.
22. Taylor B, Mannino D, Brown C, Crocker D, Twum-Baah N, Holguin F. Body mass index and asthma severity in the National Asthma Survey. *Thorax*. 2008;63:14–20.
23. Mendelson DS, Roggeveen M, Levin SM, Herbert R, de la Hoz RE. Air trapping detected on end-expiratory high resolution CT in symptomatic World Trade Center rescue and recovery workers. *J Occup Environ Med*. 2007;49:840–845.