Air Trapping Detected on End-Expiratory High-Resolution Computed Tomography in Symptomatic World Trade Center Rescue and Recovery Workers

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Objectives: *We utilized end-expiratory chest computed tomography (CT) to investigate air trapping (AT) in symptomatic former World Trade Center (WTC) workers, and correlated the findings with clinical, physiological, and exposure-related characteristics.* ***Methods:*** *Twenty-nine WTC workers with lower respiratory symptoms were evaluated. Clinical data included symptom inventories, quantitative respiratory symptom scores, WTC dust exposure duration, pulmonary function tests, and inspiratory and end-expiratory high-resolution chest CT scans. The latter were scored quantitatively for AT (by two methods) and interstitial changes, and those scores were correlated with the clinical data.* ***Results:*** *The two AT scoring methods yielded highly correlated results. AT was demonstrated in 25 of 29 patients, with scores ranging from 0 to 24 (mean, 10.6). There was a statistically significant correlation between AT and the duration of dust exposure. AT scores were significantly higher in patients with restrictive lung function data, and in lifetime nonsmokers.* ***Conclusions:*** *Our data suggest that AT from small airways disease may account for some of the reported clinical and pulmonary functional abnormalities in WTC dust-exposed workers, and support the use of high-resolution CT scans in the investigation and characterization of the pulmonary ailments of selected workers.* (J Occup Environ Med. *2007;49:840–845*)

In the aftermath of the September 11, 2001 terrorist attacks in New York City, a large number of rescue and recovery workers and volunteers flocked to the World Trade Center (WTC) site and were exposed to particulate material and fumes created by the crumbling towers and the fires that ensued. The "WTC dust cloud" contained a complex (if incompletely characterized) mixture of caustic cement particles, glass fibers, polycyclic aromatic hydrocarbons (PAHs), combustion products, and many others.[1] Exposure to WTC dust has been linked to the development of upper and lower respiratory symptoms in exposed workers,[2–4] as well as bronchial hyperreactivity, asthma,[2] and evidence of prolonged airway inflammation.[5] However, instead of a typical obstructive ventilatory impairment expected from irritant-induced airway injury, an unexpectedly high proportion of exposed workers have had spirometric changes demonstrating declines in 1-second forced expiratory volume (FEV_1) and forced vital capacity (FVC), with preservation of their ratio.[2–4,6] This pattern, which is most commonly interpreted as representing ventilatory restrictive impairment, can also result from airway obstruction (usually at the bronchiolar level) with gas trapping.[7,8] Given the well-known difficulty in diagnosing small airways disease by pulmonary function testing (PFT),[9,10] the diagnostic characterization of many

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Part of this work was presented in abstract form at the 2004 Annual Meeting of the Radiologic Society of North America.

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DOI: 10.1097/JOM.0b013e3180d09e87

WTC responders' clinical conditions has been rather difficult. We report on the findings of paired inspiratory and end-expiratory chest computed tomography (CT), which was employed to assist in the characterization of the patients' respiratory complaints and, more specifically, the investigation of air trapping (AT). We investigated the correlation of AT on expiratory chest CT with WTC dust exposure duration, respiratory symptom severity scores, smoking status, and pulmonary function tests results.

Materials and Methods

Study Subjects and Clinical Data

Subjects were evaluated at the WTC Health Effects Treatment Program, a philanthropically funded clinical program established in January of 2003 at The Mount Sinai Medical Center to provide diagnostic and treatment services to former WTC rescue and recovery workers and volunteers, after they have been screened at other programs in New York City. Of the first 453 patients evaluated between January and October of 2003, 222 had symptomatic lower respiratory disease that began while or shortly after working at the WTC site. Patients were referred for CT evaluation if their clinical diagnosis could not be clearly characterized, and their spirometry was either normal or showed a decreased vital capacity or (less frequently) a mild obstructive impairment, without either clear spirometric or clinical response to bronchodilator administration. Patients with clear clinical and functional evidence of asthma, chronic obstructive pulmonary disease (COPD), or other lung diseases were excluded from the study. The study group thus consisted of the first 29 patients (27 men and 2 women, with an average age of 47 years, ranging from 34–62 years) who met the previously mentioned criteria. They underwent a standardized history and physical examination, chest radiography, as well as office spirometry. Respiratory symptom severity was assessed by means of the asthma score component (which rates symptoms of dyspnea, wheezing, and cough, with a maximum possible score of 40) of a previously described and validated respiratory symptom score.[11] A detailed occupational history was obtained, with particular attention to the nature, duration (in weeks), and timing (in relation to the terrorist attack) of the workers' exposures to dust at the WTC site. WTC work duration was utilized as a quantitative measure of cumulative dust and respiratory irritant exposure. Patients were subsequently sent for detailed pulmonary function tests, and a combination of inspiratory and end-expiratory chest CT studies (described below). Chest CT scans were obtained a median of 2.4 years (range, 2.1–2.9 years) after September 11, 2001. A patient was considered a lifetime nonsmoker if he or she had smoked less than 20 packs of cigarettes (or 12 ounces of tobacco) in a lifetime, or less than 1 cigarette/d (or 1 cigar/wk) for 1 year.[12] A minimum of 12 months was required to deem a patient a former smoker. For analytical purposes, the patients' smoking status was categorized as ever smokers or lifetime nonsmokers. The Institutional Review Board of the Mount Sinai School of Medicine approved this study.

Chest CT Technique

Noncontrast high-resolution CT (HRCT) was performed on a Siemens Somatom 16-slice multidetector CT unit using a 512 × 512 reconstruction matrix, 120 kVp, and a Caredose protocol that automatically adjusted tube current (mA) according to patient size. The scans were obtained from above the lung apices to below the costophrenic sulci with the patient in the supine position. Scans were obtained at suspended full inspiration with a 0.75-mm slice thickness followed by scans at suspended full expiration. The scans were reconstructed at 1 mm using a lung algorithm, as well as at 5 mm with a soft tissue algorithm. The patients were coached with breathing instructions and allowed to rehearse before inspiratory and expiratory scanning. A radiologist monitored all studies.

Chest CT Evaluation

Each end-expiratory chest CT evaluation was scored globally for severity of AT (development of a mosaic pattern on end-expiratory CT only) and interstitial lung disease (ILD) changes on an integer scale of 0 to 3 as follows: 0, no regions; 1, 1% to 25% of total lung parenchyma; 2, 26% to 50% of total; 3, 51% to 100% of total. These scores were global in that they were an overall assessment of both lung fields. In addition, a more detailed zonal evaluation of the lungs was performed to assess AT, using a system similar to that described by other authors.[13] Three zones were defined in each lung as follows: upper zone, above the level of the carina; middle zone, between the level of the carina and the level of the inferior pulmonary veins; and lower zone, below the level of the inferior pulmonary veins. The following five-point integer scoring scale was used: 0, no regions of AT; 1, 1% to 25% of cross-sectional area involved; 2, 26% to 50% of area; 3, 51% to 75% of area; 4, 76% to 100% of area. The scores of each of the six lung zones were then added, giving a maximum possible score of 24. With regard to ILD, we evaluated the scans for intra- and interlobular lines, reticular density, ground glass density, and nodules, and scored them utilizing a global 0 to 3 severity scale as described above for AT. Other structural changes were also noted and tabulated, but not quantified. All 1-mm slices were reviewed. Two radiologists (D.S.M., with 24 years experience, and M.R., a third-year radiology resident), blinded to functional information, reviewed the HRCT images together and reached decision by consensus.

Pulmonary Function Testing

PFT included pre- and post-bronchodilator spirometry, plethysmographic lung volume measurement, and diffusion capacity by the single-breath method. In addition, in 14 of 29 patients, pulmonary function evaluation included methacholine bronchoprovocation testing. A decreased FEV_1/FVC ratio defined obstruction, a decreased total lung capacity defined restriction, and an increased residual volume defined overinflation. A 20% decrease in FEV_1 by a concentration of methacholine (PC_{20}) not exceeding 10 mg/mL was considered evidence of significant bronchial hyperreactivity. All testing and interpretation followed published American Thoracic Society recommendations, and confidence intervals were used to determine normality categorically for all pulmonary function measurements.[14]

Statistical Analyses

Statistical analyses were performed using SPSS software.[15] The Mann-Whitney and χ^2 tests were used to determine significant differences between any two groups (eg, ever smokers vs lifetime nonsmokers) on continuous and categorical variables, respectively. In order to identify statistically significant correlations between two continuous variables, the Spearman's ρ (ρ) correlation coefficient was used. Two-tailed statistical significance testing with a P level less than 0.05 was used throughout.

Results

Subjects reported having worked a median of 12 weeks at the disaster site (duration range, 1 day to 44 weeks), with 16 patients (55%) having arrived at the WTC site on September 11, 2001 and 21 patients (72%) within the first 48 hours of the attack. All workers reported having been provided no respiratory protective equipment and having been provided with it only after days or weeks of unprotected exposure or infrequent resupplies (ie, new masks or respirator cartridge replacements). They also indicated that the characteristics of their work made it very difficult to wear such equipment during a complete shift. None of the workers was a resident of Lower Manhattan, where the WTC was located. Table 1 summarizes the characteristics of the study group. The median asthma symptom score was 13, ranging from 4 to 35. The majority of patients were lifetime nonsmokers (n = 15, 52%). The ever-smoking group included current (n = 7, 24%) and former (n = 7, 24%) smokers.

TABLE 1
Patient Characteristics

	n (%)
Male sex	27 (93)
Smoking category	
Lifetime non-smokers	15 (52)
Ever smokers	14 (48)
Occupation at WTC site	
Laborers	9 (31)
Firefighters	8 (28)
Engineers	2 (7)
Ironworkers	2 (7)
Symptoms	
Exertional dyspnea	26 (90)
Non-exertional dyspnea	15 (52)
Dry cough	20 (69)
Productive cough	20 (69)
Office spirometry	
Decreased vital capacity	16 (55)
Normal	9 (31)
Obstruction	4 (14)
WTC-related comorbidities	
Gastroesophageal reflux disease	23 (79)
Chronic rhinitis ± sinusitis	20 (69)
Psychological illness	14 (48)
Chronic musculoskeletal conditions	6 (20)

The two AT scoring systems were very highly correlated (Spearman's ρ = 0.887, $P < 0.001$), all correlations were equally significant with either system, and the detailed zonal system (with a maximum score of 24) will be used hereafter to report all findings. AT scores ranged from 0 (4 patients) to 24 (mean 10.6 ± 7.7, median 10.0). Figure 1 shows a chest CT scan in a patient with a score of 20. Although AT scores tended to be higher in the lower lung zones, the differences in AT score among the three lung zones (upper, middle, lower) did not reach statistical significance.

There was a statistically significant correlation between the AT score and the duration of WTC dust exposure (ρ = 0.429, P = 0.020). The correlation between AT score and the asthma symptom severity score was of similar magnitude but failed to reach statistical significance (ρ = 0.401, P = 0.052). Patients with relatively higher AT scores (defined arbitrarily as 6 or more, corresponding to a minimum of 25% cross-sectional degree of involvement) were more likely to be lifetime nonsmokers (12 of 18 or 66.7%) than were those with AT scores of less than 6 (3 of 11 or 27.2%, P = 0.039). In a post hoc analysis, there appeared to be no correlation between age and

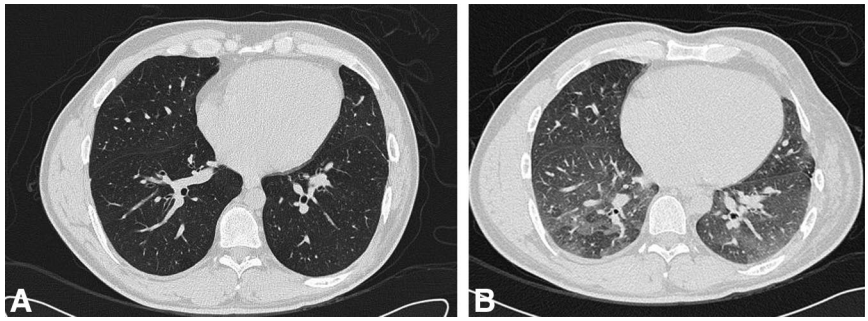

Fig. 1. Patient with an AT score of 20 (maximum possible score of 24). Figure 1A demonstrates a section of the lower zone from the end-inpiratory CT, and Figure 1B is a similar level from the end-exspiratory examination. The mosaic pattern can be noted on the end expiratory portion of the examination. The same level appears normal on the inspiratory image. This combination is indicative of AT.

AT in our patient group ($\rho = 0.007$, $P = 0.971$).

Analyses of PFTs revealed obstruction or overinflation in 8 patients, restriction in 12 patients, decreased diffusion capacity in 8 patients (7 with restriction, and 1 with overinflation), and only 4 of 14 (28.6%) methacholine bronchoprovocation tests revealed significant bronchial hyperreactivity. Most abnormalities were mild, and nine patients (31%) had completely normal PFTs. The AT score was significantly higher in patients with evidence of restriction ($P = 0.030$), but not in those with evidence of obstruction, overinflation, or diffusion abnormality ($P = 0.254$, 0.207, 0.374, respectively).

The chest CT scans also demonstrated a few isolated and mild structural abnormalities, which did not exhibit any correlation with any patient exposure, demographic, imaging, or lung functional characteristic. Very mild interstitial changes (scattered linear densities for the most part) were found with low ILD scores (mean, 0.9 ± 0.86; median,1.0), with 10 patients having a score of 0, and 14 patients having a score of 1. The ILD scores did not demonstrate any correlation with the AT score ($\rho = -0.176$, $P = 0.361$) or with any of the pulmonary functional measurements, including restriction ($P = 0.516$). Nine patients had isolated, minimal bronchiectatic changes, and five (3 former and 1 present smoker and 1 lifetime nonsmoker) had mild emphysematous changes on their CT scans. There were 41 pulmonary nodules detected in 18 of the 29 patients, with a maximum of five in one of the patients. The nodule diameters ranged from 1 to 15 mm, with an average size of 3.9 mm.

Discussion

Our study demonstrated AT (and presumably small airway dysfunction) in persistently symptomatic workers exposed to WTC dust in the course of their rescue, cleanup, and service restoration duties at the WTC site. The AT score was higher in patients with pulmonary functional evidence of restriction, was correlated with the duration of exposure to dust and irritants at the WTC site, and showed a borderline significant correlation with the asthma symptom score.

Disease at the level of the small airways is present in many lung diseases and contributes significantly to functional impairment. Diagnostic testing for small airway disease remains challenging, since noninvasive pulmonary function tests have failed to demonstrate their sensitivity, or clinical practicality,[10,16] to obviate the need for an open lung biopsy. Small airway disease has also been known to be one possible result from exposures to respiratory irritants, eg, in the occupational setting.[16,17] Moreover, a recent case report suggested an association of bronchiolitis obliterans with WTC dust exposure.[18] The patient on that report had a normal routine (ie, inspiratory) chest CT scan. The patients in this study presented with respiratory symptoms and findings suggestive of bronchial disease and/or asthma, but exhibited only minimal initial pulmonary functional findings (Table 1). This group underwent inspiratory CT and end-expiratory CT to allow evaluation of the more peripheral airway segments which might have been preferentially injured by particulates in the respirable range and/or relatively more lipophilic.[19] AT, manifested as the failure of a portion of lung to increase its attenuation homogeneously with adjacent segments during expiratory CT scans, indicates gas retention within that portion of the lung,[20] is a sensitive indicator of small airway disease,[21,22] and has been readily detected in pulmonary diseases known to be associated with bronchiolitis.[13,23–25]

Data from the largest surveys of WTC responders have documented the high prevalence of new or aggravated and persistent symptoms of respiratory disease, which can be frequently characterized as asthma or COPD. A remarkably consistent finding has been the high proportion of individuals with reduction in their FVC.[2–4] This pattern is more frequently interpreted as a restrictive impairment, as opposed to the obstructive pattern more typical for asthma. This apparent restriction can, however, result from AT distal to heterogeneously distributed obstructed bronchioles.[7,8,26] The presence of true restriction in our patients is not surprising since this is a frequent manifestation of small airway disease,[27] which has been hypothesized to result from subtraction of distal lung units in parallel and decreased lung distensibility.[28–30]

There was limited sampling of the WTC dust cloud, which limited visibility of the southern end of Manhattan for many months after the September 11, 2001 attack. The dust was a complex mixture, which probably varied in its characteristics along time. Components of the WTC dust included cement particles, glass fibers, PAHs, and polychlorinated biphenyls, among others. The pH of the particles ranged from 9.5 to 11,[1] and the concentrations of PAHs were about threefold higher than those in relatively polluted urban areas. There were particulates of respirable aerodynamic diameter in the WTC dust, which would be expected to reach the peripheral airways. Different lines of evidence suggest that WTC dust induces inflammatory and obstructive airway changes. WTC particulate matter induced cytokine release by primary human lung macrophage cell cultures[31] and bronchial hyperresponsiveness in exposed mice.[32] WTC dust exposure has been associated with prolonged airway inflammatory changes manifested in the induced sputum of New York firefighters,[5] and exposure intensity (particularly within the first 48 hours of the towers collapse) has been associated with increased risk of spirometric abnormalities, and persistent

bronchial hyperreactivity.[2,6,33] Likewise, we found that the chest CT scan-derived AT score was correlated with the duration of the patient's WTC dust exposure. It needs to be noted that almost three of four of these patients were also present at the WTC site within 48 hours of the towers collapse.

Two additional observations with regard to the AT scoring systems deserve comments. The first was the high correlation between the two AT scores that we derived. This correlation suggests that the global score, simpler to estimate during a reading session, could be an acceptable methodology for subjectively assessing the presence and degree of AT. The more detailed zonal scoring system is a step toward a quantitative approach, yet still falls short of providing a refined quantification of AT, given that it remains a visual assessment. The second related observation was that AT was more easily assessed in the lower lung zones (as defined in the Materials and Methods section), to the point of being most easily predictive of the overall AT score compared with the upper and mid lung zones. Lee et al[34] reported a similar distribution. Further research is warranted to provide a robust, easily reproducible measure of lung disease, which can be deployed in routine clinical practice.

The extent of AT that can be identified in "normal" individuals, as well as the influence of age and smoking on this finding,[34] remain to be established. Our study was not designed to address those issues. Using a similar technique, however, Lee et al[34] reported that the AT found in their asymptomatic individuals never exceeded 25% of the cross-sectional lung area. Most of our patients with AT (18 of 25, 72%) exceeded that proportion. With regard to smoking, our patients with higher AT scores were clearly more likely to be lifetime nonsmokers, and in a post hoc analysis, there was no suggestion of a correlation between AT scores and age. The very high proportion of patients with concurrent rhinosinusitis is likely to be a result of upper respiratory irritant exposure, and an association between rhinitis and small airway dysfunction has been suggested.[35] Less clear and established, but increasingly suggested by our observations and those of others, is the potential association of gastroesophageal reflux disease with irritant-induced lung disease and bronchiolitis.[36,37] Finally, the finding of nodules, and of mild emphysematous and bronchiectatic changes may be due, respectively, to preexisting disease or sequelae of previous disease. At least in some of the cases, however, they may represent changes induced by small airway disease.[38]

In conclusion, our data suggest that high-resolution chest CT scans with expiratory and inspiratory views might provide a tool in the diagnostic evaluation of symptomatic workers who were subjected to dust and irritant inhalation at the WTC site, in order to investigate the presence of AT (and presumably small airway disease). Our data suggest that CT scans should be particularly useful in the subset of patients who present with symptoms but unclear or no pulmonary functional findings consistent with asthma or COPD, and with similar decreases in FEV_1 and FVC or evidence of restriction by PFT. Scoring methods expand the characterization of the extent of those findings, and should allow longitudinal follow-up of these abnormalities.

Acknowledgments

The authors acknowledge the contributions of Mr Diego Levy and Mr Oscar Castillo to data gathering, entry, and database management. The authors thank Dr Paul Landsbergis for his critical review of the manuscript and suggestions.

This work was made possible by the support of the American Red Cross, the September 11 Fund, the Robin Hood Foundation, and the Bear Stearns Charitable Foundation.

References

1. Lioy PJ, Weisel C, Millette JR, et al. Characterization of the dust/smoke aerosol that settled east of the World Trade Center (WTC) in lower Manhattan after the collapse of the WTC 11 September 2001. *Environ Health Perspect*. 2002; 110:703–714.
2. Prezant DJ, Weiden M, Banauch GI, et al. Cough and bronchial responsiveness in firefighters at the World Trade Center site. *N Engl J Med*. 2002;347:806–815.
3. Salzman SH, Moosavy FM, Miskoff JA, Friedmann P, Fried G, Rosen MJ. Early respiratory abnormalities in emergency services police officers at the World Trade Center site. *J Occup Environ Med*. 2004;46:113–122.
4. Levin SM, Herbert R, Moline JM, et al. Physical health status of World Trade Center rescue and recovery workers and volunteers—New York City, July 2002–August 2004. *Morb Mortal Wkly Rep*. 2005;53:807–812.
5. Fireman EM, Lerman Y, Ganor E, et al. Induced sputum assessment in New York City firefighters exposed to World Trade Center dust. *Environ Health Perspect*. 2004;112:1564–1569.
6. Feldman DM, Baron SL, Bernard BP, et al. Symptoms, respiratory use, and pulmonary function changes among New York City firefighters responding to the World Trade Center disaster. *Chest*. 2004;125:1256–1264.
7. Colp C, Williams MH. Total occlusion of airways producing a restrictive pattern of ventilatory impairment. *Am Rev Respir Dis*. 1973;108:118–122.
8. Gilbert R, Auchincloss JH. What is a 'restrictive' defect? *Arch Intern Med*. 1986;146:1779–1781.
9. Schachter EN. Small airway function: the tests and their evaluation. In: Miller A, ed. *Pulmonary Function Tests in Clinical and Occupational Lung Disease*. Orlando, FL: Grune & Stratton; 1986:123–132.
10. Hayes GB, Christiani DC. Measures of small airways disease as predictors of chronic obstructive pulmonary disease. *Occup Med*. 1993;8:375–395.
11. Wasserfallen J-B, Gold K, Schulman KA, Baraniuk JM. Development and validation of a rhinoconjunctivitis and asthma symptom score for use as an outcome measure in clinical trials. *J Allergy Clin Immunol*. 1997;100:16–22.
12. American Thoracic Society. Epidemiology standardization project. *Am Rev Respir Dis*. 1978;118:1–120.
13. Tanaka N, Kim JS, Newell JD, et al. Rheumatoid arthritis-related lung dis-

eases: CT findings. *Radiology*. 2004;232: 81–91.
14. American Thoracic Society. Lung function testing: selection of reference values and interpretative strategies. *Am Rev Respir Dis.* 1991;144:1202–1218.
15. SPSS Inc. *SPSS for Windows. Ver. 12.0.* Chicago: SPSS Inc; 2003.
16. de la Hoz RE, Schlueter DP, Rom WN. Chronic lung disease secondary to ammonia inhalation injury: a report on three cases. *Am J Ind Med*. 1996;29:209–214.
17. de la Hoz RE, Berger KI, Klugh TT, Friedman-Jiménez G, Goldring RM. Frequency dependence of compliance in the evaluation of patients with unexplained respiratory symptoms. *Respir Med*. 2000; 94:221–227.
18. Mann JM, Sha KK, Kline G, Breuer F-U, Miller A. World Trade Center dyspnea: bronchiolitis obliterans with functional improvement: a case report. *Am J Ind Med*. 2005;48:225–229.
19. Balmes JR. Acute pulmonary injury from hazardous materials. In: Sullivan JB, Krieger GR, eds. *Hazardous Materials Toxicology. Clinical Principles of Environmental Health.* Baltimore: Williams & Wilkins; 1992:425–432.
20. Austin JHM, Müller NL, Friedman PJ, et al. Glossary of terms for CT of the lungs: recommendations of the Nomenclature Committee of the Fleischner Society. *Radiology*. 1996;200:327–331.
21. Lucidarme O, Coche E, Cluzel P, Mourey-Gerosa I, Howarth N, Grenier P. Expiratory CT scans for chronic airway disease: correlation with pulmonary function test results. *Am J Roentgenol*. 1998; 170:301–307.
22. Mastora I, Remy-Jardin M, Sobaszek A, Boulenguez C, Remy J, Edme J-L. Thin-section CT finding in 250 volunteers: assessment of the relationship of CT findings with smoking history and pulmonary function test results. *Radiology.* 2001;218:695–702.
23. Perez T, Remy-Jardin M, Cortet B. Airways involvement in rheumatoid arthritis: clinical, functional, and HRCT findings. *Am J Respir Crit Care Med*. 1998;157:1658–1665.
24. Franquet T, Díaz C, Domingo P, Giménez A, Geli C. Air trapping in primary Sjögren syndrome: correlation of expiratory CT with pulmonary function tests. *J Comput Assist Tomogr*. 1999;23:169–173.
25. Bartz RR, Stern EJ. Airways obstruction in patients with sarcoidosis: expiratory CT scan findings. *J Thorac Imaging*. 2000;15:285–289.
26. Macklem PT, Mead J. Resistance of central and peripheral airways measured by a retrograde catheter. *J Appl Physiol*. 1967; 22:395–401.
27. Epler GR, Colby TV, McLoud TC, Carrington CB, Gaensler EA. Bronchiolitis obliterans organizing pneumonia. *N Engl J Med*. 1985;312:152–158.
28. Mead J. The lung's "quiet zone" [editorial]. *N Engl J Med.* 1970;282:1318–1319.
29. Hudgel DW, Cooper D, Souhrada JF. Reversible restrictive lung disease simulating asthma. *Ann Intern Med*. 1976;85: 328–332.
30. Guerry-Force ML, Müller NL, Wright JL, et al. A comparison of bronchiolitis obliterans with organizing pneumonia, usual interstitial pneumonia, and small airways disease. *Am Rev Respir Dis*. 1987;135:705–712.
31. Payne JP, Kemp SJ, Dewar A, et al. Effects of airborne World Trade Center dust on cytokine release by primary human lung cells in vitro. *J Occup Environ Med.* 2004;46:420–427.
32. Gavett SH, Haykal-Coates N, Highfill JW, et al. World Trade Center fine particulate matter causes respiratory tract hyperresponsiveness in mice. *Environ Health Perspect.* 2003;111:981–991.
33. Banauch GI, Alleyne D, Sánchez R, et al. Persistent hyperreactivity and reactive airway dysfunction in firefighters at the World Trade Center. *Am J Respir Crit Care Med*. 2003;168:54–62.
34. Lee KW, Chung SY, Yang I, Lee Y, Ko EY, Park MJ. Correlation of aging and smoking with air trapping at thin-section CT of the lung in asymptomatic subjects. *Radiology*. 2000;214:831–836.
35. Morgan EJ, Hall DR. Abnormalities of lung function in hay fever. *Thorax*. 1976; 31:80–86.
36. Ghanei M, Khedmat H, Mardi F, Hosseini A. Distal esophagitis in patients with mustard-gas induced chronic cough. *Dis Esophagus*. 2006;19:285–288.
37. Ghanei M, Mokhtari M, Mirmohammad M, Aslani J, Alaeddini F. High resolution computerized tomography of chest in patients exposed to sulfur mustard. *Iran J Radiol.* 2003;1:1–6.
38. Hartman TE, Swensen SJ, Müller NL. Bronchiolar diseases: computed tomography. In: Epler GR, ed. *Diseases of the Bronchioles.* New York: Raven Press; 1994:43–57.