Giles F. Filley Lecture

Emerging Exposures and Respiratory Health
World Trade Center Dust

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The attack on the World Trade Center (WTC) on 9/11/2001 produced a massive dust cloud with acute exposure, and the rubble pile burning over 3 months exposed more than 300,000 residents, rescue workers, and clean-up workers. Firefighters in the New York City Fire Department had significant respiratory symptoms characterized by cough, dyspnea, gastroesophageal reflux, and nasal stuffiness with a significant 1-year decline in FVC and FEV_1. Bronchial hyperreactivity measured by methacholine challenge correlated with bronchial wall thickening on CT scans. Compared with the NHANES III data for FVC and FEV_1, 32% of 2,000 WTC dust-exposed residents and clean-up workers were below the lower 5th percentile. The most common abnormality was a low FVC pattern, a finding similar to that also described for individuals in rescue and recovery activities. Among those complaining of respiratory symptoms and normal spirometry, almost half had abnormalities detected with impedance oscillometry consistent with distal airways' disease. Follow-up with the WTC Health Registry and the WTC Environmental Health Center will help discern whether treatment with anti-inflammatory medications or bronchodilators in those with respiratory symptoms may prevent the development of chronic obstructive pulmonary disease.

Keywords: World Trade Center Dust; distal airway

The collapse of the World Trade Center (WTC) twin towers (over 107 stories tall) created a massive plume of dust from over 1.2 million tons of construction material. The collapse on 9/11/2001 occurred at velocities over 150 miles per hour, pulverizing computers, wallboard, steel fixtures, glass, and so on, releasing a dust mixture over 90% of which was greater than 10 μm; yet there were 11,000 tons of $PM_{2.5}$. The construction material was primarily gypsum consisting of calcium carbonate, silicate, and sulfate with other metals such as vanadium, chromium, nickel, iron, silicon, and mercury also detected. Half of the South tower had been insulated with chrysotile asbestos, which was found in the pile, and millions of tons of fibrous glass. Fires from the jet fuel released polyorganics, including polycyclic aromatic hydrocarbons (1), benzene, naphthalene, dioxins, PCBs, and other fire retardants and powdered concrete. Most of these particles had soot-like coatings. Fires continued in the pile until mid-December 2001. The subsurface of the collapse piles remained hot for months, with portions of steel beams glowing red despite massive amounts of water to cool them. Measurement peaks on October 3 were 247 $\mu g/m^3$ for PM_{10} and 196 $\mu g/m^3$ for $PM_{2.5}$, although most samples were in the range of 20 $\mu g/m^3$ for 1-hour averages. Importantly, most pH analyses found the particles to be alkaline, with pH ranging from greater than 9 to 11.

New York City firefighters arrived en masse at Ground Zero and incurred very high dust exposures (as well as 343 lost lives from the collapse). The FDNY workers were categorized as high exposure if they were present the morning of the collapse, intermediate exposure if they arrived in the afternoon of the day of the collapse or the next day, or low exposure if they arrived 48 hours after the collapse. A stratified random sample of 362 firefighters with 41% in the high-exposure group, 39% in the intermediate, 8% in the low, and 12% unexposed reported that 19% did not wear a respirator during the first 2 weeks, 50% only rarely, with about 70% of firefighters wearing a half-face respirator or disposable mask (10%) by the end of the second week (2). Respiratory symptoms (cough, shortness of breath, wheeze, chest pain) were registered by almost 80% in high- and intermediate-exposed groups, with 46% in low exposure and 9% among unexposed when evaluated October 1–5, 2001. Similar prevalences were found for eye and upper respiratory complaints, and almost half had skin irritation. Spirometry was available in the previous year for most of the exposed subjects, and FVC and FEV_1 immediately after the dust exposure declined a mean of -268 ml for FVC and -264 ml for FEV_1. Both declined significantly for the high and intermediate exposure groups with a striking dose–response. Respiratory symptoms were significantly correlated with FVC and FEV_1 declines. This mutual decline in FVC and FEV_1 seems characteristic of the alkaline WTC Dust exposure. It is likely that the large particle size and its alkaline pH allowed for deposition in the upper airways, causing the significant upper airway and nasopharyngeal irritation and cough.

A firefighter working on the pile for the first two weeks presented to Bellevue Hospital with acute shortness of breath, bilateral pleural effusions and pulmonary infiltrates on September 24, 2001 (3). He responded to antibiotics and steroids, but cultures were negative. A bronchoalveolar lavage revealed 70% eosinophils, consistent with a clinical diagnosis of acute eosinophilic pneumonia. Electron microscopy of the eosinophils showed intact granules and major basic protein more typical of a benign self-limited process rather than a chronic tropical pulmonary eosinophilia from filariasis, where the granules are extruded and pulmonary fibrosis and damage may be irreversible. IL-5, an eosinophil chemoattractant, was increased in the BAL cell supernatants, BAL fluid, and serum. Mineralogical analyses by scanning/transmission electron microscopy showed 305 fibers per million alveolar macrophages, including chrysotile and amosite as well as chromium and degraded glass fibers. There were also fly ash and many silicates. Many of the cases of acute eosinophilic

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pneumonia reported previously in the literature had acute, high dust exposures.

Prezant and colleagues reported World Trade Center cough (WTC Cough) defined as cough serious enough to require medical leave for four weeks, and bronchial hyperresponsiveness in FDNY firefighters (4). In the first six months after 9/11/2001, WTC cough occurred in 128 of 1,636 firefighters with high-level exposure (8%), 187 of 6,958 FDNY with moderate-level exposure (3%), and 17 of 1,320 with low-level exposure (1%). Impressively, 95% had symptoms of dyspnea, 87% had gastroesophageal reflux, and 54% had nasal congestion. Among the cohort with severe WTC cough before treatment, 63% had a response to bronchodilator and 24% had bronchial hyperreactivity (defined as a PC_{20} of 8 mg of methacholine/ml or less). Even in those without severe WTC cough, bronchial hyperreactivity was present in 77 (24%) firefighters with high exposure and 8% with intermediate exposure. The cough was productive, with sputum usually black to grayish and infiltrated with "pebbles or particles." The use of respiratory protection was not associated with a significantly decreased risk of lower-airway symptoms, decreased pulmonary function, or airway hyperreactivity, probably because of the hypervigilant rescue efforts during the first two weeks after the collapse with only intermittent use of respirators. Again, the magnitude of drops in FVC and FEV_1 reported showed a drop of at least 0.5 L in 58% and 54% of firefighters, respectively. Lung volumes and carbon monoxide diffusing capacity were within normal limits in 108 firefighters with WTC cough who were tested. High-resolution inspiratory and expiratory CT scans were done on 78 firefighters with normal chest radiographs; air trapping was seen in 48 (51%), and 12 of these patients (30%) had bronchial wall thickening. Seven of 38 subjects without air trapping (18%) had bronchial wall thickening. Over the 6-month follow-up period, practically all of the firefighters with upper airway symptoms were medically cleared to return to work, but only 34% of those with predominantly lower respiratory tract symptoms. Reactive airways dysfunction syndrome (RADS) was originally described as a brief, intense exposure to dust, fumes, or vapors in patients with no prior history of respiratory disease (5). It is characterized by persistent symptoms of airway inflammation (cough, wheeze, and dyspnea) and bronchial hyperreactivity. Empiric therapy includes nasal and inhaled corticosteroids, bronchodilators, and proton-pump therapy.

Subsequent studies of FDNY workers approached the firefighters with question of persistence of symptoms, whether those that developed new symptoms had a delayed or more chronic asthma–like picture, and whether the symptoms were severe enough to cause disability. A representative sample of 179 rescue worker firefighters found bronchial hyperreactivity at 1, 3, or 6 months to be associated with exposure intensity, independent of smoking status and airflow obstruction (6). High-exposure FDNY workers were 6.8 times more likely to have bronchial hyperreactivity than were those with intermediate exposure, and if hyperreactive at 1 or 3 months, 55% persisted at 6 months. RADS was highly correlated with hyperreactivity at 1 and 3 months. Studies in mice showed that 100 μg WTC $PM_{2.5}$ caused significant inflammation and hyperresponsiveness (7). Among 12,079 FDNY followed prospectively, over 32,000 spirometries were analyzed to calculate the annual rate of decline in FEV_1 (8). WTC dust–exposed FDNY workers experienced a significant decline in adjusted average FEV_1 during the year after 9/11/2001 (372 ml; 95% confidence interval 364–381 ml; $P < 0.001$). This exposure-related decrement equaled 12 years of aging-related decline. There was a significant exposure-related decrement, with high-exposure FDNY workers faring the worst. Respiratory symptoms predicted a further FEV_1 decrease. Induced sputum from 38 FDNY workers showed increased neutrophils, eosinophils, and matrix metalloproteinase levels compared with non–WTC dust–exposed firefighters and control subjects, consistent with an inflammatory diathesis due to WTC dust (9). The FDNY WTC monitoring and treatment programs encountered 26 new individuals diagnosed with sarcoidosis that could have been related to WTC dust or the asthma/airway hyperreactivity caused by it (10).

FDNY firefighters with respiratory symptoms or reduced spirometric values were referred to a Center of Excellence for further pulmonary testing (11). Of 1,720 FDNY workers referred (13% of total cohort), 919 had pulmonary function tests, 1,219 had methacholine challenge testing, and 419 had both; 982 had CT-scans. The median FVC was 98%, FEV_1 93%, FEV_1/FVC ratio 78%, RV 123%, TLC 101%, and D_{LCO} 104%, consistent with air trapping. Interestingly, as RV increased, there was a significantly greater decline in FEV_1, increased proportion of FDNY firefighters with bronchodilator response, and increased proportion with bronchial hyperreactivity as assessed by methacholine challenge. The CT scans revealed air trapping in 40%, bronchial wall thickening in 26%, emphysema in 8%, sarcoidosis in 4%, and pulmonary fibrosis in less than 1%. The presence of air trapping on CT did not correlate with bronchodilator response, hyperreactivity, or elevated RV. However, bronchial wall thickening was associated with significant increases in RV, declines in FEV_1, and increases in methacholine slope. As of 9/11/2008, 652 out of 1,720 (38%) firefighters in the Center of Excellence evaluation were awarded pulmonary disability pensions—a three- to four-fold increase compared with the 7 years before 9/11/2001.

An estimated 40,000 workers were involved in the clean-up of Ground Zero and the Staten Island landfill during the days, weeks, and months after September 11, 2001, including a variety of first responders: police, construction workers, ironworkers, laborers, and public sector workers (12). The WTC Worker Medical Screening Program was established at Mt. Sinai with clinic sites also at SUNY-Stony Brook, Queens College, UMDNJ-RWJ New Jersey Medical School, and New York University-Bellevue Hospital. Of 9,442 responders examined in 2002–2004, 69% reported new or worsened respiratory symptoms while performing WTC work, and these persisted until the time of examination in 59% of them. Sixty percent of these workers reported to be in the dust cloud on 9/11/2001. Upper respiratory symptoms, dry cough, cough with phlegm, dyspnea, chest tightness, and wheeze were the most common symptoms. They observed a significant association between low FVC and time of arrival, with abnormality in those who arrived earlier. There were 3,160 who had baseline and follow-up spirometry, with 20% with low FVC on the first examination and 16% on the second (13); 8% had obstruction at both examinations. The decline in FEV_1 was 13 ml/year, but 131 individuals lost more than 300 ml/year in FVC. No special associations were noted for this rapid decline group. Bronchodilator responsiveness was associated with an increase in prebronchodilator spironmetry, but respiratory symptoms at examination 1 were not predictive of lung function change.

There were 60,000 residents below Canal Street who bore the effects of the dust cloud, although many evacuated, and 300,000 commuters were at work there. In addition, more than 15,000 students attended school there. In a collaboration between NYU/Bellevue Hospital WTC Environmental Health Center and the New York State Department of Health, a clinical epidemiological study was initiated in apartment building dwellers located near Ground Zero and unaffected apartment dwellers from the upper West Side (14). Questionnaires were mailed and/or hand-delivered to apartment buildings 12 ± 4 months after the collapse of the WTC. There were 2,520 cases and 292 control subjects, with

a response rate of 22%; almost 40% of cases had new onset cough without a cold, compared with 12% of control subjects (Standardized Incidence Ratio, 3.36; 95% confidence interval [CI], 2.4–4.7). Persistent (twice a week) respiratory symptoms were also three times more prevalent among the exposed, and wheeze was persistent in 10.5% of participants in the exposed area compared with 1.6% in the control area. Almost 24% of participants with a persistent symptom complained of cough on a daily basis. Among those exposed with persistent symptoms, over 20% reported using controller medication (inhaled corticosteroid, long-acting β-agonist, theophylline compound, leukotriene modifier). There was a 73% increase in unplanned medical visits in previously healthy residents in the affected areas (15). Szema and colleagues reported that visits to a health clinic for asthma and prescriptions for asthma medications both increased among pediatric patients after 9/11 (16).

Between September 2005 and May 2008, 1,898 individuals participated in the WTC Environmental Health Center centered at Bellevue Hospital (17). This population had more women (47%) and was more racially diverse than previous studies, with 42% self-reported Latino ethnicity (Columbia 33%, Ecuador 20%, Dominican Republic 10%, Puerto Rico 8%). These were local workers, residents, rescue workers, and clean-up workers. Forty-one percent had a dyspnea score of 3 or greater, corresponding with moderate to severely disabling dyspnea according to the modified British Medical Research Council dyspnea scale. A significant association was noted for dust cloud exposure and new onset and persistent Dyspnea on Exertion (odds ratio [OR], 1.4; 95% CI, 1.1–1.8). Spirometry was within normal limits, but there was a slight but significant reduction in pre-bronchodilator FEV_1/FVC in residents exposed to the dust cloud compared with those not exposed (75.7 versus 78.1, respectively, $P = 0.03$). Compared with the NHANES III data for FVC and FEV_1, 32% of WTC dust-exposed individuals were below the lower 5th percentile. The most common abnormality was a low FVC pattern, a finding similar to that previously described for individuals in rescue and recovery activities. Those with normal spirometry but respiratory symptoms had methacholine challenge; 51% of 68 referred individuals had a PC_{20} less than 4 mg/ml, consistent with airway hyperreactivity. Also, among those who had a bronchodilator, there was a significant improvement in FEV_1 in those who had an obstructed pattern or low FVC. Those with MRC dyspnea 3 or more were associated with a low FVC or an obstructed plus low FVC pattern.

The NYU/Bellevue Pulmonary Function Laboratories have had an unusual experience interpreting the clinical/physiological/pathological/radiological correlations of WTC dust exposure. Oppenheimer and colleagues reported 174 subjects with normal spirometry, but with respiratory symptoms, hypothesizing that distal airway function might be abnormal (18). Impedance oscillometry was performed finding mean resistance at 5 Hz, 5 to 20 Hz, and reactance area were increased, but returned to normal after bronchodilator. Thirty-seven of 43 subjects had frequency dependence of compliance. Since spirometry results were normal in all subjects, these abnormalities reflect dysfunction in airways more distal to those evaluated by spirometry. Frequency dependence of compliance requires esophageal manometry showing that forced oscillation is a useful noninvasive test for evaluating distal airway function. Reduction of mid-expiratory flow rate was observed in fewer than 10% of subjects, and RV/TLC was elevated in approximately 33% of subjects. This study showed excellent correlation between dynamic compliance and impedance oscillometry. However, after bronchodilator, not all tests normalized suggesting heterogeneity among distal airways; bronchiolitis obliterans has been reported by open lung biopsy in a Ground Zero police officer who participated in the 9/11 rescue (19).

The New York City Department of Health and Mental Hygiene began a WTC Health Registry 2003–2004 (20). The Registry enrolled 71,437 people out of a potential 410,000 eligible candidates. Over 70% reported being in the dust cloud, and 67% of adult enrollees reported new or worsening respiratory symptoms. Three percent reported newly diagnosed asthma, with estimates translating this into 3,800 to 12,600 adults newly diagnosed with asthma. Sixteen percent screened positive for probable post-traumatic stress disorder. The WTC Health Registry had 25,748 individuals with no history of asthma, and 926 workers were newly diagnosed with asthma (3.6%)—a number very similar to earlier estimates (21). Earlier arrival and longer duration of work were significant risk factors, as were exposure to the dust cloud and pile work. Interestingly, there were increased odds ratios for delay in wearing a respirator and risk of new-onset asthma ranging from 1.63 (95% CI, 1.03–2.56) for 1 day delay to 3.44 (95% CI, 1.43–8.25) for 16 to 40 weeks of delay. A summary of WTC dust–exposed cohorts is shown in Table 1.

Exposure to a massive WTC alkaline dust cloud causes upper and lower airway irritation with penetration into the bronchial tree, distal airways, and alveoli leading to respiratory symptoms,

TABLE 1. WORLD TRADE CENTER DUST–EXPOSED COHORTS

Cohort	Number		Exposure	Pulmonary Function Tests
FDNY New York City Firefighters	>12,000	Screening and treatment program	High: first responders	Spirometry before/after 9/11 Significant decline in FVC and FEV during the 1 year after exposure, FEV_1 declined 372 ml (95% CI, 364–381, $P < 0.01$)
WTC Worker Medical Screening Program (Mt. Sinai plus 5 clinics)	>9,442	Screening and treatment program	Rescue and recovery workers, clean-up workers	Spirometry after 9/11. Reduced FVC and FEV_1 observed in ~20%.
WTC Environmental Health Center (Bellevue Hospital and 2 additional clinics)	>4,000	Treatment program (have to have symptoms to enroll)	Residents, local workers, clean-up workers Varied exposure: initial dust cloud, resuspended dusts, gasses and fumes	Spirometry after 9/11, reduced FVC and FEV_1 observed in 32% of initial patients studied using NHANES III normal values.
WTC Health Registry NYC Department of Health and Mental Hygiene	71,437	Questionnaire, no treatment	70% WTC Dust Cloud	Post 9/11, 3% reported newly diagnosed asthma correlated with recovery, clean-up, and not wearing a respirator.

pulmonary function changes, and inflammation (22). Characteristic pulmonary function findings relate to the distal airways where frequency dependence of compliance, abnormal oscillometry, reduced FVC and FEV_1, bronchial hyperreactivity, and response to bronchodilator were observed. This will likely be a contributing risk factor for the development of chronic obstructive pulmonary disease; importantly, treatment with anti-inflammatories and bronchodilators will be important in longitudinal studies to prevent this from happening. It is imperative for public policy leaders to fund continued follow-up and research of those exposed and at risk.

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