

## Small Airway Dysfunction As A Mechanism For Persistence Of Lower Respiratory Symptoms Despite Treatment In Patients Exposed To World Trade Center Dust

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**Introduction:** Exposure to World Trade Center (WTC) dust resulted in respiratory symptoms (cough, wheeze, dyspnea, chest tightness) in populations of community members exposed to this disaster. Treatment has been applied using a standardized treatment algorithm for asthma based on published guidelines that include use of “controller” therapies for persistent respiratory symptoms. Despite this approach, many patients report continued symptoms and remain on long term high dose ICS and are at risk for the adverse health effects of long term corticosteroid treatment. We hypothesize that WTC dust subjects exposed with persistent lower respiratory symptoms have evidence for either small airways disease and/or bronchial hyper-responsiveness.

**Methods:** Patients enrolled in the Bellevue Hospital WTC Environmental Health Center (WTC EHC) with physician diagnosis of asthma and therapy with ICS/LABA were studied. All subjects had normal large airway function as assessed by FEV<sub>1</sub>. Subjects were assessed over a 3 month protocol that included measures of drug adherence, symptom control (Asthma Control Test [ACT]), small airway function (forced oscillation testing [FOT]) and bronchial hyper-reactivity (methacholine challenge test).

**Results:** 27 patients were studied (age  $56 \pm 9$ yr, height  $1.67 \pm 0.08$ m, weight  $85 \pm 14$ kg). Although subjects were required to demonstrate normal FEV<sub>1</sub> at study entry, lower respiratory symptoms were uncontrolled (ACT < 20 in 25 patients; average =  $13.6 \pm 3.4$ ). Following 3 months of therapy with ICS/LABA symptoms remained uncontrolled in all but 2 patients (ACT  $14.1 \pm 4.0$ ). Bronchial hyper-reactivity (PC20 < 4mg/dl) was noted in only 9/27 patients. In contrast, FOT demonstrated abnormalities in R<sub>5</sub>, R<sub>5-20</sub> and AX ( $5.30 \pm 1.93$  cmH<sub>2</sub>O/l/s,  $1.38 \pm 0.91$  cmH<sub>2</sub>O/l/s,  $10.4 \pm 9.6$  cmH<sub>2</sub>O/l, respectively). Abnormal FOT values were noted in a total of 17/27 patients. In addition, abnormal FOT values were noted in 9 of the 18 patients that did not demonstrate bronchial hyper-reactivity.

**Conclusions:** Lower respiratory symptoms remained uncontrolled in the majority of patients independent of adherence to therapy. Bronchial hyper-reactivity may be responsible for symptoms in a minority of subjects. Small airway dysfunction that was not evident on spirometry persisted in the majority of subjects, providing an additional mechanism for persistence of lower respiratory symptoms.

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