Similar Exposure To World Trade Center (WTC) Dust Produced Variable Lung Function Decline: Defining Most And Least Effected Subgroups In The FDNY Cohort

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Background: The terrorist attack on 9/11/2001 produced a well-defined, intense irritant exposure in FDNY rescue workers. Airway obstruction predominates in 1720 FDNY personnel who required treatment for respiratory symptoms (Weiden et al. 2009). Moderate reduction of serum alpha-1-antitrypsin (14.9 ± 3.2 μM/L vs. 23.9 ± 3 μM/L for normal AAT) identifies a subgroup of FDNY personnel with 150ml/yr excess FEV1 decline.

Methods: PFTs were obtained: (**1)** pre 9/11 **(2)** within nine months post 9/11 and **(3)** upon entry into treatment. From the 1720 treatment cohort, we identified 100 patients with the and 100 patients with the smallest FEV1 decline. A biorepository of serum drawn on the first post 9/11 exam includes samples from the most and least effected subgroups.

Results: The first PFT after 9/11 occurred 3 months post 9/11 (IQR 2-4). Treatment entry PFT occurred 32 months post 9/11 (21-54) for both best and worst groups. Both groups had equal exposure intensity but marked differences in FEV1 decline. The least affected had no decline in FEV1 over the three PFTs. The most affected subgroup lost 0.875 L of FEV1 (0.58-1.10) from pre- to first post-9/11 PFT; an additional 0.410L FEV1 declined (IQR, 0.09-1.03) at treatment entry. The most affected had marked increase in airway reactivity 8-31%) vs. 3%; (2%-8%), $p< 0.01$) and MCT slope (0.09; (0.05-0.41) vs. 0.05; (0.03-0.10), $p< 0.01$). Surprisingly, the most affected had significantly higher BMI at the first post 9/11 PFT (29; (27-31) vs. 28; (26-30) $p< 0.01$).

Conclusions: Symptomatic patients with similar WTC exposure had divergent changes in FEV1, defining subgroups with differential susceptibility to lung injury. AAT is one biomarker of individual susceptibility to accelerated FEV1 decline. Case control studies using serum drawn in 2001-2002 will define biomarkers of lung injury at a time of active disease; these results will be validated in the whole cohort. We will assay serum from this early point using Luminex for 100 analytes probing a broad array of pathways that may be activated or suppressed during lung injury. BMI differences between the most and least effected point to metabolic markers as one fruitful avenue of investigation. Defining a comprehensive set of serum biomarkers may identify those at greatest risk for lung injury following irritant exposure and focus treatment efforts on the vulnerable subgroup.

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