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Relationship Between Allergen Challenge, Lung Inflammation, Lung Dysfunction in Murine Models of Asthma

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Background:

Most studies use a single HDM challenge concentration to produce maximal inflammation and airway dysfunction. This does not define the mechanisms of a full range of pathophysiologic severity, as exists for human asthma.

Objective:

Using two common strains of mice we tested relationship between airway responsiveness and inflammation in response to repeated inhaled challenge with different concentrations of HDM.

Methods:

Female 8-9 week old BALB/c and C57BL6/NJ mice were challenged for two weeks, with intranasal HDM (6, 12 or 25 µg). Lung function in response to nebulized methacholine was measured using a flexiVent small animal ventilator 48 hours after final HDM challenge. Inflammation was measured by total and differential cell analysis of bronchoalveolar lavage (BAL). Significant differences ($p<0.05$) between mean values in each group was assessed by linear multivariate analysis, and Bonferroni post-hoc testing.

Results:

BALB/c- 6, 12 and 25 ug HDM induced an increase in total cell number 1198 % ($p<0.001$), 1719 % ($p<0.001$) and 4316 % ($P<0.0001$). Eosinophils increased from 28% of total cells in 6 µg to 40% in 25 µg whereas in C57BL6/NJ- 382 % ($p<0.001$), 506 % ($p<0.001$) and 1695 % ($p<0.0001$). 6 µg HDM induced maximum eosinophil influx (75%).
BALB/c- significant increase in total lung resistance (Rrs) ($p<0.0001$), tissue damping (G) ($p<0.0001$), tissue elastance (H) ($p<0.0001$). C57BL6/NJ- magnitude of increase in Rrs, Rn, G, and H was lower than BALB/c. Changes in lung function were not HDM dose-dependent in both.

Conclusion:

Low concentrations of inhaled HDM are sufficient to perturb lung dysfunction and induce lung inflammation in two common mouse strains. Increasing HDM concentration increase inflammation but no further worsening lung dysfunction. A threshold of lung inflammation may exist to trigger asthma-like lung dysfunction. Independent mechanisms appear to govern inflammation and changes in lung function. Unraveling these may provide insight about factors that determine pathophysiological severity of asthma.