**Low-dose Australian air pollution promotes neutrophilic, steroid-insensitive, experimental asthma**

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**Introduction**. Particulate matter <2.5 μm (PM2.5) is an airborne pollutant and a critical global health threat. Epidemiological studies show that PM2.5 exposure is associated with the development and increased severity (including reduced symptom control with corticosteroids) of asthma. However, the pathobiology of PM2.5 exposure at levels present in Australia is relatively unexplored.

**Aims**. To investigate how chronic Sydney PM2.5 exposure influences the phenotype of experimental asthma and response to corticosteroids.

**Methods**. Mice (*n*=12/group) were exposed daily to PM2.5 (i.n.; 10 μg) or Sham (PBS) control. In some groups, experimental asthma was superimposed by sensitising with ovalbumin, (Ova; i.p.; 50 μg; day 21) or saline, followed by challenge (i.n; 20 μg Ova; days 33, 34, 54, 55) and corticosteroid treatment (i.n.; 2 mg/kg dexamethasone; days 53-55) or vehicle control. At endpoint (day 56), we measured lung function and airway hyperresponsiveness (AHR), airway inflammation (bronchoalveolar lavage fluid), and lung leukocytes (flow cytometry).

**Results**. In Ova-sensitised mice, PM exposure resulted in an 18% reduction in inspiratory pulmonary capacity compared to sham (*n*=8/group; *p*<0.05), although no changes in the magnitude of AHR or total airway leukocyte numbers occurred. Analysis of bronchoalveolar lavage fluid revealed that Ova-sensitised, sham-exposed mice had airway eosinophilia; however, Ova-sensitisation with PM exposure caused a significant shift to airway neutrophilia (*n*=12/group; *p*<0.001), but a >40% and >70% increase in both eosinophils and neutrophils in lung tissue (*n*=8/group; *p*<0.01). In Ova-sensitised mice, PM-exposure reduced the ability of corticosteroid treatment to suppress AHR and inflammation back down to baseline levels observed in corticosteroid-treated, sham-exposed groups, indicating steroid insensitive disease.

**Discussion**. Our data show that PM exposure promotes a neutrophilic inflammatory phenotype and reduced responsiveness to corticosteroid treatment in experimental asthma. Next, characterising cytokine, chemokine, and histopathological changes will help elucidate our findings and determine the potential relevance to other diseases.