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Title: LSC 2013 abstract - Age of first allergen exposure is critical in determining the development of allergic airway disease

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Body: The immunological landscape of adult and neonatal lungs are different. While adult lungs are immunologically mature and able to mount both innate and adaptive immune responses, neonatal lungs are developing and undergoing immune maturation. Failure of development of allergic airway disease (AAD) following inhaled house dust mite (HDM) commencing at 14 days of age in neonatal mice has been described. However, we have documented robust AAD in neonatal mice when HDM exposure is commenced from day 3 of life. We hypothesised that age at first allergen exposure is critical in determining development of allergic immune responses and aimed to investigate disease progression when allergen exposure is commenced at different ages. Intranasal HDM or saline was administered intermittently for 3 weeks, with the first dose administered from day 3, 7, 14, 21, 28 or 42 of life. Airway hyperresponsiveness (AHR) to methacholine, inflammation in lung and broncho-alveolar lavage, cytokine mediators of AAD in the lungs, and serum Ig E were measured. HDM exposure at day 3 or 7 of life resulted in the development of AHR, eosinophilic inflammation and increased Th2 cytokines (IL-4 and IL-13) in the lung, with elevated serum IgE. In contrast, allergen exposure from day 14 or 21 of life did not result in the development of AAD, with AHR, serum IgE and Th2 cytokines remaining at control levels. The development of AAD in response to HDM exposure was restored when allergen was administered from day 28 and 42 of life. This study demonstrates the critical role of immune maturation and lung development in determining the development of allergic immune responses and the development of neonatal AAD.