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Influenza-Induced Exacerbation In A Murine Chronic House Dust Mite (HDM) Asthma Model
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Abstract Body

Introduction. Allergic asthma is a chronic inflammatory airways disease controlled by T helper 2 (Th2) cells as exemplified by local eosinophilia and the production of Th2-cytokines. Viral airway infections cause acute worsening of asthma symptoms (exacerbation) paralleled by additional accumulation of neutrophils and CD8+ T cells in the lungs. The mechanisms that underlie virus-induced exacerbations are being researched intensely. Here we aimed to develop an adequate murine model of exacerbating asthma. Methods. Mice were sensitized intranasally (i.n.) to HDM extract (25ug/dose) or saline for 5 days/week for 5 consecutive weeks. On the first day of the fifth week the mice were infected i.n. with 20 TCID50 influenza A/X31 or PBS and sacrificed 8 days after infection. Cellular influx was assessed in bronchoalveolar lavage fluid (BALF) by flow cytometry and cytokines were measured in lung lysate. PenH was determined as a measure of airway hyperresponsiveness (AHR). Results. At 8 days after influenza A/X31 infection of sensitized mice, the recruitment of eosinophils, neutrophils and lymphocytes into the lungs was boosted as compared to that in sensitized uninfected mice and non-sensitized infected mice. CD4 and CD8 T cells recruitment is consistent with the induction of a virus-specific immune response. In BALF of sensitized infected mice, eosinophils are more activated (MHC-II, CD80 and CD86) in comparison to that in PBS-challenged sensitized mice. Sensitized infected mice lose more body weight (20%) and show a markedly enhanced PenH (4) at day 7 although the AHR was similar to that in infected non-sensitized mice. Further results are pending. Conclusion. Influenza infection of sensitized mice aggravates allergic airway inflammation at day 8, similar to that in exacerbating asthma patients. These findings contrast with those obtained in an acute model of allergic asthma reported earlier. We did not find a significant difference in PenH for infected sensitized mice compared to non-sensitized mice. This was not due to having reached a plateau value, as in fact happened in sensitized mice exposed to the more virulent influenza A/PR/8/34. We are currently extending the data to other time points. The study is supported by The U-BIOPRED consortium that receives funding from the European Community and from the European Federation of Pharmaceutical Industries and Associations as an IMI JU funded project.