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Title: Cigarette smoke exposure facilitates allergic sensitization to house dust mite and aggravates the asthmatic phenotype in mice

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Body: Background: Cigarette smoke (CS) exposure has been associated with increased sensitization and asthma development in children and adults. Aims and objectives: We wanted to design a novel mouse model to unravel the impact of CS on the different stages of asthma pathogenesis, specifically during the initial sensitization and acute asthma development. Methods: Mice were exposed to 25µg house dust mite (HDM) extract (intranasaly, 1/week) for 3 consecutive weeks, combined with air or CS exposure (3 times/day, 5 days/week) during 3 weeks or only during the first week. Results: Mice concomitantly exposed to HDM and CS for 3 weeks, showed a significant increase in eosinophils, goblet cells, airway hyperresponsiveness and HDM-specific serum IgG1, compared to sole HDM or CS exposure. Interestingly, exposure to CS only during the first week was sufficient to induce an aggravated asthmatic phenotype after rechallenge with HDM allergens. To further investigate the effect of CS during mucosal sensitization, mice were exposed to HDM (just once) and 3 days of CS, followed by the assessment of DC trafficking and early Th2 responses in the lymph nodes. This short CS exposure amplified DC-mediated transport of HDM allergens to the lymph nodes and was sufficient to generate a Th2 response, characterized by IL-4, IL-5 and IL-13 production in the draining lymph nodes. Conclusions: CS facilitates the development of HDM-induced allergic asthma. Only a few days of smoke exposure are sufficient to facilitate allergic sensitization to common aeroallergens. Funding: IUAP - Belgian Science Policy P6/35 and BOF/GOA 01251504.