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Title: Persistence of the asthmatic response in two animal models with exposure to high and low molecular weight agents

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Body: Introduction: Aim: to compare the persistence of bronchial hyperresponsiveness (BHR) and pulmonary inflammation after the end of exposure to soybean (high-molecular-weight agent, HMW) and ammonium persulfate (AP) (low-molecular-weight agent, LMW) in two animal models of asthma. Methods: In the AP model, BALB/C mice received dermal applications of AP or dimethylsulfoxide on days 1 and 8 and a single intranasal instillation of AP or saline on day 15. In the soybean model, BALB/C mice received intranasal instillation of soy extract or saline on 5 consecutive days for 5 weeks. BHR was assessed using methacholine challenge. Pulmonary inflammation was evaluated in bronchoalveolar lavage (BAL) 1, 4, 8, 24, 48 and 72 hours after the last exposure to the causal agent. Results: AP-treated mice presented a sustained increase in BHR which lasted four days after intranasal instillation. Conversely, soybean-treated mice showed a peak response four hours after intranasal instillation. There was a significant increase in the percentage of neutrophils within 24 hours of the challenge, reaching a peak eight hours after exposure (42.35%) in the AP model. In the soybean model, the peak was reached four hours after the challenge (58.44%). The percentage of eosinophils was significantly increased in soybean-treated mice (15.76%, 1 hour after challenge) while no eosinophils were found in BAL of AP-treated mice. Conclusion: With the LMW agent BHR persisted over time, whereas with the HMW agent the inflammatory profile is characterized by an increase in percentage of eosinophils. Neutrophilic inflammation is present in both models of asthma, although it is more persistent in the AP model.