Acute, But Not Resolved, Influenza A Infection Enhances Susceptibility to House Dust Mite-Induced Allergic Disease


**PURPOSE OF THE STUDY.** To examine the consequences of exposure to a low dose of the common aeroallergen house dust mite (HDM) during the course of an influenza A infection.

**METHODS.** The response to allergen exposure was evaluated at 3 distinct time points, relative to influenza infection. To evaluate responses to allergen exposure during the acute phase of infection, mice were inoculated intranasally with influenza type A virus and then exposed to a low dose of HDM daily for 10 days during the peak of acute inflammation. The second experiment investigated whether HDM-associated changes in the inflammatory response were transient or long-lasting. The mice were inoculated with influenza A and challenged with HDM as described previously, but the animals were allowed to rest for a period of ≥30 days, after which they were reexposed to HDM for 3 consecutive days. In the final experiment, mice were exposed to HDM after resolution of the influenza infection.

**RESULTS.** In mice inoculated with influenza A, there was a preferential increase in the activation of CD8+ T cells over CD4+ T cells and an increase in antigen-presenting cells, particularly plasmacytoid dendritic cells, as expected after a viral infection. Exposure to a low dose of HDM during the acute phase of influenza infection led to significantly increased numbers of mononuclear cells and eosinophils in the lung. Flow cytometry revealed a robust increase in the number of CD4+ T cells, specifically T-helper 2 (Th2) cells, and this increase in Th2 cells was much stronger in the influenza-infected HDM group, compared with the HDM-alone group. Exposure to HDM during the acute phase of influenza infection also resulted in significantly elevated levels of HDM-specific immunoglobulin G1 (IgG1) and IgG2a. Mice exposed to HDM allergen during the acute infection also demonstrated enhanced lung dysfunction and significantly greater goblet cell metaplasia and mucus production, compared with mice treated with HDM allergen alone. Mice that were rechallenged with HDM (experiment 2) showed responses similar to those listed above. Finally, mice with a first exposure to HDM that occurred after resolution of the influenza infection had an attenuated HDM-associated inflammatory response.

**CONCLUSIONS.** The study shows that the Th1 immune environment created during the acute phase of influenza infection leads to enhanced, rather than attenuated, allergic sensitization and inflammation in response to aeroallergen exposure and that these effects are long-lasting. In contrast, allergen exposure that occurs after the resolution of influenza infection does not result in an enhanced inflammatory response.

**REVIEWERS’ COMMENTS.** There has been great interest in finding ways to divert the immune system away from a Th2 allergic profile. Previous studies suggested that viral infection may afford protection against allergic disease by promoting Th1 responses. This study clearly shows that, despite the Th1 state induced by influenza A infection, the immune system is driven to a robust response to concomitant allergen exposure. Whether influenza or other viruses play a similar role in humans remains to be seen.
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