



CORBIS

 ASTHMA

The secret face of *H. pylori*

It has been proposed that the increasing incidence of asthma in developed countries is due to the lack of early exposure to microbial antigens, which may contribute to the maturation of the airway immune system. Now, Arnold *et al.* report that early infection of mice with the gastric pathogen *Helicobacter pylori* increases the number of CD4⁺ regulatory T (T_{Reg}) cells in the airways and thereby prevents the development of asthma.

Chronic infection with *H. pylori*, which is the causative agent of gastric ulcers and gastric cancers, has been inversely correlated with the development of asthma. To investigate the underlying mechanisms of this correlation, the authors infected neonatal and adult mice with virulent *H. pylori* prior to the induction of

allergic airway inflammation. Both *H. pylori*-infected and uninfected mice that were sensitized with ovalbumin generated ovalbumin-specific IgE antibodies and primary T cell responses to the antigen. However, following challenge with the aerosolized antigen, the mice that had been previously infected with *H. pylori* showed reduced airway hyperresponsiveness and decreased numbers of immune cells in the bronchoalveolar lavage (BAL) fluid and in the lungs, compared with uninfected mice. Interestingly, mice that had been infected with *H. pylori* as neonates showed lower levels of allergic airway inflammation than mice infected during adulthood, and this effect was even more prominent in a model of allergic response to house dust mite allergen.

So, why does early infection with *H. pylori* prevent the development of airway inflammation? In a previous study, the authors had shown that early infection with *H. pylori* induces the development of long-lived T_{Reg} cells. Indeed, the numbers of pulmonary T_{Reg} cells were increased in mice infected with *H. pylori* as neonates compared with the numbers in uninfected mice. Moreover, depletion of CD4⁺CD25⁺ T_{Reg} cells during allergen challenge resulted in allergic airway inflammation and high numbers of inflammatory immune cells in the BAL fluid of mice that had been neonatally infected with *H. pylori*. Finally, transferred CD4⁺CD25⁺ T_{Reg} cells from neonatally *H. pylori*-infected mice, but not lymph node cells from uninfected mice, prevented airway hyperresponsiveness and lung inflammation.

Thus, this study suggests that early infection with *H. pylori* induces the development of T_{Reg} cells and thereby contributes to the prevention of airway inflammation and asthma. Based on the observation that the numbers of immature dendritic cells are increased together with the numbers of T_{Reg} cells in the lungs of neonatally infected mice, the authors speculate that *H. pylori*-induced T_{Reg} cells may contribute to protection against airway inflammation by preventing the maturation of dendritic cells in the lung.

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