

Images in Allergy and Immunology

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Mycoplasma in severe asthma

Editor's note: This feature, Images in allergy and immunology, is designed to highlight current concepts of the immunopathology of allergic diseases and other common immunologically mediated diseases. The presentation will appear as sets of images that involve cross-pathology, histopathology, and molecular pathology and will cover a range of topics of interest to allergists and immunologists.

Bacteria are well known to exacerbate asthma and pose significant problems for patients and their clinicians. Bacterial organisms can increase airway hyperresponsiveness and inflammation in the patient with known asthma, but now the question arises of whether these same mechanisms might be responsible for the development of asthma. This latter observation is controversial and not conclusively proved. The data appear most compelling in regard to specific organisms, such as *Mycoplasma pneumoniae*.

M pneumoniae is an extracellular pathogen without a cell wall. It attaches to ciliated airway epithelial cells in the respiratory tract and is responsible for community-acquired infections in adults and children, including pneumonia, tracheobronchitis, bronchiolitis,

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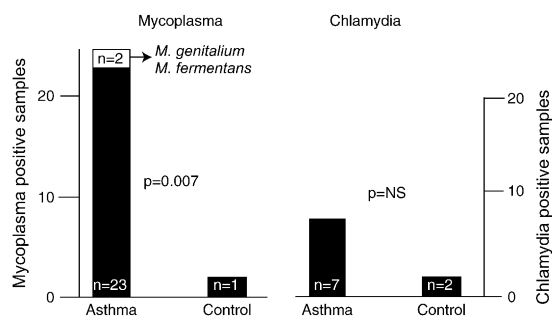


FIG 1. The number of subjects with positive PCR results for *Mycoplasma* and *Chlamydia* species in patients with asthma and healthy control subjects. In regard to *Mycoplasma* species, 25 of 55 subjects had positive results, and 1 of 11 control subjects had positive results. Of the 25 asthmatic subjects with positive results, 23 had *M pneumoniae* and 2 had either *Mycoplasma fermentans* or *Mycoplasma genitalium*. There were 7 of 55 asthmatic subjects with positive results for *Chlamydia pneumoniae*, of whom 1 also had a positive result for *M pneumoniae*. Two control subjects had positive results for *C pneumoniae*.

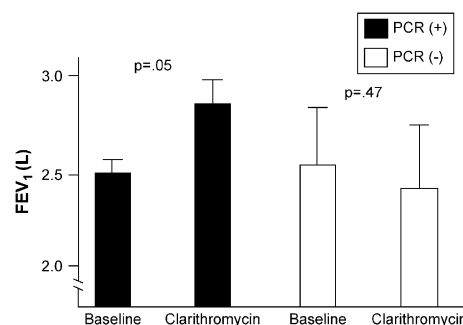


FIG 2. The FEV₁ before and after treatment in the clarithromycin groups in subjects with positive (+) and negative (-) PCR results are shown. The filled bars denote the subjects with positive PCR results, and the open bars denote the subjects with negative PCR results.

and interstitial pneumonitis. The challenges in the diagnosis of *M pneumoniae* infection include the significance of serology in the diagnosis of chronic infection and that PCR, which is very sensitive and specific, does not distinguish between nonviable organisms.¹ Culture is the gold standard but very insensitive because of the fastidiousness of the organism.

With regard to the relationship between *M pneumoniae* and asthma, several studies have reported an association between infection and exacerbation of asthma.² In chronic asthma Martin and colleagues³ demonstrated an association with *M pneumoniae*, as measured in the airway by means of PCR and stable chronic asthma (Fig 1). In 55 asthmatic subjects, 23 of 55 demonstrated the presence of *Mycoplasma* species in the lower airway, the majority (21/55) of which was *M pneumoniae*. Treatment with the macrolide clarithromycin, an antibiotic with activity against *M pneumoniae*, resulted in improvement in lung function but only in those asthmatic subjects who demonstrated *M pneumoniae* by means of PCR in their airways (Fig 2).⁴ *Mycoplasma* species infection is mainly

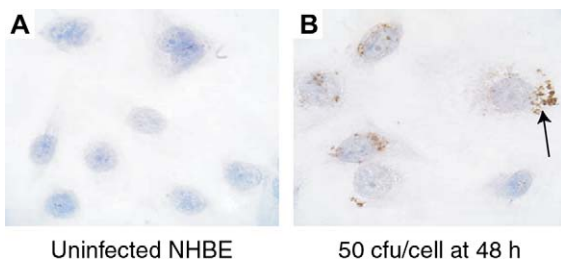


FIG 3. Immunoperoxidase detection of *M pneumoniae* in normal human bronchial epithelial cell (NHBE) culture. **A**, Uninfected normal human bronchial epithelial cell stained with a polyclonal rabbit antibody. **B**, *M pneumoniae*-infected normal human bronchial epithelial cell (50 colony-forming units/cell). Note the presence of particle aggregates on the surface of infected cells.

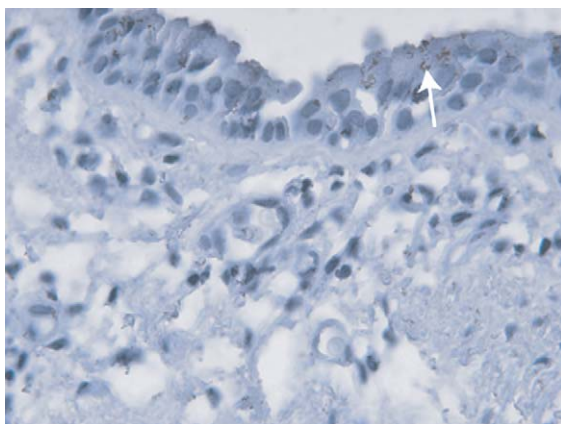


FIG 4. Immunoperoxidase detection of *M pneumoniae* in a bronchial biopsy specimen taken from a patient with severe asthma. Note that particle aggregates are found on the epithelial surface.

associated with epithelial cells (Fig 3). We have shown recently, using immunocytochemistry, that severe asthma is associated with high levels of *Mycoplasma* species immunoreactivity that is located mainly in the epithelial layer compared with mild asthma (Fig 4).

At the cellular level, *M pneumoniae* has been shown to increase expression of IL-8 and TNF- α from airway epithelial cells. Asthmatic subjects who had positive PCR results for the organism demonstrated significantly more mast cells in their airway tissue. Studies have also demonstrated that *M pneumoniae* might exacerbate neurogenic inflammation (Fig 5). In a murine model the presence of *M pneumoniae* infection after ovalbumin sensitization and challenge increased T_H2 inflammation⁵ and enhanced *MUC5* gene expression and airway hyperresponsiveness (Fig 6). Work is

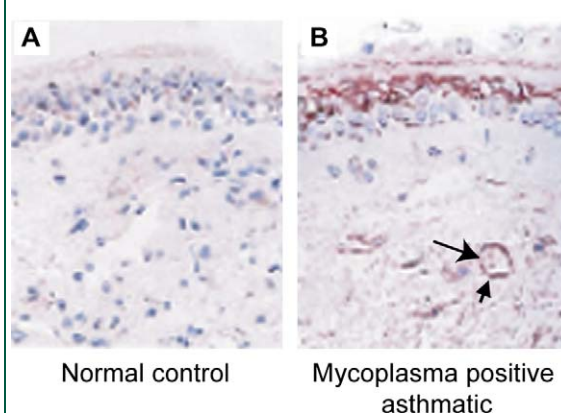


FIG 5. Representative photomicrographs of NK-1 immunostaining in endobronchial biopsy specimens from a healthy control subject (**A**) and an asthmatic subject with positive PCR results (**B**). The arrow denotes NK-1 immunostaining in the submucosa.

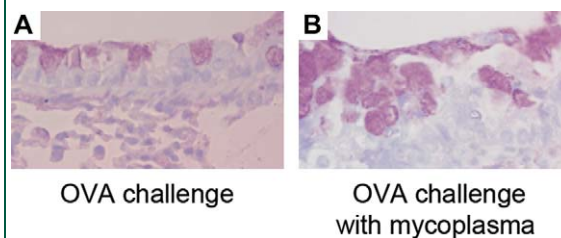


FIG 6. *MUC5AC* expression in mice sensitized and challenged with ovalbumin (OVA; **A**) and after ovalbumin plus infection with *M pneumoniae* (**B**).

ongoing, but studies are beginning to demonstrate that chronic *M pneumoniae* infection might exacerbate airway inflammation in asthma and might contribute to its severity and persistence.

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