

Correspondence

***Chlamydia pneumoniae* and asthma: More than just exacerbations**

To the Editor:

I would like to clarify a statement made by Nagy et al¹ in their interesting article describing associations of mannose-binding lectin (MBL) variant alleles with increased risk of asthma in children with serologic evidence for *Chlamydia pneumoniae* (Cpn) infection. They stated that Cpn-asthma associations have been “mainly restricted to the exacerbation of asthma symptoms in adults with known asthma,”¹ and quoted my article² describing 9 patients with acute wheezing during acute Cpn infection. The main thrust of my article² was to document strong associations of “preexisting” Cpn antibody (indicating previous exposure or possible chronic infection) with asthma. In addition to the 9 patients cited, 4 others were diagnosed with chronic asthma after infection, not before. In addition to an association with asthma exacerbations, emerging evidence also suggests an important association of Cpn previous exposure and/or persistent infection with chronic asthma severity.³ It appears that the link(s) between Cpn and asthma are more complex than stated in their background information.

In children with MBL variant alleles, Nagy et al¹ reported that the highest risk of asthma occurred in subjects with possible chronic or recurrent infection (Cpn IgG and IgA seropositive), but no increased risk was seen in children with acute (IgM positive) infection. Other seroepidemiologic investigations have also linked non-acute Cpn IgG and IgA with asthma.³ Thus, the findings of Nagy et al¹ provide additional data supporting an association of nonacute Cpn infection with asthma. Their original contribution is to document interactions between host factors (in this case MBL variant alleles) and environmental factors (indicated by Cpn antibodies) that are associated with the asthma phenotype.

Various strategies for designing antibiotic treatment trials are available to investigate whether such infection-asthma associations are causal. It is generally accepted that asthma is a multifactorial condition, and I submit that this multifactorial model applies to environmental and to host factors equally. I do not advocate the use of Cpn antibodies to select patients for treatment (since other organisms might also be involved and/or antibody detection may be insensitive). Nor do I support the suggestion that MBL gene polymorphisms be used to identify “those who can benefit more likely from the antibiotic therapy”¹ (since other genes are also likely to be involved). Only antibiotic trials that enroll a broadly representative sample of patients with asthma and that perform relevant subgroup analyses can test hypotheses of multifactorial environmental (multiple pathogens) and host (multiple asthma genes) factors producing the asthma phenotype. For example, my colleagues and I recently detected significant asthma symptom improvement 3 months after com-

pleting 6 weeks of azithromycin in a small (n = 45), randomized, placebo-controlled trial that enrolled a community sample of adults with stable persistent mild to moderate asthma. Neither clinical (age, sex, smoking, allergy, or severity) nor biological (Cpn IgG or IgA) factors significantly predicted the improvement. Limiting research trials or treatment to a narrow subgroup precludes such analyses and might (in my opinion) delay effective treatment for many asthma sufferers.

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