Correspondence: W.C. Webley, Dept of Microbiology, 639 North Pleasant Street, 203 Morrill IV N, Amherst, MA 01003, USA. E-mail: wilmore@microbio.umass.edu

Statement of Interest: None declared.

REFERENCES

1 Wang F, He XY, Baines KJ, *et al*. Different inflammatory phenotypes in adults and children with acute asthma. *Eur Respir J* 2011; 38: 567–574.
2 Webley WC, Tilahun Y, Lay K, *et al*. Occurrence of *Chlamydia trachomatis* and *Chlamydia pneumoniae* in paediatric respiratory infections. *Eur Respir J* 2009; 33: 360–367.
3 Martin RJ, Kraft M, Chu HW, *et al*. A link between chronic asthma and chronic infection. *J Allergy Clin Immunol* 2001; 107: 595–601.
4 Zucker M. Asthma associated with bacterial infection. www.respiratoryreviews.com/jul01/rr_jul01_bactasthma.html Date last accessed: July 26, 2011.
5 Schröder NW, Crother TR, Naiki Y, *et al*. Innate immune responses during respiratory tract infection with a bacterial pathogen induce allergic airway sensitization. *J Allergy Clin Immunol* 2008; 122: 595–602.

DOI: 10.1183/09031936.00071711

From the authors:

We thank W.C. Webley and D.L. Hahn for their correspondence regarding our article [1]. In our study, we hypothesised that *Chlamydophyla pneumoniae* infection may be an aetiological agent for noneosinophilic forms of asthma and sought to test this hypothesis using a sensitive and validated PCR for *C. pneumoniae*. We did not detect *C. pneumoniae* and concluded that *C. pneumoniae* infection was unlikely to be the cause of noneosinophilic asthma. We stand by these results because we studied a large number of subjects, who were carefully classified into inflammatory asthma phenotypes and who were assessed using valid methods. Induced sputum samples material from the lower airways, as evidenced by the recovery of pulmonary macrophages in the sample. It is a useful technique for assessing lower respiratory tract infection, and widely used for this purpose [2]. In particular, induced sputum can detect *C. pneumoniae* infection when it is present [3]. A recent multicentre study, which used bronchoscopic biopsy, reported a similar rate of *C. pneumoniae* detection to ours (one out of 92 samples) [4].

W.C. Webley and D.L. Hahn propose that *C. pneumoniae* may preferentially reside in lower airway cells that are out of the sampling range of induced sputum. This hypothesis could be directly tested by a study comparing induced sputum to bronchoalveolar lavage samples for *C. pneumoniae* detection. However, we think this is biologically implausible based on other published data [3, 4]. Furthermore, how does *C. pneumoniae* infection cause inflammation and asthma in airways (*e.g.* large airways, for example) in which it is not present, and yet it does not cause an inflammatory reaction in parts of the lung where it is proposed to be present (*e.g.* alveoli)?

Defining the role of *C. pneumoniae* in airway diseases such as asthma and chronic obstructive pulmonary disease is an important issue. Research in this area has been held back by the inability to reliably and reproducibly detect *C. pneumoniae* in airway samples, and the inconsistent results of treatment studies. PCR has now been able to overcome many of these technical limitations [3, 4]. If *C. pneumoniae* is indeed relevant to chronic inflammatory airway disease, we may need to consider different mechanisms other than the simple chronic infection hypothesis. For example, the timing of *C. pneumoniae* infection and the resulting immune reprogramming may influence the development and phenotypic expression of asthma. Based on our recent modelling work, *C. pneumoniae* infection during active sensitisation may induce a neutrophilic asthma phenotype through immune reprogramming and does not require chronic *C. pneumoniae* infection for the expression of neutrophilic asthma [5]. Our recently published data are consistent with this hypothesis [1], and this may also explain why studies of treatment directed at *C. pneumoniae* are not clearly positive in asthma. In childhood asthma, the timing of *C. pneumoniae* infection in early life may induce immune reprogramming and subsequent asthma [6]. These mechanisms might also explain the associations between *C. pneumoniae* antibody (immune) responses that are linked with asthma, often in the absence of detectable organisms.

We think it is time to accept that the published data do not support chronic infection as the main mechanism in the modulation of asthma through *C. pneumoniae*. There are other possibilities, which focus on the timing of infection and subsequent immune reprogramming; our efforts could be put to use designing studies that test for these effects in human asthma.

F. Wang* and P.G. Gibson*,#,¶
*Dept of Pathogenobiology, Norman Bethune College of Medicine, JiLin University, Changchun, China. #Centre for Asthma and Respiratory Disease, University of Newcastle, Callaghan, and ¶Dept of Respiratory and Sleep Medicine, Hunter Medical Research Institute, John Hunter Hospital, New Lambton, New South Wales, Australia.

Correspondence: F. Wang, Dept of Pathogenobiology, Norman Bethune College of Medicine, JiLin University, 126, Xin Min Street, Chang Chun, China. E-mail: wf@jlu.edu.cn

Statement of Interest: A statement of interest for P.G. Gibson can be found at www.erj.ersjournals.com/site/misc/statement.xhtml

REFERENCES

1 Wang F, He XY, Baines KJ, *et al*. Different inflammatory phenotypes in adults and children with acute asthma. *Eur Respir J* 2011; 38: 567–574.
2 Simpson JL, Moric I, Wark PA, *et al*. Use of induced sputum for the diagnosis of influenza and infections in asthma: a comparison of diagnostic techniques. *J Clin Virol* 2003; 26: 339–346.
3 Harju TH, Leinonen M, Nosko-Koivisko J, *et al*. Pathogenic bacteria and viruses in induced sputum or pharyngeal secretions of adults with stable asthma. *Thorax* 2006; 61: 579–584.
4 Sutherland ER, King TS, Ictovic N, *et al*. A trial of clarithromycin for the treatment of suboptimally controlled asthma. *J Allergy Clin Immunol* 2010; 126: 747–753.
5 Horvat JC, Starkey MR, Kim RY, *et al*. Chlamydial respiratory infection during allergic sensitization drives neutrophilic allergic airways disease. *J Immunol* 2010; 184: 4159–4169.
6 Horvat JC, Beagley KW, Wade MA, *et al*. Neonatal chlamydial infection induces mixed T-cell responses that drive allergic airway disease. *Am J Respir Crit Care Med* 2007; 15: 556–564.

DOI: 10.1183/09031936.00076011