

**IS *CHLAMYDIA PNEUMONIAE* A MISSING LINK IN THE "DUTCH HYPOTHESIS" AND CHRONIC NON-SPECIFIC LUNG DISEASE (CNSLD)?**  
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The "Dutch Hypothesis" states that bronchitis, asthma and COPD are a disease continuum (chronic non-specific lung disease - CNSLD) defined by a common host response to environmental factors.<sup>1</sup> Research has traditionally focused on adaptive immunity and atopy as a key host characteristic. More recently, *Chlamydia pneumoniae* (*Cpn*) chronic infection has been associated with asthma and COPD.<sup>2</sup> On this basis it has been suggested that *Cpn* may contribute to the pathogenesis of CNSLD and that innate immune response to *Cpn* may be an important factor in causation.<sup>3</sup> Most published associations of *Cpn* and airways disease have focused on asthma and COPD, with less known about the relationship of chronic *Cpn* infection and uncomplicated acute bronchitis (UAB). Nevertheless, UAB has been implicated as a risk factor for the development of asthma,<sup>4</sup> raising the question whether a common etiologic factor is present for CNSLD. We therefore studied whether *Cpn* chronic infection is also associated with UAB in patients with acute respiratory illnesses (ARI).

We studied 402 outpatients (mean age 34.2 years) with ARI diagnosed as upper respiratory illness (URI, n=115), UAB (n=189) or acute exacerbations of reactive airways disease (RAD, n=98) and obtained acute and convalescent serum specimens for *Cpn*, *Chlamydia trachomatis* (*Ct*) and *Mycoplasma pneumoniae* (*Mpn*) antibodies, and throat swabs for *Cpn* culture. Subjects with evidence for an acute infection by *Cpn*, *Ct* or *Mpn* were excluded.

*Cpn* seropositivity (polyvalent MIF titer  $\geq 1:16$ ) was 47% in URI, 57% in UAB and

76% in RAD (P-trend  $<.01$  after controlling for age, sex, smoking, allergy, *Ct* and *Mpn* titers).

The results are consistent with a previous report linking *Cpn*-specific antibodies with the spectrum of respiratory illnesses including bronchitis, asthma and COPD (CNSLD).<sup>5</sup> Defects in innate immunity have recently been reported in association with *Cpn* infection in asthma.<sup>6</sup> *Cpn*-specific IgA antibodies suggesting chronic infection have been associated with both UAB and asthma but *Cpn*-specific hsp60 antibodies were associated only with asthma.<sup>7</sup> Thus, development of asthma instead of just UAB after acute *Cpn* infection may depend on, in addition to chronic infection, a pathogenic host response involving chlamydial heat shock protein-60 (hsp60) that has been implicated in the pathogenesis of other chronic chlamydial diseases.<sup>8</sup> Taken together, these results suggest that research focusing on host innate immune response to infectious agents such as *Cpn* may be important to understand the etiopathogenesis of CNSLD.

#### References

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