IS *CHLAMYDIA PNEUMONIAE* A MISSING LINK IN THE "DUTCH HYPOTHESIS" AND CHRONIC NON-SPECIFIC LUNG DISEASE (CNSLD)?

D.L. Hahn*,[1,2] M.B. Plane[1]

[1]Dept. Family Medicine, U. Wisconsin Medical School, Madison, WI USA, [2]Dean Medical Center, Madison, USA

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.[1] 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.[2] 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.[3] 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,[4] 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).[5] Defects in innate immunity have recently been reported in association with *Cpn* infection in asthma.[6] *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.[7] 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.[8] 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

1. Sluiter HJ et al. Eur Respir J 1991; 4:479-489
2. Hahn DL. Ann Allergy Asthma Immunol 1999; 83:271-292
3. Hahn DL Chest 2002; 122:1510-1512
4. Williamson HA et al. J Fam Pract 1987; 24:35-38
5. Falck G et al. Chest 2002; 122:1587-1593
6. Nagy A et al. J Allergy Clin Immunol 2003; 112:729-734
7. Hahn DL et al. Ann Allergy Asthma Immunol 2000; 84:227-233
8. Huittinen T et al. Eur Resp J 2001; 17:1078-1082