Lack of Serum Oligoclonal Antibody Responses to *Chlamydomydia pneumoniae* in Multiple Sclerosis

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Dear Sir,

Dr. Chapman and colleagues [1] demonstrated patients with multiple sclerosis (MS) do not exhibit serum oligoclonal antibody responses to *Chlamydomydia pneumoniae* antigens using Western blotting (WB). The authors concluded that systemic *C. pneumoniae* infection is not associated with MS.

Although one would expect reactive serum oligoclonal bands to *C. pneumoniae*, should the bacterium be present and pathogenic, WB may not be the most sensitive measurement of *C. pneumoniae* antibody responses [2]. This may explain the discrepancy between the lower frequency of serum antibody detected by WB in this study compared to the authors' previous study using the microimmunofluorescence (MIF) test [3]. Several studies have confirmed a high prevalence of *C. pneumoniae* IgG antibodies in both MS patients and controls using MIF [3]. This is expected given the high frequency of antibodies in western populations, in general [4].

Certain surface *C. pneumoniae* epitopes, particularly the major outer membrane protein (MOMP), are prone to denaturing and cannot be detected using WB [2]. MIF tests and commercially available enzyme-linked immunosorbent assays (ELISA) use whole organisms as the antigenic target with struc-

tural conservation of immunogenic proteins such as MOMP. Although the antigenicity of each *C. pneumoniae* surface protein is not well characterized, a broader range of antibody responses would be detected using these tests.

Presumably, to increase specificity, the authors used WB. Certainly, isolated positive results using MIF or ELISA are difficult to interpret because they may represent acute, chronic or previous infection. *C. pneumoniae* antibody testing in this way is discouraged [5]. However, it is difficult to exclude systemic *C. pneumoniae* infection in patients with MS using antibody testing alone, considering the technical difficulties with WB. To do this, antigen-specific testing of sera is required, either to detect free antigen or immune complexes, a method used in studies of cardiovascular disease [6].

C. pneumoniae is a common cause of respiratory infection in western populations and may become chronic. The majority of serological studies do not support *C. pneumoniae* as an aetiological agent in MS. However, the rate of systemic infection should be characterised, using antigen-specific methods, as chronic bacterial infection in susceptible MS patients may exacerbate the autoimmune pathogenesis.

References

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Reply

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The two complementary studies [1, 2] were performed simultaneously on the same cohorts. Seropositivity was determined by WB [1] and ELISA on all samples, positives on ELISA being followed up with MIF [2]. CSF samples were analysed by PCR and culture [2] to replicate the work of Sriram [3] whilst all paired samples were analysed by IEF for oligoclonal IgG [1].

We agree with Dr. Parratt that MIF is the diagnostic gold standard but it cannot distinguish between high and low affinity antibody and whether that antibody response is polyclonal or oligoclonal. When the hypothesis is that *C. pneumoniae* may be an infectious cause of MS, these are important considerations. Our original intention was to follow up serum positives with

IEF of paired samples, to investigate the clonality of serum and CSF, followed by antigen immunoblotting and probing with thiocyanate to investigate affinity. However, as both studies [1, 2] reported identical incidences of seropositivity by all methods in MS patients and controls it was felt unnecessary to do this.

References

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