

Dear Mr Tuttle

The following are the essential points I would make regarding "Clinical Diagnosis and Testing" in patients with persisting symptoms, aka "Persistent Lyme disease", "Post-treatment Lyme disease syndrome", "Chronic Lyme disease":

- The diagnosis in such patients is primarily a clinical diagnosis, based on a typical combination of persisting symptoms, and exclusion of other clear diagnostic possibilities.

- Current serology testing, ie two-tiered testing (the screening ELISA test, followed by Western Blot testing only if the ELISA is positive), is insufficiently sensitive in such patients to exclude the diagnosis if the ELISA is negative. The reasons for this are likely that patients with persistent symptoms, as compared to for example patients who have Lyme arthritis-who generate robust immune responses against the causative organisms and who do well with limited courses of antibiotic treatment, mount limited, often muted or no immune responses to *B.burgdorferi*. This explanation is supported by both the results of animal model studies, including the non-human primate model, and extensive clinical observations, with the primary findings that *B.burgdorferi* somehow subverts the host immune response such that there is interference with the normal transition of IgM to IgG response. Further support is provided by the clinical observations that Lyme Western Blot testing in many such patients show limited, primarily IgM responses and a few if any IgG responses, and probably more importantly demonstration of one or more immune responses to highly specific *B.burgdorferi* proteins, ie the 23kd and/or 39kd proteins, in addition to the commonly seen but less specific 41kd protein. And successful treatment of these patients using specific antibiotic regimens for a sufficient duration of time, results in resolution of the IgM responses.

- Based on the above results, it could be recommended that Western Blot testing be directly ordered, bypassing the ELISA test, in patients with possible persisting Lyme disease, its value in potentially supporting the clinical diagnosis, but recognizing that even negative Western Blot tests do not exclude the clinical diagnosis, and the likely basis for empiric antibiotic treatment as the ultimate diagnostic tool.

- If, and until one or more specific markers can be discovered that can more definitively answer the question of whether there is or is not persisting infection by *B.burgdorferi*, the diagnosis and management of patients with persistent Lyme disease rests on the clinical evaluation and experience of health care providers.

I look forward to further participation in this important meeting.

Best regards  
Dr Donta