Reviewer's report

Title: Mapping of Hormones and Cortisol Responses in Patients after Lyme Neuroborreliosis.

Version: 3 Date: 19 December 2009

Reviewer: John J Halperin

Reviewer's report:

Major compulsory revisions: While I thank the authors for their clarifications, I think the responses only add to my initial concerns about this work. As the authors make clear on pages 8 and 9, the cortisol response correlates entirely with the presence of subjective symptoms (most of which are nonspecific) and not with any objective measure of neurologic disease. Since these subjective symptoms are commonly present in the normal population, any suggestion that these patients had persistent symptoms or problems causally related to Lyme neuroborreliosis or its sequelae can only be established in an appropriate controlled trial. Since similar cortisol responses have been shown to occur in patients with depression, this essential control group must be included to understand the implications of these findings. At the very least, a control group of non-LNB patients with comparable symptoms (and matched for demographics such as age) would seem to be essential.

On the other hand, the study does provide several observations worth emphasizing. This group of patients thought to have had neuroborreliosis had no persisting endocrine abnormalities, and persisting symptoms did not correlate with IL6, used as a measure of ongoing inflammation. Persisting subjective symptoms were unrelated to any persisting objective evidence of neurologic damage.

Minor essential revisions:

p. 7. The authors state: “No other pathological neurological signs were noted in these patients. In four patients, ataxia, disturbed motor and sensory functions were found.” These two sentences appear to be mutually exclusive.

The “arbitrarily chosen cut off level of four” remains a post hoc analysis. Even though other selected cut-offs were also stated to be statistically significant, such analyses remain post hoc and of dubious statistical import.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a
statistician.

**Declaration of competing interests:**
I declare that I have no competing interests