

The lymphocyte transformation test for the diagnosis of Lyme borreliosis could fill a gap in the difficult diagnostics of borreliosis

V. von Baehr

Immunology, IMD Berlin, Berlin, Germany

Corresponding author: V. von Baehr, IMD Berlin, Nicolaistr. 22, 12247 Berlin, Germany
E-mail: v.baehr@imd-berlin.de

Sir,

We would like to comment on the article “The lymphocyte transformation test for the diagnosis of Lyme borreliosis has currently not been shown to be clinically useful” by Dessau *et al.* in *Clin Microbiol Infect.* 2014 Feb 13. doi: 10.1111/1469-0691.12583.

Mr. Dessau criticises in his article that the clinical inclusion criteria for the assignment of the 94 patients with clinical Lyme borreliosis were not clearly defined and that the control group consisted only of seronegative patients. This leads him to the conclusion that due to this “selection bias” the specificity of the LTT for borreliosis antigens may be overestimated.

We would like to give following comments:

Our publication indicates the fact that clinical characterisation is difficult. This is in agreement with other studies and it is generally known that it is a problem to select a distinct characterised patient population. However, our study did not intend to distinguish between the immunological phenomena of different borrelia manifestations. The aim of this study was to investigate and confirm that the result obtained by LTT allows a statement on the borrelia specific immune response. As irrelevant for the study objective, we adopted clinical diagnoses, as for example Bannwarth Syndrome, from the patients' health records.

The investigation of seronegative patients was performed in order to show the specificity of the antigens used in the LTT as it is often criticised that the detected T-cell reactivity is not specific to borreliosis but simply a general T-cell reactivity of patients with other inflammatory diseases. For this reason, a seronegative healthy collective was used to investigate the analytical specificity and to ensure that those patients or rather probands have no borreliosis specific memory T-lymphocytes. It is certainly correct that the specificity is lower when also clinical healthy seropositive patients are included. To show this point, a clinically healthy

seropositive control group ($n = 48$) was investigated as well, as shown in table 1. And indeed, with 91.6% the specificity was lower than the specificity of the seronegative group, however, this is clearly shown and also addressed in the discussion section.

Despite the criticism regarding our patient selection, the quintessences should be accepted:

1. The fact that 1.3% of healthy seronegative (and therefore very likely not infected) and only 8.4% of healthy seropositive patients showed positive results speaks for a high analytical specificity.
2. The fact that 92.1% of patients in the early infection phase and 53.3% of patients with late manifestations forms showed a decline or negative LTT results under antibiotic treatment argues for the specificity of the analysis, because it is not explainable why antibiotic treatment should influence an unspecific T-cell reactivity.

In our article we emphasize that clinical evaluation is essential for diagnosis, but that the LTT is able to give additional evidence. Mr. Dessau did not address the available scientific literature regarding LTT in his comment. However, this would have shown that other authors confirm our results [1–5]. It is important to ensure the specificity of the technically sophisticated LTT. This strongly depends on the selection of antigens. The specificity must be tested prior to use for each antigen lot on an adequate amount of healthy people. The LTT is, provided that it is validated *lege artis* by the performing laboratory, a reproducible laboratory method which should be used as extension to serological methods and when the clinical picture does not give sufficient certainty. The LTT should not replace serological methods and clinical evaluation.

Transparency Declaration

The author has no conflicting interest to declare.

References

1. Krause A, Brade V, Schoerner C, Solbach W, Kalden JR, Burmester GR. T cell proliferation induced by *Borrelia burgdorferi* in patients with Lyme borreliosis. *Arthritis Rheum* 1991; 34: 393–402.
2. Schempp C, Bocklage H, Owsianowski M, Lange R, Orfanos CE, Gollnick H. In vivo und in vitro Nachweis einer Borrelieninfektion bei einer morpheaähnlichen Hautveränderung mit negativer Borrelienserologie. *Hautarzt* 1993; 44: 14–18.
3. Breier F, Klade H, Stanek G *et al.* Lymphoproliferative responses to *Borrelia burgdorferi* in circumscribed scleroderma. *Br J Dermatol* 1996; 134: 285–291.

4. Buechner SA, Lautenschlager S, Itin P, Bircher A, Erb P. Lymphoproliferative responses to *Borrelia burgdorferi* in patients with erythema migrans, acrodermatitis chronica atrophicans, lymphadenosis benigna cutis, and morphea. *Arch Dermatol* 1995; 131: 673–677.
5. Valentine-Thon E, Ilsemann K, Sandkamp M. A novel lymphocyte transformation test (LTT-MELISA[®]) for Lyme borreliosis. *Diagn Microbiol Infect Dis* 2007; 57: 27–34.