Usefullness of quantitative IgG assays Borrelia VLSE LIAISON® and the new VIDAS® Lyme for serological follow-up of patients with Lyme borreliosis

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INTRODUCTION

Diagnosis of Lyme borreliosis relies on serology by screening for IgG and IgM to Borrelia burgdorferi sensu lato, confirmed by immunoblots if results are positive or equivocal. In Europe epidemiological situation is complicated by IgG seroprevalence varying from 10 to 20%. Seroprevalence increases with age and depends on risks of contact with ticks during leisure or professional activity. Positive predictive value is below 50% without anamnesis of tick bite and good clinical examination. VIsE discovered in the 2000's was thought to be the answer as a marker of disease activity. Unfortunately seroprevalence was also detected and tempered enthusiasm for this specific antigen. We used quantitative values of Borrelia IgG LIAISON assay for follow-up of patients. Using the new VIDAS® Lyme IgG in routine, we observed similar variations. Our goal was to compare these 2 assays (VIDAS Lyme IgG and LIAISON Borrelia IgG) for serological follow-up of patients at different stages of Lyme borreliosis. A retrospective analysis was initiated with collection of precise clinical data from all included patients.

MATERIALS AND METHODS

The VIDAS Lyme IgG is a qualitative assay. VLSE antigen is the main constituent of this new assay. Linearity range was determined for the VIDAS Lyme IgG assay, as well as reproducibility. The Borrelia IgG LIAISON assay is only constituted of VIsE antigen. This assay was performed according to manufacturer instructions but dilutions 1/10 were performed starting with value $\geq$200 AU/ml.

A total of 296 sera from 97 patients with early, disseminated and late symptoms of Lyme borreliosis were evaluated. Clinical data were collected for all the patients. A control group composed of 2 samples, 3 to 12 months apart from seropositive and seronegative blood donors (N=38 and N=52 respectively) was included. Concordance of both methods was calculated based on both groups, blood donors and patients. Patients were evaluated according to clinical stages. Concordance of tendencies was established between the 2 assays.

Blood donors (N=90)

Discrimination positive-negative between both assays was 97.8%. Correlation of tendencies was 95.6 % : stable values (N=82) or significant increase (N=3) or decrease (N=1). In addition 4 discrepant results were observed with LIAISON : 2 significant increasing value (above 30%) and 2 decreasing value . These 4 cases showed stable values with VIDAS.
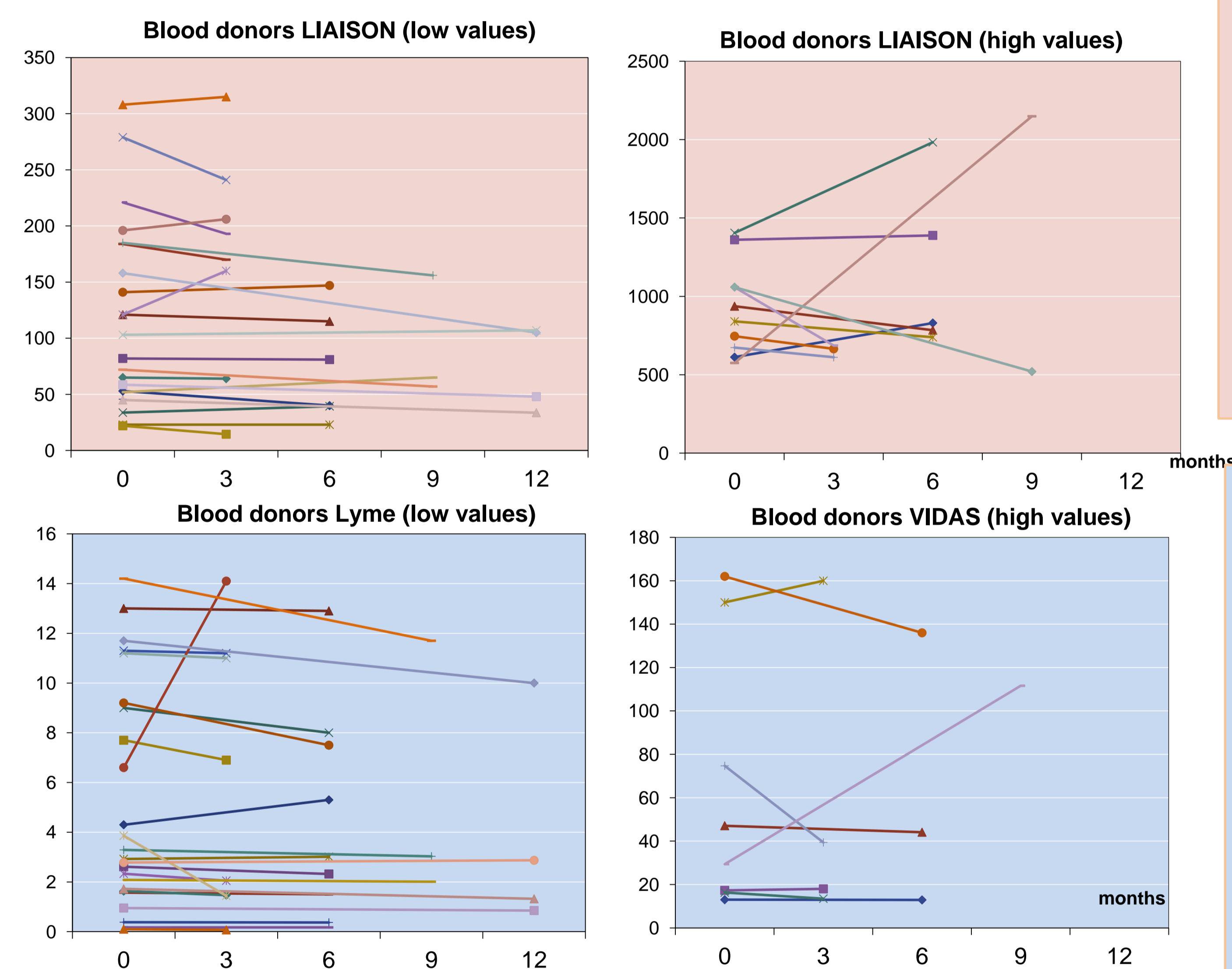No significant variations was observed for 91% of blood donors
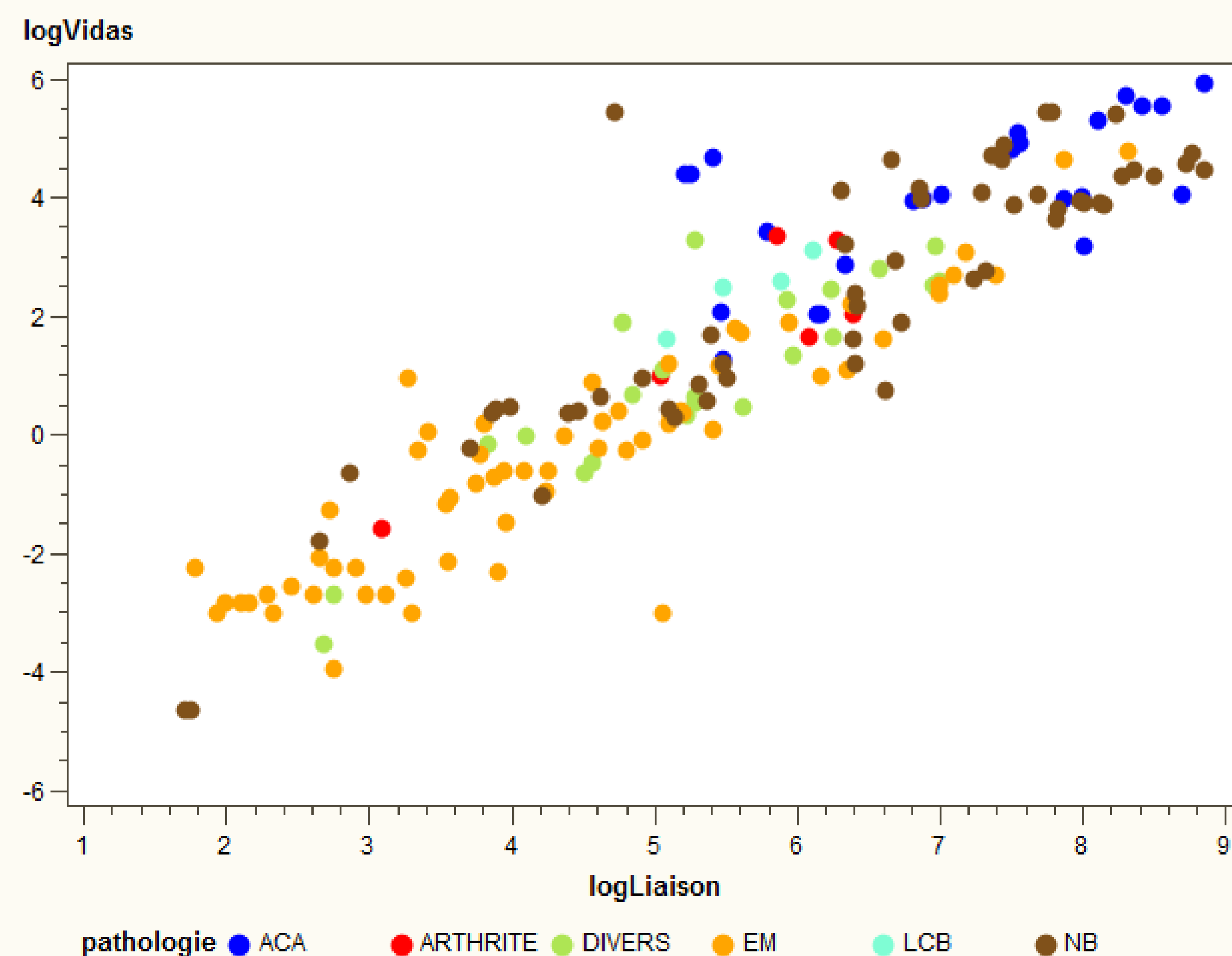
Patients (N=97)

Linearity for the VIDAS assay was established between 0.4 and 4.0 TV (Test Value). For the LIAISON assay linearity was found between 5 and 200 AU/mL. Concordance between both assays was good. We observe increasing values with duration of symptoms. Usually patients with EM have LIAISON values <200 AU/ml and VIDAS values <2.0, except in case of a second EM. Patients with ACA or arthritis have values >500 AU/ml (LIAISON) or >50.0 (VIDAS). Patients with neuroborreliosis have a wide range of values going from <10 to 6'934 AU/ml (LIAISON) or <0.2 to 236 (VIDAS) depending on duration of disease.
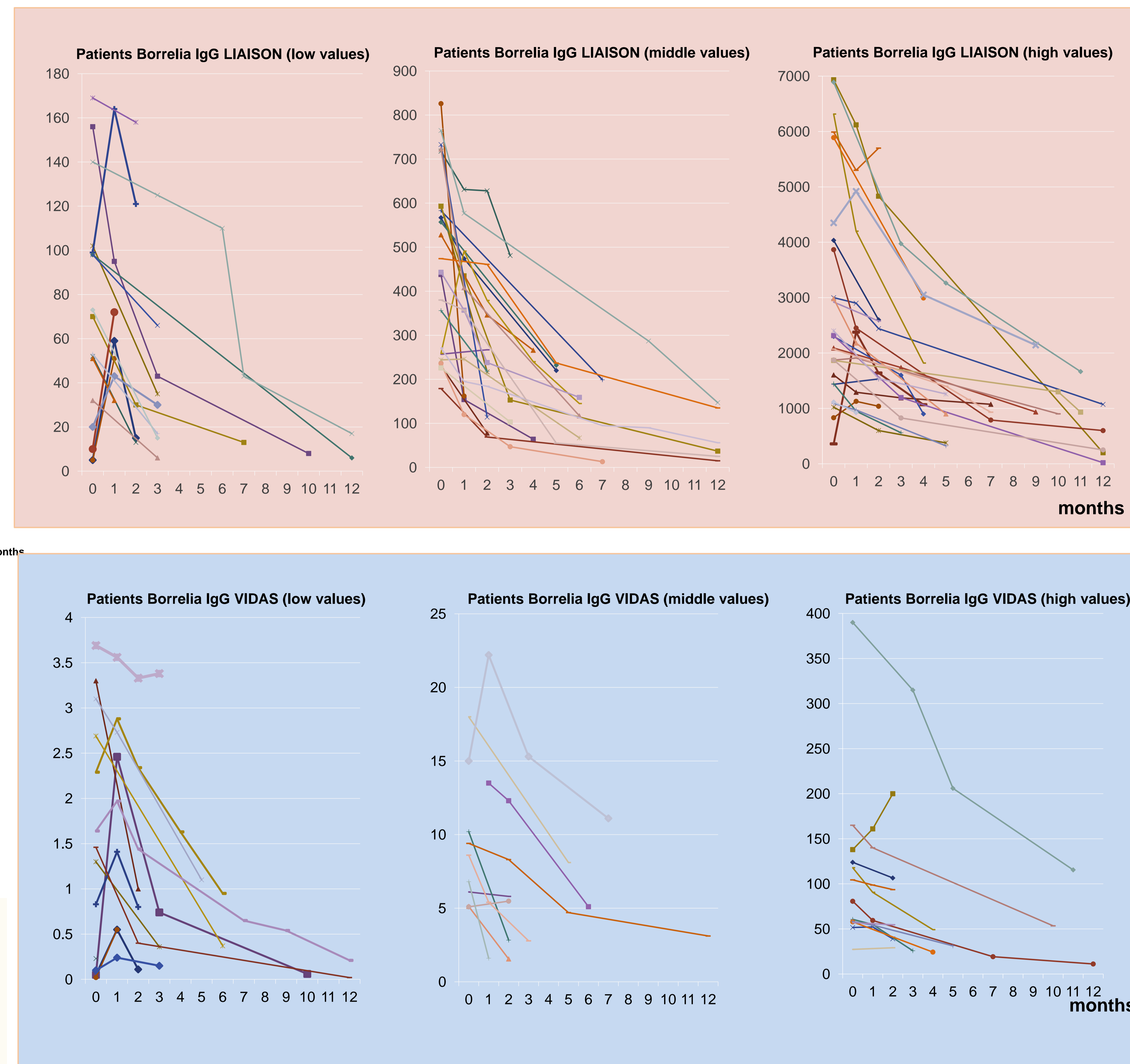
RESULTS

Variations observed among **blood donors (N=90)**

Blood donors LIAISON (low values)

Blood donors LIAISON (high values)

Blood donors Lyme (low values)

Blood donors VIDAS (high values)

Concordance of values between LIAISON and VIDAS assays
Serum of patients with EM, neuroborreliosis, LCB, ACA, Lyme Arthritis.

pathologie ● ACA ● ARTHRITE ● DIVERS ● EM ● LCB ● NB

RESULTS

Patients Borrelia IgG LIAISON (low values)

Patients Borrelia IgG LIAISON (middle values)

Patients Borrelia IgG LIAISON (high values)

months

Patients Borrelia IgG VIDAS (low values)

Patients Borrelia IgG VIDAS (middle values)

Patients Borrelia IgG VIDAS (high values)

months

Follow-up serums (N=296)

Concordance between LIAISON and VIDAS assays was good given that the 2 assays are basically different : technology (CLIA- ELFA), antigens (VIsE – VIsE, OspC, DbpA) , scales… Concordance of tendencies is 82.7% with EM patients (seroconversion appears in few cases later with VIDAS) and 96.7% with neuroborreliosis , ACA and Lyme arthritis patients. Patients with early infections (EM or neuroborreliosis) demonstrated a clear increase in test value and a quick decrease after initiation of treatment. For patients experiencing late infections (ACA or Lyme Arthritis), test values were usually high and decline was marked but slower than for the test values observed with early Lyme borreliosis.

CONCLUSION

Using this methodology for the follow-up of patients for several years we are convinced that quantification of IgG to *B. burgdorferi* sensu lato makes sense and gives useful laboratory results to the clinicians regarding activity of infection and effectiveness of treatment. The fact that both assays show similar variations supports prediction of either a current infection or seroprevalence or cure. Variations with these 2 assays were rapid, within a few weeks depending on clinical stages. Observed variations seem to reflect disease activity as previously described in initial papers.[1,2]
These results need to be confirmed by a prospective multicentre study.

1. Philipp M.T. et al, J. Clin. Microbiol. 2003, 41:4955-60
2. Marangoni A. et al Clin. Vaccin. Immunol. 2006, 13:529-9