

# T-Helper 17 Cell Cytokine Responses in Lyme Disease Correlate With *Borrelia burgdorferi* Antibodies During Early Infection and With Autoantibodies Late in the Illness in Patients With Antibiotic-Refractory Lyme Arthritis

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## Abstract

### Background.

Control of Lyme disease is attributed predominantly to innate and adaptive T-helper 1 cell (T<sub>H</sub>1) immune responses, whereas the role of T-helper 17 cell (T<sub>H</sub>17) responses is less clear. Here we characterized these inflammatory responses in patients with erythema migrans (EM) or Lyme arthritis (LA) to elucidate their role early and late in the infection.

### Methods.

Levels of 21 cytokines and chemokines, representative of innate, T<sub>H</sub>1, and T<sub>H</sub>17 immune responses, were assessed by Luminex in acute and convalescent sera from 91 EM patients, in serum and synovial fluid from 141 LA patients, and in serum from 57 healthy subjects. Antibodies to *Borrelia burgdorferi* or autoantigens were measured by enzyme-linked immunosorbent assay.

### Results.

Compared with healthy subjects, EM patients had significantly higher levels of innate,  $T_H1$ , and  $T_H17$ -associated mediators ( $P \leq .05$ ) in serum. In these patients, the levels of inflammatory mediators, particularly  $T_H17$ -associated cytokines, correlated directly with *B. burgdorferi* immunoglobulin G antibodies ( $P \leq .02$ ), suggesting a beneficial role for these responses in control of early infection. Late in the disease, in patients with LA, innate and  $T_H1$ -associated mediators were often >10-fold higher in synovial fluid than serum. In contrast, the levels of  $T_H17$ -associated mediators were more variable, but correlated strongly with autoantibodies to endothelial cell growth factor, matrix metalloproteinase 10, and apolipoprotein B-100 in joints of patients with antibiotic-refractory LA, implying a shift in  $T_H17$  responses toward an autoimmune phenotype.

### Conclusions.

Patients with Lyme disease often develop pronounced  $T_H17$  immune responses that may help control early infection. However, late in the disease, excessive  $T_H17$  responses may be disadvantageous by contributing to autoimmune responses associated with antibiotic-refractory LA.

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**Keywords:** [Lyme disease](#), [erythema migrans](#), [Lyme arthritis](#),  [\$T\_H17\$](#) , [antibodies](#)

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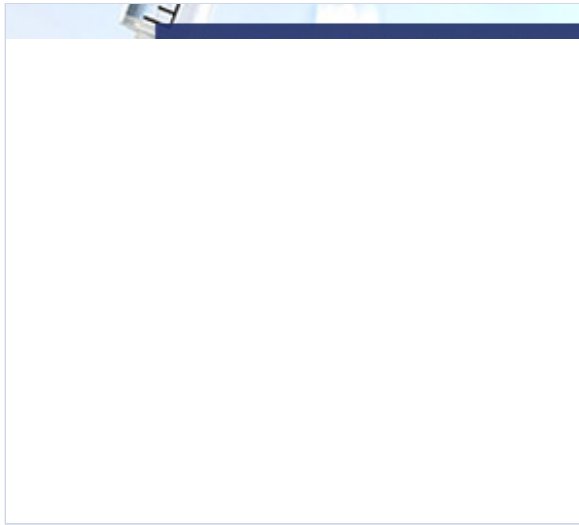
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