Temporal patterns of early cytokine immune response to infection with *B. burgdorferi*

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Background:
Early Lyme disease is caused by *Borrelia burgdorferi* infection of the skin. Serologic testing by ELISA is commonly negative in the first weeks of infection. Convalescent serologies are often negative in patients after prompt antibiotic therapy. It is unknown how immune response may vary before, during, and after treatment and how specific biomarkers may relate to clinical serology.

Methods:
Sera were drawn at 4 time points over 4 months of follow-up from 17 patients with early Lyme disease. A total of 30 cytokines were measured using the Luminex bead based system and compared to 12 uninfected controls. Serostatus by ELISA and confirmatory western blot was measured by a commercial lab.

Results:
Patients with early, untreated Lyme disease had elevated levels of 9 cytokines when compared with controls ($p<.10$), including Eotaxin, IL-12, IL-7, IP-10, IL-IRA, MCP-1, MIP1, MIG and HGF. Following treatment, these differences disappeared for IL-IRA, IP-10 and MIG, while the remaining six cytokines remained significantly elevated across all time points. While not initially elevated, RANTES levels increased post-treatment and remained significantly elevated as well. Seropositivity pre-treatment was associated with elevations in 8 cytokines, including EGF, FGF-β, G-CSF, IFNα, IL-1β, IL-7, MCP-1 and MIP-1α ($p<.10$). Patients with delayed seroconversion during treatment showed increasing levels of 6 of these cytokines over this period, whereas those that remained persistently sero-negative maintained or decreased their levels. Eotaxin levels did not differ significantly by serostatus.

Discussion:
Immune response to early Lyme disease may show temporal patterns, including initial elevations of certain cytokines (such as IP-10) as well as later elevations of others (such as RANTES). Eotaxin was significantly elevated compared to controls at all time points but seems unrelated to patient serostatus. Elevation of other cytokines appears to correspond with seroreactivity. The relationship between underlying immune response and clinical outcomes warrants further research.