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77 : The immune system cannot generate immunological memory during infection with the Lyme disease agent *B. burgdorfer*

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In vertebrates including humans, mice and dogs, the bacteria *Borrelia burgdorferi* (Bb) causes a chronic, non-resolving infection known as Lyme disease, which requires antibiotic treatment to clear the bacteria. Re-infections are common in endemic regions. Similarly, mice can be re-infected with the same strain of Bb, implying a lack of functional immune responses. The mechanisms underlying this lack of effective short and long-term immunity to Bb are unknown. Using a mouse model of Bb-infection we show that infection with Bb produces strong T-dependent and T-independent serum antibodies, characterized by the unusual continued presence of IgM. Remarkably, both T-dependent and T-independent antibodies disappear rapidly when infection is controlled by antibiotic treatment and Bb-specific memory B cells could not be recovered. Thus, maintenance of Bb-specific humoral responses requires ongoing infections. Histological and flow cytometric examination of germinal centers, birthplaces of long-term humoral immunity, demonstrate their induction within 2 weeks of a primary infection and the presence of germinal center follicular helper T and B cells. However, the apparent normal induction of germinal centers is followed by their rapid and global collapse in multiple lymphoid organs by day 45. To determine whether the lack of memory formation is due to the nature of the Bb-antigens or is a sign of Bb-infection-mediated immune suppression, we vaccinated mice with influenza virus during an ongoing Bb-infection. Remarkably, in Bb infected mice the early antibody response to this unrelated antigen was skewed towards increased IgM production compared to that in non-infected mice, and influenza specific IgG responses were strongly reduced. Together our data demonstrate that Bb infection suppresses the development of long-lived antibody production and immunological memory formation and indicates that Bb may achieve this by suppressing the function and/or causing the rapid and global collapse of germinal centers. Supported by NIH AI073911 and T32 AI060555.