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Retention of Virus-specific Antibody Secreting Cells within the CNS

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Infection by the neurotropic JHM strain of mouse hepatitis virus (JHMV) produces an acute demyelinating encephalomyelitis, followed by ongoing chronic demyelination associated with viral persistence. While cellular immunity initially eliminates infectious virus by two weeks post infection (p.i.), viral persistence in the central nervous system (CNS) is predominantly controlled by humoral immunity. Serum anti-viral Ab were maximal at day 14 p.i. and were maintained after clearance of infectious virus. Virus specific Ab secreting cells (ASC) were measured in cell suspensions from the CNS, spleen and bone marrow to better understand the kinetics and distribution of humoral immune responses following CNS infection. Virus specific ASC peaked in the spleen at day 10 p.i. and in the CLN at day 14 p.i., but declined to undetectable levels after virus clearance. By contrast, in the CNS virus specific ASC peaked at day 21 p.i. and were maintained at high levels out to 90 days p.i. Surprisingly, analysis of the bone marrow showed no significant increase of frequency in virus specific ASC following the resolution of primary infection. At day 90 p.i., the frequency of virus specific ASC within CNS was 12 fold higher than in the bone marrow. To assess a correlation between ASC persisting in the CNS and ongoing demyelination, mice were infected with a variant of JHMV with similar growth characteristics but only little or no capacity for inducing encephalitis or demyelination. No differences of virus specific ASC levels in the peripheral lymphoid organs or within the CNS were uncovered in groups of mice infected with either variant. These data confirm the CNS as an organ for delayed, but sustained retention of ASC compared to T cells following viral infection and suggest that events associated with demyelination do not affect the preferential long term retention of ASC in the CNS.

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