Sequential control of hepatitis B virus in a mouse model of acute, self-resolving hepatitis B.

Abstract:
The determinants of an immune response to the human hepatitis B virus (HBV) are poorly understood. As studies in man and chimpanzees are limited, we aimed at developing a model of self-limiting hepatitis B in mice that helps to dissect the control of HBV by humoral and cellular immune responses. Adenoviral vectors containing 1.3-fold HBV genomes allowed an efficient and reproducible transfer of HBV genomes into mouse livers and initiated HBV replication in mice. HBV transcripts were detected in mouse livers for more than 3 months. HBsAg and HBeAg peaked around day 6 and slowly declined thereafter. A two-phase mild to moderate liver inflammation with elevated serum alanine transaminase activities was observed around day 7 and around day 70 when the vast majority of HBV-specific T cells were detected in the liver. HBV was initially controlled when specific and nonspecific T cells infiltrated the liver and intrahepatic interferon-" levels peaked around day 7, but replicated again from day 10 to day 24 and persisted at low levels thereafter despite the presence of HBV-specific T cells. Finally, HBV replication was terminated after a sufficient B-cell response had been mounted- indicated by anti-HBs seroconversion around day 35. HBV-specific T cells infiltrated the liver a second time around day 70 postinfection. This demonstrates that
the established mouse model allows studying the onset and termination of HBV infection and will help to dissect the determinants of HBV control and clearance by the immune response.

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