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The role of e-antigen in immunological tolerance and activation during HBV infection

The presence of circulating hepatitis B e-antigen may promote hepatitis B chronic infection by serving as an immunotolerance agent capable of inducing T-cell clonal deletion, ignorance and anergy. Sudden loss of e-antigen leads to the restoration of T-cell effector function and consequently to liver cell death. Using mathematical models, we investigate the host-virus interactions, determine the factors that lead to viral persistence when e-antigen is present and study the changes in these dynamics when e-antigen is lost as a result of e-antigen seroconversion or virus mutation. Using the seroconversion model, we show that high antibody levels, which completely remove e-antigen, successfully restore effector function to anergic T-cells while reducing the overall liver cell death. Using the mutation model, we show that intermediate mutation rates are associated with high levels of liver cell death, while complete loss of the wild virus is associated with mild liver disease and emergence of low mutant virus levels. The results are compared with virus concentrations and immune activation markers from patients with prenatal HBV infections.