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THE IMMUNPATHOGENESIS OF HEPATITIS C VIRUS

MARGARET JAMES KOZIEL, MD;

Beth Israel Deaconess Medical Center

and Harvard Medical School,

Boston MA, USA

Hepatitis C virus (HCV) is notable for the high rate of chronic infection, which occurs in nearly all individuals who become infected. The immune response to HCV is polyclonal and multispecific, both in terms of antibody and cellular immune responses. In hepatitis C, numerous antibodies develop during the course of chronic infection, but it has been difficult to determine which antibody response correlates best with recovery from acute viral infection. Emerging evidence indicates that cellular immunity mediated by both CD4+ and CD8+ T cells is more important in recovery from acute HCV. Individuals who recover from acute HCV infection appear to have quantitatively more vigorous CD4+ proliferative responses against one or more HCV proteins compared to those individuals who develop chronic disease. Recent data also suggests that HCV-specific cytotoxic T lymphocyte (CTL) responses may play a critical role in recovery, and may persist for years after acute infection. However, HCV-specific CTL can be readily isolated from the liver and PBMC of chronically infected individuals, and recognize multiple epitopes. These CD8+CTL may also cause tissue damage once chronic infection is established. Cytokines produced by these and other cells likely play a role in liver fibrosis. Mechanisms of viral escape include interference with host cell proteins and mutations in B- and T cell epitopes. Furthermore, the liver may play an important role in facilitating persistence. The normal liver has an abundance of non-classical T cells, and the role of these cells in chronic HCV will be discussed.