

Medical Writers' Circle

a series of articles
written by medical
professionals about
the management
and treatment of
Hepatitis C

José Azócar, MD

Medical Director
Northgate Medical,
Springfield, MA

The Role of the Immune System in Determining Viral Outcome After Hepatitis C Viral (HCV) Infection.

Infection by the hepatitis C virus (HCV) is a growing public health concern. In the general population the prevalence of HCV antibodies in the United States has been reported to be 1.8%. However, this figure is higher in other countries or in populations at high risk for infection (1, 2, 3). After infection, 70 to 80% of the infected subjects develop chronic viremia, characterized by the presence of HCV-RNA in plasma. Some of these subjects develop chronic liver disease, mainly cirrhosis of the liver and hepatocellular carcinoma several years after the initial infection (4). The remaining 20 to 30% of the people infected by HCV are able to control the infection, clear the virus spontaneously, and remain free of liver disease, although positive for anti-HCV IgG in plasma (1, 4). It is generally accepted that genes within the Major Histocompatibility Complex (MHC) play a central role in the development of the immune response against HCV (5, 6). Several studies have addressed the issue of the association of Class II HLA alleles with the clinical outcome after initial HCV infection. However, which genes are associated with one outcome or another seems to depend on the ethnicity of the infected subject.

In Caucasians, spontaneous clearance of HCV has been described as being associated mainly with the HLA alleles DQB1*0301, DRB1*01, DRB1*0501, and DRB1*1101. In the same ethnic group, persistent infection has been associated with the DRB1*0301, DQB1*0201 and DRB4*0101 (5-8).

In African American subjects, however, viral clearance was mainly associated with the DQB1*0301 (9). In other ethnic groups, diverse associations have been made between HLA alleles and the outcome of HCV infection (10, 11). In Hispanics a strong anti HCV immune reaction and viral clearance is associated with the Class II HLA allele DQB1-0501 (12), just the opposite of what occurs in Caucasians (5-8). How could the same allele be associated with different outcomes? In one ethnic group it is associated with chronic viremia, while in another it is associated with spontaneous viral clearance.

A primary cause for the difference in results published by different authors may be due to the great variability of the frequency of HLA alleles in different ethnic populations. However, Azócar et al. suggested that this might be the result of the linkage disequilibrium between certain class II genes and the other genes involved in the regulation of the immune response and clinical

outcome after the initial HCV infection (12).

The variability in the association of HLA alleles and the response to HCV infection related to ethnicity requires further studies to rule out the possible role of Class II HLA alleles in HCV viremia, and should include studies of several genetic markers within the MHC in several ethnic groups or nationalities.

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