

gene. Patients resolving the infection, and patients with chronic infection, had different DNA sequences in this promoter.

The fact that some people infected with HCV spontaneously recover, while others progress and suffer from chronic HCV, has further bases in the immune system. Most people infected with HCV mount CD8⁺ T cell responses. However, what distinguishes people who recover from acute HCV and those who progress to chronic HCV is that those who quickly recover also mount an effective CD4⁺ T cell response (in addition to the CD8⁺ T cell response), while those who progress to chronic HCV mount only CD8⁺ T cell responses, but fail to mount an effective CD4⁺ T cell response (15). In other words, although increased numbers of viral antigen-specific CD8⁺ T cells are present in most patients, these cells are not maximally activated, where inadequate inactivation occurs because of lack of CD4⁺ T cell response. Smyk-Pearson et al. (16) characterized CD8⁺ T cells that specifically recognize and kill HCV infections, but that have not been helped by CD4⁺ T cells, as follows. These CD8⁺ T cells are helpless, impaired in the ability to generate a secondary response upon rechallenge, where the unhelped memory CTLs divided less and were unable to provide complete protection against HCV.

IV. DRUGS AGAINST HEPATITIS C VIRUS

Ribavirin and pegylated interferon- α -2 are the most commonly used drugs for HCV infections. Details on safety, efficacy, dosing, and warnings on these two drugs are provided on the package inserts, as cited (17,18). Two new drugs, telaprevir and boceprevir, were approved by the FDA in 2011 for use in combination with ribavirin and IFN.

Interferon- α -2 is a naturally occurring cytokine, but when used as a drug it is modified by the attachment of polyethylene glycol (PEG). PEG is an inert polymer that, when covalently attached to the interferon, increases its half-life in the bloodstream. Thus the drug is called “pegylated interferon.” When used as a drug, interferon- α , also known as “alpha interferon,” has a success rate against chronic HCV of 40 to 90%, depending on the genotype of the infecting HCV virus (19). The addition of ribavirin to interferon- α therapy increases response rates for patients with chronic HCV infection (20).

¹⁵ Smyk-Pearson S, Tester IA, Klarquist J, et al. Spontaneous recovery in acute human hepatitis C virus infection: functional T-cell thresholds and relative importance of CD4 help. *J Virol.* 2008;82:1827–1837.

¹⁶ Smyk-Pearson S, Tester IA, Klarquist J, et al. Spontaneous recovery in acute human hepatitis C virus infection: functional T-cell thresholds and relative importance of CD4 help. *J Virol.* 2008;82:1827–1837.

¹⁷ Package insert. COPEGUS™. Hoffmann-La Roche, Inc. 2004 [24 pages].

¹⁸ Package insert. PEGASYS™. Hoffmann-La Roche, Inc. 2010 [51 pages].

¹⁹ Abdel-Hakeem MS, Bédard N, Badr G, et al. Comparison of immune restoration in early versus late alpha interferon therapy against hepatitis C virus. *J Virol.* 2010;84:10429–10435.

²⁰ Chevaliez S, Brillet R, Lázaro E, Hézode C, Pawlotsky JM. Analysis of ribavirin mutagenicity in human hepatitis C virus infection. *J Virol.* 2007;81:7732–7741.