

Hepatitis C

Genetic Variation Predicts Response

A human genetic variation, or polymorphism, helps explain differences in response to interferon-based therapy for hepatitis C, according to a study reported in the August 6 advance online edition of *Nature*. D. Ge and colleagues analyzed genetic material from 1,671 participants in the IDEAL trial, which comparing pegylated interferon alfa-2a (Pegasys) against two doses of pegylated interferon alfa-2b (PegIntron), all with weight-adjusted ribavirin.

The researchers found that a variation (designated rs12979860) in a single nucleotide at a specific position on chromosome 19, near the IL28B gene – which encodes interferon-lambda-3 – was associated with nearly a three-fold in-

crease in treatment response rate. Patients with the CC genotype had a sustained virological response (SVR) rate of about 80%, compared with about 30% for those with the CT or TT genotypes. The polymorphism was associated with improved treatment response in people of all racial/ethnic groups, but the likelihood of having the mutation varied. People of East Asian descent were most likely to carry the favorable pattern, followed by European-Americans, Hispanics, and African-Americans. The researchers concluded that the rs12979860 polymorphism "explains approximately half of the difference in response rates between African-Americans and patients of European ancestry."

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Statins Active Against HCV

Statin drugs (HMG CoA reductase inhibitors) demonstrated anti-HCV activity themselves and increased the antiviral activity of interferon and directly-targeted agents in a laboratory study reported in the July 2009 issue of *Hepatology*. L. Delang and colleagues assessed the activity of various statins against HCV replicons in cell cultures. Among the five statins tested, mevastatin (not approved) and simvastatin (Zocor) exhibited the strongest *in vitro* activity. Lovastatin (Mevacor) and fluvastatin (Lescol) had moderate antiviral activity, while pravastatin (Pravachol) was "devoid of an antiviral effect."

When the researchers combined the statins with interferon-alfa or HCV polymerase and protease inhibitors, they observed additive antiviral activity. While neither statins alone nor any of the tested anti-HCV agents alone completely cleared HCV from cell cultures, a combination of HCV polymerase or protease inhibitors plus mevastatin or simvastatin produced efficient clearance. Furthermore, adding mevastatin inhibited the emergence of HCV replicons with resistance to the

investigational polymerase inhibitor HCV-796 (no longer in development). "A combination of specific HCV inhibitors with statins may result in a more profound antiviral effect and may delay or prevent the development of resistance to such inhibitors," they concluded.

Steatosis

Two recent studies looked at the natural history and progression of steatosis, or fat accumulation in liver cells, among people with hepatitis C. In the first study, reported in the June issue of *Hepatology*, A. Lok and colleagues assessed the evolution of steatosis among participants in the HALT-C trial, which evaluated long-term pegylated interferon monotherapy as a maintenance regimen to slow liver disease progression in patients without sustained response to combination therapy. Out of 1,000 total trial participants (more than 90% with HCV genotype 1), 892 had at least one follow-up liver biopsy and 699 had their last biopsy 3.5 years after randomization to the maintenance therapy or no further treatment arms.

In the second study, published in the July 2009 *Journal of Viral Hepatitis*,

T. J. Cross and colleagues performed a retrospective analysis of 112 chronic hepatitis C patients who underwent two liver biopsies separated by a median of 50 months. Participants were not treated for hepatitis C (i.e., they had mild fibrosis, declined therapy, or had contraindicating conditions). On the first liver biopsy, 54% had stage S0 steatosis (less than 5% of liver cells affected), 30% had stage S1 (5% to 33% of cells), 11% had stage S2 (33% to 66% of cells), and 5% had stage S3 (more than 66% of cells). Presence of steatosis was associated with HCV genotype 3.

About one-fifth (21%) exhibited fibrosis progression on the second biopsy (increase of at least one Ishak stage). In a multivariate analysis, baseline steatosis was the only significant predictor of fibrosis progression, with an odds ratio of 14.3. "The finding that steatosis was significantly associated with fibrosis progression indicates that, independent of baseline fibrosis stage, patients should be considered for antiviral treatment if steatosis is present," the researchers recommended.

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Cardiovascular Risk

People with chronic hepatitis C are more likely than those without to develop cardiovascular disease, according to a study reported in the July 15 *Clinical Infectious Diseases*. A. Butt and colleagues looked at the link between HCV infection and coronary artery disease among 82,083 HCV positive and 89,582 HCV negative patients receiving care at Veterans Affairs medical facilities.

In a multivariate analysis, HCV positive patients were about a 25% more likely than HCV negative patients to have coronary artery disease. This was the case even though people without HCV were older on average, had higher blood lipid (cholesterol and triglyceride) levels, and were more likely to have high blood pressure and diabetes – all established cardiovascular risk factors. “Despite a favorable risk profile, HCV infection is associated with a higher risk of coronary artery disease after adjustment for traditional risk factors,” the investigators concluded. They suggested that the elevated risk might be due to ongoing inflammation and immune activation related to chronic viral infection.



Understanding HCV: A Patient Pocket Guide by Alan Franciscus

This pocket guide is designed to help you make informed choices about various aspects of living with hepatitis C. Starting with basic information about hepatitis C prevention, disease progression and management, this booklet goes on to provide you with the tools you need to advocate for the best possible medical care and treatment.

