

Caring Ambassadors Hepatitis C Program  
Monthly Literature Review  
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## IN THE NEWS

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### **Caring Ambassadors Program releases *Hepatitis C Choices, 4th Edition***

“The Caring Ambassadors Hepatitis C Program is pleased to announce the publication of the 4th edition of *Hepatitis C Choices*, a comprehensive book that addresses all aspects of hepatitis C and its treatment. In accordance with its mission to provide state-of-the-art information, Caring Ambassadors has sought out the most recent advancements on the various aspects of the disease and included these updates in the newest edition.’ We are extremely excited about the new chapters in the 4th edition that were authored by nationally renowned experts,’ said Lorren Sandt, Hepatitis C Program Director. ‘We have added important new information on mental health, hepatitis C in women and children, immunological research, and a number of other important topics that affect the hepatitis C community.’” [Read more...](#)

### **FDA approves comprehensive system to test donated blood for HIV, hepatitis B and hepatitis C**

“The Food & Drug Administration (FDA) today approved a new nucleic acid test from Roche to screen donated blood for HIV-1 Group M RNA, hepatitis C RNA and hepatitis B DNA in a single, automated assay. The test, called the cobas TaqScreen MPX Test for use on the cobas s 201 system, is a qualitative in vitro test for comprehensive single-assay detection of HIV-1 Group M RNA, HIV-1 Group O RNA, HIV-2 RNA, hepatitis C virus RNA and hepatitis B virus DNA in human plasma. The test, which is not intended for use as an aid in diagnosis, is designed to further increase the safety of blood supplies by identifying infections earlier than traditional serology tests.” [Read more...](#)

### **Peg-Intron/Rebetol combination therapy approved for pediatric hepatitis C**

“The FDA has approved Schering-Plough’s Peg-Intron (peginterferon alfa-2b) and Rebetol (ribavirin) combination therapy for the treatment of previously untreated chronic hepatitis C in children  $\geq 3$  years old. This approval was based on a clinical trial of 107 treatment-naïve children ages 3 to 17 years of age with chronic hepatitis C and compensated liver disease. The study showed a safe and efficacious result from the pediatric patient population. Peg-Intron and Rebetol combination therapy is already indicated for chronic hepatitis C in adults with compensated liver disease.”

### **New test can predict success of hep C drugs**

“The genetic code of hepatitis C contains telltale patterns that reveal whether a patient will respond to the available drugs for the virus. Studying the viruses of 94 people infected with hepatitis C, the scientists found sections of code that were always linked to drug failure. And John Tavis of the Saint Louis University school of medicine and his team of researchers say that a genetic test could be deployed that would prevent unnecessary treatment.” [Read more...](#)

### **Program helps ex-inmates reintegrate**

“The Hepatitis Support Network of Hawaii has established a program to help ex-offenders reintegrate into the community with social, health and economic services. Andy Botts, director of the Prisoner Reintegration and Family Reunification program, will see relatives of ex-offenders and prisoners from 9 to 11 a.m. on Mondays and Thursdays at 1286 Queen Emma St. The program started Dec. 18. Botts became involved with the Hepatitis Support Network after learning he had hepatitis C when tested in prison. He was treated and cured by Dr. Alan Tice, medical director of Infections Limited Hawaii. A nonviolent drug offender, Botts had been in and out of institutions, including five years in a Thai prison, a release from the network said. Botts will join with volunteers and faith-based and community organizations to help ex-offenders and their families. "Costwise, a sensible approach to the management of nonviolent offenders would be better on the outside of a prison instead of inside," Tice said. He said treatment for infectious diseases such as hepatitis C "can change a person's perspective on life." [Read more...](#)

### **‘You feel like you’re talking to an angel’**

“As a nurse who deals with liver disease — a particularly trying medical field with a steady drumbeat of dispiriting news — Martha Shea does everything but get away from it after hours. “I’m just passionate about what I do,” said Ms. Shea, 57, on a recent weekend in a moment of rare repose at her home in Wallingford. Ms. Shea is described as tough but compassionate by patients she has seen over the years at the Veterans Affairs hospital in West Haven. She has worked there since 1979, first running a hepatology research lab and since 1987, as a nurse — now the nurse-manager of the hepatitis C resource center.” [Read more...](#)

### **Needle/syringe programmes and opioid substitution therapy should be widely available in prisons to help prevent HIV transmission.**

“Prisons should have needle and syringe programmes (NSPs), opioid substitution therapy (OST) and other preventive measures in place to prevent HIV transmission between inmates. These are the conclusions of a Review published in the January edition of *Lancet Infectious Diseases*, written by Dr Ralf Jürgens, a consultant for HIV/AIDS based in Quebec, Canada, and colleagues on behalf of WHO. The high prevalence of HIV infection and drug dependence among prisoners, combined with the sharing of injecting-drug equipment, make prisons high-risk environments for the transmission of HIV and also hepatitis C. The authors reviewed the effectiveness of interventions to reduce risky behaviour in this context. This Review forms part of a broader review of interventions to address HIV in prisons commissioned by WHO, together with the UN Office on Drugs and Crime, and UNAIDS, to guide countries in their efforts to scale-up towards universal access to HIV prevention, treatment and care by 2010.” [Read more...](#)

### **Study shows dramatic drop in needlestick risks for healthcare workers**

“When working with needles, healthcare workers always have to be concerned about contracting a life-altering or even life-threatening infection from HIV, hepatitis B or hepatitis C. But after 20 years of intense regulatory and legislative activity and innovative changes to the design and handling of needles, U.S. healthcare workers are now significantly safer from needlestick injuries, according to a new study from the University of Virginia International Healthcare Worker Safety Center. "Since the U.S. Needlestick Safety and Prevention Act was passed in 2000, American healthcare workers have benefited from an unprecedented level of protection from occupationally transmitted diseases," says Janine Jagger, M.P.H., Ph.D., director of the Center and co-author of the study published in the December 8 issue of the *Journal of Infection and Public Health*.” [Read more...](#)

### **Fresno County, Calif., officials approve needle-exchange program**

“The Fresno County Board of Supervisors in California on Tuesday approved a one-year needle-exchange pilot program, the Fresno Bee reports. Supervisors voted 3-2 in support of the program, which was proposed by County Health Officer Edward Moreno and will provide injection drug users with clean needles in an effort to curb the spread of HIV and other bloodborne diseases. Supervisors said that they understand concerns from some law enforcement officials about illegal drug use but that the county needs ways to reduce the spread of diseases such as HIV and hepatitis C. Volunteers have been illegally dispensing 6,000 to 8,000 clean needles each Saturday to IDUs in the county, according to advocate Dallas Blanchard, who has been distributing clean needles for about 13 years. According to the Bee, although these efforts have been tolerated

by police, an official program previously had never been endorsed by the Board of Supervisors, which last voted against a needle-exchange program in 2006.” [Read more...](#)

### **Controversy of care**

“A recent study, out of the University of California at Los Angeles offered a controversial, yet straightforward, answer to the legal and medical debate over standards of care for inmates with hepatitis C. The researchers concluded treating chronic hepatitis C in the prison population with interferon and antiviral drugs creates cost savings and improves the quality of life for all inmates, sick or not. If the medical community is starting to move in this direction, they’re not alone. An up-and-coming legal challenge is also looking to continue the momentum swing towards increased access to treatment. The law firm of Khorrami, Pollard & Abir is currently filing hundreds of individual lawsuits on behalf of California inmates against the California Department of Corrections and Rehabilitation for failure to properly treat inmates with hepatitis C. The firm expects the total number of plaintiffs to grow into the thousands. “This is an important problem nationally, it’s not just a California problem,” says Mark Ravis an attorney representing the inmates.” [Read more...](#)

### **Sixth Annual Hepatitis C Summit**

“The Hepatitis C Task Force of Los Angeles brought the medical and prevention community together on November 21 to discuss the state of the hepatitis C epidemic in Los Angeles County. Drug Policy Alliance (DPA) Southern California led the charge in prevention strategies for reducing the further outbreak of the disease at this Sixth Annual Hepatitis C Summit held at the California Endowment. Meghan Ralston, DPA’s Harm Reduction Coordinator, gave a highly energetic presentation about how pharmacies in the Los Angeles County are able to sell syringes without a prescription to those who need them. The Disease Prevention Demonstration Project (DPDP) is a pilot program put together by Senate Bill 1159, the Drug Policy Alliance, California Endowment and the LA Department of Public Health to stop the ever increasing rates and spread of HIV and Hepatitis C. DPDP has signed up over 300 pharmacies in the county and the number is still increasing, with new ground being broken for those in the Antelope Valley area.” [Read more...](#)

### **Hepatitis C outbreak: Infections prompt U.S. study**

“Congressional concerns about disease outbreaks in ambulatory surgery centers, including the hepatitis C outbreak at a Las Vegas endoscopy center, have prompted a nationwide study to determine what role the facilities play in the spread of health care-associated infections."There have been situations across the country that have raised concerns about the problems in those health care settings," said Cynthia Bascetta, director of health care for the federal Government Accountability Office, which is doing the study. The study, in the planning stage but expected to be complete by February, will determine to what extent data are available on the frequency and characteristics of health care-associated infections in ambulatory surgery centers. Instead of just looking at how many infections occurred in outpatient surgery centers, the study also will determine whether the facilities are following appropriate infection-control procedures, Bascetta said."One of the problems is that people aren't admitted into ambulatory surgery centers, so it is much harder to figure out what the source of an infection is if that person is being treated elsewhere," she said. Data will be collected from the Centers for Disease Control and Prevention, which conducts surveillance of disease outbreaks, and the Centers for Medicare and Medicaid Services, which regulates ambulatory surgery centers and monitors their infection-control policies.” [Read more...](#)

### **Health professionals need to raise hepatitis C awareness**

“Awareness of hepatitis C among health professionals and the public needs to increase if diagnosis rates are to continue to improve, the Health Protection Agency (HPA) has said. Although diagnosis rates are increasing, there are still many infected individuals who remain undiagnosed, the HPA says. The HPA highlights the importance of coverage of hepatitis C, including GP's coverage to coincide with World Hepatitis Day. The report also stresses the role primary care can play in increasing diagnosis rates. ‘It is likely that many prevalent infections exist in individuals who have injected drugs in the past and are no longer in contact with drugs services, or in those who acquired their infections via other routes, like transfusion,’ the HPA points out. ‘For this reason, targeted hepatitis C testing in primary care is also important.’ It adds:

‘Individuals diagnosed in these settings often have the advantage of more stable lifestyles that enable them to more easily tolerate and complete anti-viral therapy to clear their infections.’” [Read more...](#)

### Human Genome's hep C drug is halfway home

“Human Genome Sciences is halfway home. The company's hepatitis C drug, Albuferon, passed its first phase 3 trial test yesterday, but the harder test is yet to come. In a trial on patients infected with genotypes 2 and 3 of the hepatitis C virus, Albuferon worked just as well as Roche's Pegasys. (Genotypes refer to the virus's different genetic variations.) Fortunately, it didn't have to work *better* than Pegasys, because it's given every other week. The other interferon treatments, Pegasys and **Schering-Plough's** Peginteron, require weekly shots. Since injecting interferon causes unpleasant side effects, halving the number of injections should be a great selling point.” [Read more...](#)

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## CLINICAL TRIALS, COHORT STUDIES, PILOT STUDIES

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**The impact of diet on liver fibrosis and on response to interferon therapy in patients with HCV-related chronic hepatitis.** Loguercio C, Federico A, Masarone M, et al. Am J Gastroenterol. 2008 Dec;103(12):3159-66. Epub 2008 Sep 11.

[http://www.ncbi.nlm.nih.gov/pubmed/18786125?ordinalpos=109&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\\_RESULTSPanel.Pubmed\\_DefaultReportPanel.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/18786125?ordinalpos=109&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_RESULTSPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum)

**BACKGROUND AND AIMS:** A deranged metabolic status and alcohol intake may trigger induction and progression of chronic hepatitis C virus (HCV) liver disease. The aim of this study was to evaluate whether dietary composition affects the severity of liver damage and response to therapy in patients with HCV-related chronic hepatitis. **METHODS:** We enrolled 1,084 patients with biopsy-proven HCV-related chronic hepatitis (432 treated with interferon plus ribavirin) and 2,326 healthy subjects in this prospective study conducted in a university hospital. Dietary habits were recorded in enrolled individuals, and their alcohol consumption was evaluated with a questionnaire (AUDIT). Body mass index, and plasma levels of blood glucose, nitrogen, creatinine, cholesterol, and triglycerides were also measured. All individuals underwent routine liver tests and HCV genotyping. **RESULTS:** At study onset, there were no differences in metabolic status or alcohol consumption between patients and controls. About 50% of each group was overweight, and about 60% consumed alcohol. Patients and controls had similar dietary habits. Intake of carbohydrates, lipids and polyunsaturated fatty acids, and alcohol consumption were independent factors of liver damage at histology (logistic regression analysis). Some dietary components (unsaturated fatty acids, iron, zinc, vitamin A, and niacin) and alcohol intake differed significantly ( $P < 0.05$  and  $P 0.01$ , respectively; univariate analysis) between responders and nonresponders to interferon therapy. Genotype, age, body mass index, steatosis, and fibrosis were independent predictors of therapy outcome ( $P < 0.02$ ; multivariate analysis). **CONCLUSIONS:** The severity of HCV-related chronic hepatitis depends on a variety of factors. Our results show that dietary composition is related to the extent of liver damage. Although traditional risk factors independently affected treatment response, some dietary components were associated with nonresponse to therapy in our patients. This suggests that HCV patients may benefit from instructions regarding their diet.

**Peginterferon alfa-2a relapse rates depend on weight-based ribavirin dosage in HCV-infected patients with genotype 1: results of a retrospective evaluation.** Zopf S, Herold C, Hahn EG, Granslmayer M. Scand. J. Gastroenterol. 2008 Dec 31:1-5. [Epub ahead of print] [http://www.ncbi.nlm.nih.gov/pubmed/19117241?ordinalpos=1&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\\_RESULTSPanel.Pubmed\\_DefaultReportPanel.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19117241?ordinalpos=1&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_RESULTSPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum)

**OBJECTIVE.** The cumulative dosage of ribavirin per kilogram of body-weight prevents relapse

and thus is a significant predictor of sustained virological response (SVR). Comparison of peginterferon (peg-IFN) alfa-2b/ribavirin and peg-IFN alfa-2a/ribavirin shows that the rates of SVR are similar, but the rates of relapse are significantly lower under the peg-IFN alfa-2b regimen. Depending on the weight-based ribavirin dose, patients with >105 kg reach a maximum of 13.2 mg/kg body-weight ribavirin in the peg-IFN alfa-2b regimen as opposed to only 11.3 mg/kg in the peg-IFN alfa-2a regimen. The aim of these investigations was to determine relapse rates in a retrospective analysis of 98 patients chronically infected with hepatitis C virus (HCV) genotype (GT) 1 in relation to the weight-based ribavirin dose. **MATERIAL AND METHODS.** All patients completed treatment with peg-IFN alfa-2a/ribavirin (1000 mg/d or 1200 mg/d for patients weighing <75 kg or  $\geq$ 75 kg) for 48 weeks. Classification of a low ribavirin dose with <13.2 mg/kg body-weight was used. Patients with a ribavirin dose  $\geq$ 13.2 mg/kg were compared with those with a dose <13.2 mg/kg. **RESULTS.** Patients with a ribavirin dose  $\geq$ 13.2 mg/kg (n=84) showed a relapse rate of 19.0% in contrast to 71.4% in patients with a ribavirin dose of <13.2 mg/kg (n=14) (p=0.0013). The SVR rate was significantly higher in the  $\geq$ 13.2 mg/kg ribavirin dosed group (59.5% versus 28.6%). **CONCLUSIONS.** Weight-adapted ribavirin dosing in combination with peg-IFN alfa-2a to avoid giving low doses of ribavirin should be evaluated. This will minimize relapse, especially in HCV GT 1 patients.

### **PTPN22 C1858T polymorphism and the outcome of hepatitis C virus infection.**

Montes-Cano MA, García-Lozano JR, Aguilar-Reina J, et al. *Viral Immunol.* 2008 Dec;21(4):491-4. [http://www.ncbi.nlm.nih.gov/pubmed/19115939?ordinalpos=1&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\\_RESULTSPanel.Pubmed\\_DefaultReportPanel.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19115939?ordinalpos=1&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_RESULTSPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum)

The outcome of chronic hepatitis C virus infection varies, depending on viral and host factors. Those mechanisms involved in the control of the innate and adaptive response could have an influence on the outcome of infection. The PTPN22 gene encodes an intracellular lymphoid-specific phosphatase (Lyp) with a lymphocyte activating downregulatory effect. A single-nucleotide polymorphism (SNP) C1858T located on this gene has been associated with autoimmune diseases and bacterial infections. **The aim** of this study was to assess whether the PTPN22 C1858T polymorphism is related to the outcome of hepatitis C viral infection. A total of 69 patients with spontaneous viral clearance (SVC), 281 patients with chronic hepatitis C (CHC), and 1036 individuals not infected with hepatitis C (NIC) were included in this study. Patients with CHC were stratified according to Scheuer score of hepatic fibrosis from F0-F2 (n = 200) and F3-F4 (n = 81), and according to their response to therapy in patients with sustained responses (SR; n = 103) and non-sustained response (NSR; n = 104). Genotyping of the C1858T polymorphism was performed using TaqMan probes. No statistically significant differences in the distribution of PTPN22 C1858T polymorphism were observed upon comparison of patient group with the NIC group. Also, when the different patient groups were compared to one another, no statistically significant differences were detected: the SVC with the CHC group (10.2% versus 12.5%; p = 0.6), the F0-F2 with the F3-F4 group (11.5% versus 14.8%; p = 0.5), and the NSR with the SR group (11.5% versus 14.6%; p = 0.4). Our **results** do not support a major role of this polymorphism of the PTPN22 gene in the outcome of chronic hepatitis C virus infection in the Spanish population.

### **Impact of donor graft steatosis on overall outcome and viral recurrence after liver**

**transplantation for hepatitis C virus cirrhosis.** Briceño J, Ciria R, Pleguezuelo M, et al. *Liver Transpl.* 2009 Jan;15(1):37-48.

[http://www.ncbi.nlm.nih.gov/pubmed/19109846?ordinalpos=10&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\\_RESULTSPanel.Pubmed\\_DefaultReportPanel.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19109846?ordinalpos=10&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_RESULTSPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum)

**The aim** of this study was to determine the influence of donor graft steatosis on overall outcome, viral recurrence, and fibrosis progression in orthotopic liver transplantation (OLT) for hepatitis C

virus (HCV) cirrhosis. One hundred twenty patients who underwent OLT for HCV cirrhosis between 1995 and 2005 were included in the study. Donor steatosis was categorized as absent (0%-10%; n = 40), mild (10%-30%; n = 32), moderate (30%-60%; n = 29), or severe (>60%; n = 19). A Cox multivariate analysis for marginal donor variables and a Model for End-Stage Liver Disease index were performed. Fibrosis evolution was analyzed in liver biopsies (fibrosis < 2 or >=2) 3, 6, and 12 months post-OLT and in the late post-OLT period. Fifty-six grafts were lost (46%). The survival of the grafts was inversely proportional to donor liver steatosis: 82%, 72%, and 72% at 1, 2, and 3 years post-OLT in the absence of steatosis; 73%, 63%, and 58% with mild steatosis; 74%, 62%, and 43% with moderate steatosis; and 62%, 49%, and 42% with severe steatosis (P = 0.012). HCV recurrence was earlier and more frequent in recipients with steatosis > 30% (46% versus 32% at 3 months, P = 0.017; 58% versus 43% at 6 months, P = 0.020; 70% versus 56% at 12 months, P = 0.058; and 95% versus 69% at 3 years post-OLT, P = 0.0001). Graft survival was lower in alcoholic liver disease recipients versus HCV recipients when steatosis was >30% at 3, 6, and 12 months post-OLT (P = 0.042) but not when steatosis was <30% (P = 0.53). A higher fibrosis score was obtained 3 months post-OLT (P = 0.033), 6 months post-OLT (P = 0.306), 12 months post-OLT (P = 0.035), and in the late post-OLT period (P = 0.009). **In conclusion**, donor graft steatosis influences the outcome of OLT for HCV cirrhosis. HCV recurrence is more frequent and earlier in recipients of moderately and severely steatotic livers. Fibrosis evolution is higher when graft steatosis is >30%. OLT with >30% steatotic donor livers should be precluded in HCV recipients.

**Does interferon use prior to liver transplant influence hepatitis C outcomes following transplantation?** Smallwood GA, Devine R, Fasola C, et al. *Transplantation*. 2008 Dec 27;86(12):1795-8.

[http://www.ncbi.nlm.nih.gov/pubmed/19104424?ordinalpos=29&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\\_RESULTSPanel.Pubmed\\_DefaultReportPanel.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19104424?ordinalpos=29&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_RESULTSPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum)

**BACKGROUND:** The most frequent reason for orthotopic liver transplantation (OLT) in the United States is due to complications of hepatitis C (HCV). Recent reports have shown decreased survival for HCV after OLT. Of note, the use of interferon (IFN) products has become wide spread with the majority of HCV patients being treated before transplant. **AIM:** To review the outcomes of HCV patients who have received IFN products before liver transplant compared with HCV patients those who have never received IFN. **METHOD:** Single-center, retrospective review of patients transplanted for HCV since December 1998 (n=131). Primary endpoint is the effect of IFN exposure before transplant on posttransplant outcomes. **RESULTS:** Patients receiving before transplant (pre-IFN group; n=45) had a more aggressive recurrence of HCV with earlier recurrence (181.1+/-236 days vs. 303.4+/- 327 days; P=0.031), frequency of recurrence [41/45 (91.1%) vs. 62/86 (72.1%); P=0.013], and 1-year recurrence free survival [20% (+/-0.06) vs. 48.2% (+/-0.05); P=0.005]. Survival difference was noted in the pre-IFN group at 1 year and 3 years [79.7% (+/-0.06) vs. 90.5% (+/-0.03); 65.7 (+/-0.08) vs. 75.9% (+/-0.05); P=0.05] when compared with patients not receiving IFN (n=86) before transplant. **CONCLUSIONS:** Based on this study, interferon use before transplant for the HCV patient indicates poor outcomes After OLT. Because of the increasing numbers of HCV patients coming to transplant, validation of these results should be of utmost importance

**Genome-wide hepatitis C virus amino acid covariance networks can predict response to antiviral therapy in humans.**

Aurora R, Donlin MJ, Cannon NA, Tavis JE. *J Clin Invest*. 2008 Dec 22. pii: 37085. doi: 10.1172/JCI37085. [Epub ahead of print]

[http://www.ncbi.nlm.nih.gov/pubmed/19104147?ordinalpos=31&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\\_RESULTSPanel.Pubmed\\_DefaultReportPanel.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19104147?ordinalpos=31&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_RESULTSPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum)

Hepatitis C virus (HCV) is a common RNA virus that causes hepatitis and liver cancer. Infection is treated with IFN-alpha and ribavirin, but this expensive and physically demanding therapy fails in half of patients. The genomic sequences of independent HCV isolates differ by approximately 10%, but the effects of this variation on the response to therapy are unknown. To address this question, we analyzed amino acid covariance within the full viral coding region of pretherapy HCV sequences from 94 participants in the Viral Resistance to Antiviral Therapy of Chronic Hepatitis C (Virahep-C) clinical study. Covarying positions were common and linked together into networks that differed by response to therapy. There were 3-fold more hydrophobic amino acid pairs in HCV from nonresponding patients, and these hydrophobic interactions were predicted to contribute to failure of therapy by stabilizing viral protein complexes. Using our analysis to detect patterns within the networks, we could predict the outcome of therapy with greater than 95% coverage and 100% accuracy, raising the possibility of a prognostic test to reduce therapeutic failures. Furthermore, the hub positions in the networks are attractive antiviral targets because of their genetic linkage with many other positions that we predict would suppress evolution of resistant variants. Finally, covariance network analysis could be applicable to any virus with sufficient genetic variation, including most human RNA viruses.

**A randomized study of extended treatment with peginterferon alpha-2b plus ribavirin based on time to HCV RNA negative-status in patients with genotype 1b chronic hepatitis C.** Ide T, Hino T, Ogata K, et al. *Am J Gastroenterol.* 2009 Jan;104(1):70-5.

[http://www.ncbi.nlm.nih.gov/pubmed/19098852?ordinalpos=47&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\\_RESULTSPanel.Pubmed\\_DefaultReportPanel.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19098852?ordinalpos=47&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_RESULTSPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum)

**OBJECTIVES:**The treatment of patients with hepatitis C virus (HCV) genotype 1 with peginterferon plus ribavirin treatment for more than 48 weeks demonstrated high sustained virological response (SVR) rates. Although many studies extended the duration of therapy from 48 weeks to 72 weeks, the optimal duration has not yet been determined. **METHODS:**A total of 113 genotype 1b patients with high viral load were randomized at baseline to the standard (n=56) or extended (n=57) treatment group. The standard group patients received 48 weeks of peginterferon plus ribavirin treatment. In the extended group, the treatment was performed for 44 weeks after patients became negative for HCV RNA (total duration 48-68 weeks). **RESULTS:**The SVR rate of the standard and extended group was 36% (20 of 56) and 53% (30 of 57; P=0.07). However, the extended group patients who became negative for HCV RNA between weeks 16 and 24 had a significantly higher SVR rate (78%; 7 of 9) than that of standard group (9%, 1 of 11; P=0.005). The predictive factors for the SVR were the treatment regimen (the standard vs. extended treatment) and the time to HCV RNA negative-status. **CONCLUSIONS:**The extended treatment significantly increased the SVR rate in patients who were HCV RNA negative at 16-24 weeks.

**Four-week pegylated interferon alpha-2a monotherapy for chronic hepatitis C with genotype 2 and low viral load: A pilot, randomized study.** Tsubota A, Satoh K, Aizawa M, et al. *World J Gastroenterol.* 2008 Dec 21;14(47):7220-4.

[http://www.ncbi.nlm.nih.gov/pubmed/19084937?ordinalpos=75&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\\_RESULTSPanel.Pubmed\\_DefaultReportPanel.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19084937?ordinalpos=75&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_RESULTSPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum)

**AIM:** To assess the efficacy and advantages of 4-wk pegylated interferon alpha-2a (peg-IFN-alpha2a) monotherapy for chronic hepatitis C patients with strong predictors of sustained virologic response (SVR). **METHODS:** Patients (n = 33) with genotype 2 and low viral load (< 100 KIU/mL), who became HCV RNA negative after 1 wk of IFN treatment, were randomly allocated to receive a 4- or 12-wk treatment course at a ratio of 2:1, respectively, with a subsequent 24-wk follow-up period. Peg-IFN-alpha2a was administered subcutaneously at a dose of 180 mug or 90 mug once weekly. SVR was defined as absence of serum HCV RNA at the end of the follow-up

period. **RESULTS:** All patients completed the treatment schedule, and more than half were symptom-free during the treatment. In the 4-wk treatment group, 20 of 22 (91%) patients achieved SVR. Two patients relapsed, but achieved SVR following re-treatment with peg-IFN-alpha2a alone. In the 12-wk treatment group, 11 of 11 (100%) patients attained SVR. **CONCLUSION:** Our **results** show that a 4-wk course of peg-IFN-alpha2a monotherapy can achieve a high SVR rate in "IFN-sensitive" patients, without negatively affecting outcome.

**Hepatitis C virus infection and primary Sjögren's syndrome: a clinical and serologic description of 9 patients.** Ceribelli A, Cavazzana I, Cattaneo R, et al. *Autoimmun Rev.* 2008 Dec;8(2):92-4. Epub 2008 Aug 8.

[http://www.ncbi.nlm.nih.gov/pubmed/18692602?ordinalpos=118&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\\_RESULTSPanel.Pubmed\\_DefaultReportPanel.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/18692602?ordinalpos=118&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_RESULTSPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum)

**OBJECTIVE:** To define the clinical and immunologic profile of 9 patients with Sjögren's Syndrome (SS) and Hepatitis C virus (HCV) infection. **PATIENTS:** 9 out of 305 patients with SS, diagnosed according to the criteria proposed in 2002, had repeated positive serology for HCV. **RESULTS:** 9 female patients were studied. The mean age at onset of SS was 59 years, with a mean period of follow-up of 7.1 years. All the patients had glandular manifestations and they were all positive for dacryologic tests. Salivary gland biopsy was performed in 4 patients, all showing characteristic lymphocytic infiltrate. The main extraglandular features were arthralgias, photosensitivity, purpura, thyroiditis. All the patients were positive for anti-nuclear antibodies (ANA): 6 anti-Ro/SSA, 3 anti-Ro/SSA and anti-La/SSB positive. HCV-positive SS were compared with 296 patients with primary SS. They showed higher mean age ( $p=0.01$ ), higher prevalence of photosensitivity ( $p=0.0266$ ) and circulating cryoglobulins ( $p=0.0372$ ). In primary SS, most patients had anti-Ro/SSA antibodies alone (49.8%) or associated to anti-La/SSB (46.5%). Five patients (1.8%) had other ANA specificities. **CONCLUSIONS:** A chronic HCV infection is concomitant in about 3% of patients with pSS. They differ from patients without HCV infection for the higher prevalence of photosensitivity and cryoglobulins, without clinical manifestations of cryoglobulinemia.

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## BASIC AND APPLIED SCIENCE, PRE-CLINICAL STUDIES

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**Hepatitis C virus-specific T-cell gamma interferon and proliferative responses are more common in perihepatic lymph nodes than in peripheral blood or liver.** Moonka D, Milkovich KA, Rodriguez B, et al. *J Virol.* 2008 Dec;82(23):11742-8. Epub 2008 Aug 20.

[http://www.ncbi.nlm.nih.gov/pubmed/18715927?ordinalpos=113&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\\_RESULTSPanel.Pubmed\\_DefaultReportPanel.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/18715927?ordinalpos=113&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_RESULTSPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum)

The activation state, differentiation state, and functions of liver lymphocytes and perihepatic lymph nodes during chronic hepatitis C virus (HCV) infection are not well understood. Here, we performed phenotypic and functional analyses of freshly prepared lymphocytes isolated from the livers, perihepatic lymph nodes, and peripheral blood compartments of chronic HCV-infected and disease control subjects with end-stage liver disease undergoing liver transplantation. We measured lymphocyte subset frequency and memory T-cell gamma interferon (IFN-gamma) and proliferative responses to HCV peptide and control viral antigens in direct ex vivo assays. We found higher frequencies of CD4 cells in the lymph node compartment than in the other compartments for both HCV-infected and disease control subjects. Lymph node CD4 and CD8 cells less commonly expressed the terminal differentiation marker CD57, a finding consistent with an earlier differentiation state. In HCV-infected subjects, HCV-specific IFN-gamma-producing and proliferative responses were commonly observed in the lymph node fraction, while they were uncommonly observed in the peripheral blood or liver fractions. In contrast, control viral CD4

protein antigen and CD8 peptide antigen-specific IFN-gamma responses were commonly observed in the periphery and uncommonly observed in the lymph nodes of these same subjects. These findings are consistent with a selective defect in HCV-specific T-cell effector function or distribution in patients with advanced chronic HCV infection. The high frequency of HCV-reactive T cells in perihepatic lymph nodes indicates that a failure to generate or sustain T-lymphocyte HCV reactivity is not responsible for the paucity of functional cells even in end-stage liver disease.

### **Peripheral blood gene expression profile associated with sustained virologic response after peginterferon plus ribavirin therapy for chronic hepatitis-C genotype 1.**

Huang C, Chen H, Cassidy W, Howell CD. J Natl Med Assoc. 2008 Dec;100(12):1425-33.

[http://www.ncbi.nlm.nih.gov/pubmed/19110910?ordinalpos=4&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\\_RESULTSPanel.Pubmed\\_DefaultReportPanel.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19110910?ordinalpos=4&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_RESULTSPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum)

We investigated the relationship between global gene expression in peripheral blood mononuclear cells (PBMCs) during the first 4 weeks of peginterferon alfa and ribavirin therapy and long-term eradication of hepatitis-C genotype 1 infections in 23 patients. A sustained virologic response (SVR), defined as an undetected serum HCV ribonucleic acid (RNA) at week 72, was the virologic response endpoint. PBMC RNA was prepared at week 0 and week 4 from 23 patients (17 black and 6 white Americans), and hybridized to Affymetrix GeneChip HG-U133 plus 2.0 arrays. Compared to week 0, 269 genes were differentially expressed at week 4 of treatment, including many genes regulated by alpha interferons and associated with host immunity ( $p < 0.0001$ ), cell signal transduction ( $p < 0.001$ ) and cellular protein metabolism ( $p < 0.001$ ). Expression of these 269 genes at week 0 and week 4 did not differ significantly between patients with and without a SVR. In contrast, SVR was associated with differential expression of 98 genes at week 4 (false discovery rate  $< 0.01$ ). Many of the genes have been implicated in control of HCV lifecycle and thus may play important roles in HCV clearance during peginterferon and ribavirin therapy.

### **Discovery of pentacyclic compounds as potent inhibitors of hepatitis C virus NS5B RNA polymerase.**

Habermann J, Capitò E, Ferreira MD, et al. Bioorg Med Chem Lett. 2008 Dec 13.

[Epub ahead of print]

[http://www.ncbi.nlm.nih.gov/pubmed/19109015?ordinalpos=15&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\\_RESULTSPanel.Pubmed\\_DefaultReportPanel.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19109015?ordinalpos=15&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_RESULTSPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum)

We report a new series of inhibitors for hepatitis C virus NS5B RNA polymerase containing a constrained pentacyclic scaffold. Our SAR studies led to the identification of hexahydroindolo[2,1-a]pyrrolo[3,2-d][2]benzazepines exposing basic groups. The compounds displayed a high activity in the enzyme assay and displayed good activity in the cell-based (replicon) assay in the presence of serum proteins.

### **Debio 025, a cyclophilin binding molecule, is highly efficient in clearing HCV replicon containing cells, alone or when combined with Specifically Targeted Antiviral Therapy for HCV (STAT-C) inhibitors.**

Coelmont L, Kaptein S, Paeshuyse J, et al. Antimicrob Agents

Chemother. 2008 Dec 22. [Epub ahead of print]

[http://www.ncbi.nlm.nih.gov/pubmed/19104013?ordinalpos=33&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\\_RESULTSPanel.Pubmed\\_DefaultReportPanel.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19104013?ordinalpos=33&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_RESULTSPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum)

Debio 025 is a potent inhibitor of hepatitis C virus (HCV) replication [Hepatology, 43:761-70]. In phase I clinical studies monotherapy (dose 1200 mg BID of Debio 025) resulted in a mean maximal decrease in viral load of 3.6 log<sub>10</sub> [Hepatology, 47: 817-26], whereas a reduction of 4.6 log<sub>10</sub> was obtained in phase II studies where Debio 025 was combined with interferon [J Hepatol, 48: S2]. We here report on the particular characteristics of the in vitro anti-HCV activities of Debio 025. The combination of Debio 025 with either ribavirin (RBV) or STAT-C inhibitors [NS3 protease or

NS5B (nucleoside and non-nucleoside) polymerase inhibitors] resulted in an additive antiviral activity in short term antiviral assays. Debio 025 has the unique ability to clear hepatoma cells from their HCV replicon when used alone or in combination with interferon and STAT-C inhibitors. Debio 025, at concentrations that have been observed in human plasma (0.1 or 0.5 microM), was able to delay or prevent the development of resistance to HCV protease inhibitors as well as to nucleoside and non-nucleoside polymerase inhibitors. Debio 025 forms an attractive drug candidate for the treatment of HCV infections in combination with standard interferon-based treatment and treatments that directly target the HCV polymerase and/or protease.

### **3D cultured immortalized human hepatocytes useful to develop drugs for blood-borne**

**HCV.** Aly HH, Shimotohno K, Hijikata M. *Biochem Biophys Res Commun.* 2008 Dec 25. [Epub ahead of print]

[http://www.ncbi.nlm.nih.gov/pubmed/19103167?ordinalpos=38&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\\_RESULTSPanel.Pubmed\\_DefaultReportPanel.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19103167?ordinalpos=38&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_RESULTSPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum)

Due to the high polymorphism of natural hepatitis C virus (HCV) variants, existing recombinant HCV replication models have failed to be effective in developing effective anti-HCV agents. In the current study, we describe an in vitro system that supports the infection and replication of natural HCV from patient blood using an immortalized primary human hepatocyte cell line cultured in a three-dimensional (3D) culture system. Comparison of the gene expression profile of cells cultured in the 3D system to those cultured in the existing 2D system demonstrated an up-regulation of several genes activated by peroxisome proliferator-activated receptor alpha (PPARalpha) signaling. Furthermore, using PPARalpha agonists and antagonists, we also analyzed the effect of PPARalpha signaling on the modulation of HCV replication using this system. The 3D in vitro system described in this study provides significant insight into the search for novel anti-HCV strategies that are specific to various strains of HCV.

### **Generation of immune responses against HCV using dendritic cells containing NS5 protein-coated microparticles.**

Gehring S, Gregory SH, Wintermeyer P, et al. *Clin Vaccine Immunol.* 2008 Dec 17. [Epub ahead of print]

[http://www.ncbi.nlm.nih.gov/pubmed/19091993?ordinalpos=53&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\\_RESULTSPanel.Pubmed\\_DefaultReportPanel.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19091993?ordinalpos=53&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_RESULTSPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum)

Dendritic cells (DCs) internalize and process antigens as well as activate cellular immune responses. The aim of this study was to determine the capacity of DCs that contained antigen-coated magnetic beads to induce immunity against the nonstructural hepatitis C virus (HCV) antigen 5 (NS5). Splenocytes derived from Flt3 ligand pretreated BALB/c mice were incubated with magnetic beads coated with HCV NS5, LPS and/or anti-CD40, purified and used for immunization. Cellular immunity was measured using cytotoxic T-lymphocyte (CTL) and T-cell proliferation assays, intracellular cytokine staining and a syngeneic tumor challenge using NS5 expressing SP2/0 myeloma cells in vivo. Splenocytes isolated from animals vaccinated with DCs-beads+NS5+LPS+anti-CD40 secreted elevated levels of IL-2 and IFN-gamma in the presence of NS5. The numbers of CD4(+)IL-2(+) cells were increased >5-fold in the group immunized with DC-Beads+NS5+LPS+anti-CD40, paralleled by an enhanced splenocyte proliferative response. Immunization promoted antigen-specific CTL activity 3-fold compared to control mice and reduced significantly the growth of NS5 expressing tumor cells in vivo. Thus, strategies that employ NS5-coated beads induce cellular immune responses in mice, that correlate well with the natural immune responses that occur in individuals who resolve HCV.

### **Role of the hepatitis C virus core+1 open reading frame and core cis-acting RNA elements in viral RNA translation and replication.**

Vassilaki N, Friebe P, Meuleman P, et al. *J Virol.* 2008

Dec;82(23):11503-15. Epub 2008 Sep 17.

[http://www.ncbi.nlm.nih.gov/pubmed/18799568?ordinalpos=108&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\\_RESULTSPanel.Pubmed\\_DefaultReportPanel.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/18799568?ordinalpos=108&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_RESULTSPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum)

Four conserved RNA stem-loop structures designated SL47, SL87, SL248, and SL443 have been predicted in the hepatitis C virus (HCV) core encoding region. Moreover, alternative translation products have been detected from a reading frame overlapping the core gene (core+1/ARFP/F). To study the importance of the core+1 frame and core-RNA structures for HCV replication in cell culture and in vivo, a panel of core gene silent mutations predicted to abolish core+1 translation and affecting core-RNA stem-loops were introduced into infectious-HCV genomes of the isolate JFH1. A mutation disrupting translation of all known forms of core+1 and affecting SL248 did not alter virus production in Huh7 cells and in mice xenografted with human liver tissue. However, a combination of mutations affecting core+1 at multiple codons and at the same time, SL47, SL87, and SL248, delayed RNA replication kinetics and substantially reduced virus titers. The in vivo infectivity of this mutant was impaired, and in virus genomes recovered from inoculated mice, SL87 was restored by reversion and pseudoreversion. Mutations disrupting the integrity of this stem-loop, as well as that of SL47, were detrimental for virus viability, whereas mutations disrupting SL248 and SL443 had no effect. This phenotype was not due to impaired RNA stability but to reduced RNA translation. Thus, SL47 and SL87 are important RNA elements contributing to HCV genome translation and robust replication in cell culture and in vivo.

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## EPIDEMIOLOGY, DIAGNOSTICS, AND MISCELLANEOUS WORKS

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**Hepatitis C in the elderly: Epidemiology, natural history, and treatment.** Mindikoglu AL, Miller RR. Clin Gastroenterol Hepatol. 2008 Dec 10. [Epub ahead of print]

[http://www.ncbi.nlm.nih.gov/pubmed/19084480?ordinalpos=77&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\\_RESULTSPanel.Pubmed\\_DefaultReportPanel.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19084480?ordinalpos=77&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_RESULTSPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum)

Hepatitis C continues to be a major public health problem affecting approximately 3% of the global population. According to the World Health Organization, an estimated 170 million people have chronic hepatitis C. Ten percent to 20% of those who are chronically infected with hepatitis C will progress to cirrhosis and 5% will develop hepatocellular carcinoma. Although the safety and efficacy of hepatitis C therapies have been studied extensively in patients between the ages of 18 and 65, patients who are older than 65 still remain an understudied and difficult-to-treat population. This review discusses the epidemiology, natural history, and treatment of chronic hepatitis C in older adults.

**Fibrosis progression in African Americans and Caucasian Americans with chronic hepatitis C.** Terrault NA, Im K, Boylan R, Bacchetti P, et al. Clin Gastroenterol Hepatol. 2008

Dec;6(12):1403-11. Epub 2008 Aug 19.

[http://www.ncbi.nlm.nih.gov/pubmed/19081528?ordinalpos=85&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\\_RESULTSPanel.Pubmed\\_DefaultReportPanel.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19081528?ordinalpos=85&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_RESULTSPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum)

**BACKGROUND & AIMS:** Prior studies suggest the rate of liver fibrosis progression is slower in African Americans (AAs) than Caucasian Americans (CAs) with chronic HCV infection.

**METHODS:** With a multi-state Markov model, fibrosis progression was evaluated in a well-characterized cohort of 143 AA and 157 CA adults with untreated chronic HCV genotype 1 infection. In subjects with a history of injection drug use, duration of infection was imputed from a fitted risk model rather than assumed to be the reported first year of use. **RESULTS:** The distribution of Ishak fibrosis stages was 0 (8.7%), 1/2 (55.7%), 3/4 (29.3%), and 5/6 (6.3%) and was similar in AAs and CAs ( $P = .22$ ). After adjusting for biopsy adequacy, AAs had a 10% lower rate of fibrosis progression than did CAs, but the difference was not statistically significant (hazard ratio,

0.90; 95% confidence interval, 0.72-1.12). The overall 20-year estimates of probabilities of progression from stage 0 to stages 1/2, 3/4, and 5/6 were 59.3%, 28.8%, and 4.7%, respectively. The estimated median time from no fibrosis to cirrhosis was 79 years for the entire cohort and 74 and 83 years for CAs and AAs, respectively. In 3-variable models including race and biopsy adequacy, the factors significantly associated with fibrosis progression were age when infected, steatosis, ALT level, and necroinflammatory score. **CONCLUSIONS:** The rates of fibrosis progression were slow and did not appear to differ substantially between AAs and CAs.

#### **Sociodemographic trends in national ambulatory care visits for hepatitis C virus infection.**

Tsui JI, Maselli J, Gonzales R. Dig Dis Sci. 2008 Dec 23. [Epub ahead of print]

[http://www.ncbi.nlm.nih.gov/pubmed/19104932?ordinalpos=24&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\\_RESULTSPanel.Pubmed\\_DefaultReportPanel.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19104932?ordinalpos=24&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_RESULTSPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum)

Poor and non-white patients are disproportionately infected with the hepatitis C virus (HCV). The **OBJECTIVE** of this research is to determine sociodemographic patterns of HCV-related ambulatory care visits over time. Data from the National Ambulatory Medical Care Survey (NAMCS) and the National Hospital Ambulatory Medical Care Survey-Outpatient (NHAMCS-OPD) for the years 1997-2005 were analyzed in 3-year intervals. Demographic and other variables were compared for each period, and multivariable logistic regression was performed to examine whether the likelihood of a visit being HCV-related (versus non-HCV) was independently associated with (1) race and/or (2) Medicaid status over time. The total number of HCV-related ambulatory visits more than doubled from 3,583,585 during the years 1997-1999 to 8,027,166 during 2003-2005. During this time, the proportion of non-whites and Medicaid recipients presenting for HCV-related visits approximately doubled (non-whites: 16% vs. 33%,  $P = 0.04$ ; Medicaid recipients: 10% vs. 25%,  $P = 0.07$ ). In 2003-2005, HCV-related visits were more than twice as likely to occur among non-white patients vs. white patients (OR = 2.49; 95% CI: 1.60-3.86) and patients on Medicaid vs. non-Medicaid (3.49; 1.79-6.80). Our **RESULTS** show that HCV-associated ambulatory care visits are increasing, with a greater proportion of visits occurring among non-white patients and Medicaid recipients.

#### **Reduced quality of life in patients with chronic viral liver disease as assessed by SF12 questionnaire.**

Svirtlih N, Pavic S, Terzic D, et al. J Gastrointest Liver Dis. 2008 Dec;17(4):405-9.

[http://www.ncbi.nlm.nih.gov/pubmed/19104701?ordinalpos=27&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\\_RESULTSPanel.Pubmed\\_DefaultReportPanel.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19104701?ordinalpos=27&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_RESULTSPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum)

**BACKGROUND & AIM.** Quality of life may be reduced in patients with chronic liver diseases. The purpose of this study was to assess the impact of chronic viral liver disease on health-related quality of life (HRQOL). **PATIENTS AND METHODS.** Quality of life was prospectively investigated in 227 patients with chronic viral liver disease and 75 controls. The generic Short Form 12 questionnaire was applied to measure the HRQOL. Mental and physical component scores were expressed as numeric and categorical values (presence/absence of disability). The electronic database (SPSS for Windows) was used for statistical analysis with 95% confidence intervals. **RESULTS.** Mental and physical numeric and categorical scores for the absence of disability were significantly worse in patients compared with controls. Patients were a negative predictive factor for the absence of disability on both mental and physical components while the physical component was the significant factor in multivariate regression analysis ( $p = 0.000$ ). There was no difference in HRQOL scores among patients with hepatitis C or B virus infection. Mental and physical numeric scores were lower in patients with cirrhosis. Liver cirrhosis predicted lower components of the absence of disability in comparison to chronic hepatitis more influencing the physical component ( $p = 0.003$ ). **CONCLUSIONS.** Chronic viral liver disease reduces and predicts a lower quality of life in comparison to a healthy population impairing more the physical component. Hepatitis viruses do

not influence differently the quality of life. Liver cirrhosis has a higher negative impact on the quality of life than chronic hepatitis, especially relating to a physical component.

**Symptomatic acute hepatitis C in egypt: diagnosis, spontaneous viral clearance, and delayed treatment with 12 weeks of pegylated interferon alfa-2a.** Sharaf Eldin N, Ismail S, Mansour H, et al. PLoS ONE. 2008;3(12):e4085. Epub 2008 Dec 30.

[http://www.ncbi.nlm.nih.gov/pubmed/19115010?ordinalpos=1&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\\_RESULTSPanel.Pubmed\\_DefaultReportPanel.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19115010?ordinalpos=1&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_RESULTSPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum)

**BACKGROUND AND OBJECTIVES:** The aim of this study was to estimate the proportion of spontaneous viral clearance (SVC) after symptomatic acute hepatitis C and to evaluate the efficacy of 12 weeks of pegylated interferon alfa-2a in patients who did not clear the virus spontaneously.

**METHODS:** Patients with symptomatic acute hepatitis C were recruited from two "fever hospitals" in Cairo, Egypt. Patients still viremic three months after the onset of symptoms were considered for treatment with 12 weeks of pegylated interferon alfa-2a (180 microg/week). **RESULTS:** Between May 2002 and February 2006, 2243 adult patients with acute hepatitis were enrolled in the study.

The SVC rate among 117 patients with acute hepatitis C was 33.8% (95%CI [25.9%-43.2%]) at three months and 41.5% (95%CI [33.0%-51.2%]) at six months. The sustained virological response (SVR) rate among the 17 patients who started treatment 4-6 months after onset of symptoms was 15/17 = 88.2% (95%CI [63.6%-98.5%]). **CONCLUSION:** Spontaneous viral clearance was high (41.5% six months after the onset of symptoms) in this population with symptomatic acute hepatitis C.

Allowing time for spontaneous clearance should be considered before treatment is initiated for symptomatic acute hepatitis C.

**Laboratory evaluation of the UniCel DxI 800 analyser (Beckman Coulter) for detecting HBV and HCV serological markers.** Miedouge M, Legrand-Abravanel F, Lalanne C, et al. J Clin Virol. 2008 Dec 23. [Epub ahead of print]

[http://www.ncbi.nlm.nih.gov/pubmed/19110466?ordinalpos=&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\\_RESULTSPanel.SmartSearch&log\\$citationsensor](http://www.ncbi.nlm.nih.gov/pubmed/19110466?ordinalpos=&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_RESULTSPanel.SmartSearch&log$citationsensor)

**BACKGROUND:** Due to their high prevalence, hepatitis B virus (HBV) and hepatitis C virus (HCV) infections need accurate and rapid diagnosis tools. **OBJECTIVES:** Technical performances of the UniCel DxI 800 analyser (Beckman Coulter) and a comparison with the Vitros ECi (Ortho Clinical Diagnostics) were performed for five serological markers: HBsAg, total anti-HBc, anti-HBc IgM, anti-HBs and anti-HCV. **STUDY DESIGN:** Reproducibility was determined by repeated tests on the manufacturers' controls. The performance of the UniCel DxI 800 was assessed by testing negative and positive samples previously analysed with the Vitros ECi. The accuracy and linearity of anti-HBs assay were evaluated using the WHO international standard (W1042). **RESULTS:** The intra-assay and inter-assay coefficients of variation were: 0.8% and 4.4% for HBsAg, 2.4% and 6.2% for anti-HBc, 5% and 8.7% for anti-HBc IgM, 2.1% and 5.1% for anti-HBs and 3.7% and 7.4% for anti-HCV. The two **METHODS** were concordant: 100% agreement for the five markers except for the negative HBsAg sera (99%). The anti-HBs **RESULTS** correlated well with the Vitros ECi ( $r=0.925$  with  $p<0.0001$ ) and the WHO standard ( $r(2)=0.9996$ ). Throughput was 216tests/h. **CONCLUSION:** The high throughput, specificity and sensitivity make UniCel DxI 800 assays useful for routine diagnoses of HCV and HBV infections.

**Differences between two real-time PCR-based hepatitis C virus (HCV) assays (RealTime HCV and Cobas AmpliPrep/Cobas TaqMan) and one signal amplification assay (Versant HCV RNA 3.0) for RNA detection and quantification.** Vermehren J, Kau A, Gärtner BC, et al. J Clin Microbiol. 2008 Dec;46(12):3880-91. Epub 2008 Sep 17.

[http://www.ncbi.nlm.nih.gov/pubmed/18799708?ordinalpos=106&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\\_RESULTSPanel.Pubmed\\_DefaultReportPa](http://www.ncbi.nlm.nih.gov/pubmed/18799708?ordinalpos=106&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_RESULTSPanel.Pubmed_DefaultReportPa)

Hepatitis C virus (HCV) RNA detection and quantification are the key diagnostic tools for the management of hepatitis C. Commercially available HCV RNA assays are calibrated to the HCV genotype 1 (gt1)-based WHO standard. Significant differences between assays have been reported. However, it is unknown which assay matches the WHO standard best, and little is known about the sensitivity and linear quantification of the assays for non-gt1 specimens. Two real-time reverse transcriptase PCR-based assays (RealTime HCV and Cobas Ampliprep/Cobas TaqMan HCV [CAP/CTM]) and one signal amplification-based assay (the Versant HCV RNA, version 3.0, branched DNA [bDNA] assay) were compared for their abilities to quantify HCV RNA in clinical specimens (n = 65) harboring HCV isolates of gt1 to gt5. The mean differences in the amounts detected by RealTime HCV in comparison to those detected by the bDNA assay and CAP/CTM were -0.02 and 0.72 log(10) IU/ml HCV RNA, respectively, for gt1; -0.22 and 0.03 log(10) IU/ml HCV RNA, respectively, for gt2; -0.27 and -0.22 log(10) IU/ml HCV RNA, respectively, for gt3; -0.19 and -1.27 log(10) IU/ml HCV RNA, respectively, for gt4; and -0.03 and 0.09 log(10) IU/ml HCV RNA, respectively, for gt5. The lower limits of detection for RealTime HCV and CAP/CTM were 16.8 and 10.3 IU/ml, respectively, for the WHO standard and in the range of 4.7 to 9.0 and 3.4 to 44.4 IU/ml, respectively, for clinical specimens harboring gt1 to gt6. Direct comparison of the two assays with samples of the WHO standard (code 96/798) with high titers yielded slightly smaller amounts by RealTime HCV (-0.2 log(10) at 1,500 IU/ml and -0.3 log(10) at 25,000 IU/ml) and larger amounts by CAP/CTM (0.3 log(10) at 1,500 IU/ml and 0.2 log(10) at 25,000 IU/ml). Finally, all three tests were linear between  $4.0 \times 10^3$  and  $1.0 \times 10^6$  IU/ml (correlation coefficient,  $\geq 0.99$ ). **In conclusion**, the real-time PCR based assays sensitively detected all genotypes and showed comparable linearities for the quantification of HCV RNA, with the exception of gt1 and gt4. The previously reported differences in the absolute quantification of samples harboring gt1 were confirmed and may be explained by different calibrations to the WHO standard.

**Diagnosis of acute hepatitis C virus infection and estimated incidence in low- and high-risk English populations.** Brant LJ, Ramsay ME, Balogun MA, Boxall E, Hale A, Hurrelle M, Kaluba L, Klapper P, Lewis D, Patel BC, Parry J, Irving WL. *J Viral Hepat.* 2008 Dec;15(12):871-7. Epub 2008 Jul 10.

[http://www.ncbi.nlm.nih.gov/pubmed/18637073?ordinalpos=125&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\\_RESULTSPanel.Pubmed\\_DefaultReportPanel.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/18637073?ordinalpos=125&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_RESULTSPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum)

The diagnosis of acute hepatitis C virus (HCV) infection is not straightforward; few people exhibit clinical symptoms and genome/antigen detection techniques do not indicate when infection had occurred. Here, a strategy to detect HCV RNA in the absence of antibody ('window-period') for diagnosis of acute infection is assessed. The sentinel surveillance of hepatitis testing study was used to retrospectively identify anti-HCV negative samples from high-risk individuals (2002-2003), for testing singly for HCV RNA. Additional samples were identified prospectively (2005) and tested in pools for HCV RNA. Positive samples were genotyped. Incidence and costs of adopting the pooling strategy were estimated. In the retrospective study, 8/390 (2.1%) samples were confirmed HCV RNA positive, anti-HCV negative. Prospectively, 3237 samples were tested in 325 pools. Five positive pools identified four confirmed HCV RNA positive patients (one false positive). Estimated incidence was 12.9 per 100 person-years in injecting drug users (IDUs) (retrospective study) and 3.7 per 100 person-years among drug/alcohol services and prison attendees (prospective study). Estimated costs were pound 850 per positive sample, in areas of higher risk. The yield from a window-period strategy depends upon the population tested. Pooled HCV RNA testing of anti-HCV negative samples from the current IDUs is realistic and relatively inexpensive to identify recently infected individuals.