

Caring Ambassadors Hepatitis C Program Newsletter
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CLINICAL TRIALS, COHORT STUDIES, PILOT STUDIES

A sustained virologic response is durable in patients with chronic hepatitis C treated with peginterferon alfa-2a and ribavirin. Swain MG, Lai MY, Shiffman ML, et al.

Gastroenterology. 2010 Jul 13. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/20637202>

BACKGROUND & AIMS: A sustained virologic response (SVR) to therapy for Hepatitis C virus (HCV) infection is defined as the inability to detect HCV RNA 24 weeks after treatment has been completed. Although small studies have reported that the SVR is durable and lasts for long time periods, it has not been conclusively demonstrated. **METHODS:** The durability of treatment responses were examined in patients who were originally enrolled in 1 of 9 randomized, multicenter trials (n=1343). The study included patients who received peginterferon alfa-2a alone (n=166) or in combination with ribavirin (n=1077, including 79 patients with normal levels of alanine aminotransferase and 100 patients that were co-infected with HIV and HCV) and whose serum samples were negative for HCV RNA (<50 IU/mL) at their final assessment. Patients were assessed annually, from the date of last treatment, for a mean of 3.9 years (range 0.8-7.1). **RESULTS:** Most patients (99.1%) that achieved an SVR had undetectable levels of HCV RNA in serum samples throughout the follow-up period. Serum samples from 0.9% of the patients contained HCV RNA after a mean period of 1.8 years (range 1.1-2.9 years) after treatment ended. It is not clear if these patients were re-infected or relapsed.

CONCLUSION: In a large cohort of patients monitored for the durability of a SVR, the SVR was maintained for almost 4 years after treatment with peginterferon alfa-2a alone or in combination with ribavirin. In patients with chronic hepatitis C infection, the SVR is durable and these patients should be considered as cured.

Retreatment of hepatitis C patients with pegylated interferon combined with ribavirin in non-responders to interferon plus ribavirin. Is it different in real life? Goncales FL Jr,

Moma CA, Vignani AG, et al. BMC Infect Dis. 2010 Jul 20;10(1):212. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/20646277>

BACKGROUND: More than 50% of hepatitis C viruses (HCV)-infected patients do not respond to the classical Interferon (IFN)/Ribavirin (RBV) combination therapy. The aim of this study was to evaluate the efficacy of retreatment with Peg-Interferon alpha-2b (PEG-IFN alpha-2b) plus RBV, in patients with HCV, genotypes 1 or 3, who were non-responders to the previous standard treatment with IFN/RBV. **METHODS:** In the period 2005-2007, a total of 238 HCV chronic patients were non-responders to previous treatment with IFN plus RBV. Of these 130 agreed to be retreated with PEG-IFN alpha-2b and participated in this evaluation (90 with genotype 1 HCV

and 40 with genotype 3 HCV). Patients were retreated at assisted IFN application hubs in compliance with the country's public health system rules. They received subcutaneous PEG-IFN alpha-2b, 1.5ug, once weekly, associated with RBV, through the oral route, with doses determined according to weight (1,000mg if weight [less than or equal to] 75kg and 1,250mg if > 75kg). Patients with genotype 1 HCV were retreated for over 48 weeks and patients with genotype 3 HCV for over 24 weeks. HCV-RNA was tested by polymerase chain reaction (PCR) at baseline, at week 12, at the end of the treatment, and 6 months thereafter. The predictiveness of week 12 in the development of a sustained virologic response (SVR) was also evaluated. Patients with negative HCV-RNA at week 12 were considered as early virologic responders (EVR). **RESULTS:** EVR was observed in 25% of the patients with genotype 1 HCV and in 64% of the patients genotype 3 HCV (risk = 2.075 and p-value = 0.0414). SVR was observed in 22.2% of the patients with genotype 1 HCV and in 40% with genotype 3 HCV (intention-to-treat analysis). The positive predictive value (PPV) of the HCV-RNA testing at week 12, in order to obtain the SVR, was 65% for genotype 1 and 56% for genotype 3, and the negative predictive value (NPV) was 88% for genotype 1 and 89% for genotype 3. **CONCLUSION:** PEG-IFN alpha-2b plus weight-based ribavirin is effective in re-treating previous interferon-alpha plus RBV failure; 22.2% of the patients with genotype 1 HCV and 40% of patients with genotype 3 HCV achieved SVR.

Components of metabolic syndrome are independent predictors of mortality in patients with chronic liver disease: a population-based study. Stepanova M, Rafiq N, Younossi ZM. Inova Health System Falls Church, Virginia, USA. Gut. 2010 Jul 26. [Epub ahead of print] <http://www.ncbi.nlm.nih.gov/pubmed/20660697>

OBJECTIVE: Chronic liver disease (CLD) is a major cause of mortality and morbidity worldwide. The aim of this study was to assess the overall and liver-related mortality and their predictors in patients with CLD using population data. **METHODS:** The Third National Health and Nutrition Examination Survey (NHANES III) and linked mortality data were utilised. Participants from NHANES III (1988-1994) and their mortality status were updated by the Center for Disease Control (CDC) as of 31 December 2006. In this study, the aetiology of CLD was based on available serological tests and clinical data. Each diagnostic cohort was compared with a cohort without liver disease using stratum-specific chi(2). The Cox proportional hazard model was used for analysis, and HRs adjusted for all major confounders; overall mortality and cause-specific mortality were calculated for each type of liver disease. All analyses were run using SAS-callable SUDAAN 10.0 functions using remote access to the CDC Research Data Center server with restricted use linked mortality data. **RESULTS:** The study cohort included 15 866 NHANES III participants with complete clinical, demographic, laboratory and mortality follow-up data. Of these, 235 subjects had alcohol-related liver disease (ALD), 66 had chronic hepatitis B (CH-B), 264 had chronic hepatitis C (CH-C), 991 were presumed to have non-alcoholic fatty liver disease (NAFLD) and 505 had other liver disease. Additionally, 13 004 subjects without evidence of liver disease served as controls. The analysis shows that type II diabetes (DM) and/or insulin resistance (IR) are independent predictors of overall mortality in CH-B, NAFLD and ALD (p <0.05). Additionally, DM, IR, obesity and metabolic syndrome could be independent predictors of liver-related mortality in CH-C, NAFLD and ALD. **CONCLUSIONS:** Components of metabolic syndrome are associated with overall and liver-related mortality in subjects with CLD.

Interferon reduces the risk of hepatocellular carcinoma in hepatitis C virus-related chronic hepatitis/liver cirrhosis. Masuzaki R, Yoshida H, Omata M. *Oncology*. 2010 Jul;78 Suppl 1:17-23. Epub 2010 Jul 8.

<http://www.ncbi.nlm.nih.gov/pubmed/20616579>

The efficacy of interferon therapy against hepatitis C virus (HCV) has much improved, showing a sustained virologic response rate of 40-50% even in the genotype 1b with a high viral load. Several cohort studies conducted in Japan in the 1990s unanimously concluded that the risk of hepatocellular carcinoma (HCC) development was reduced in patients who achieved a sustained virologic response or persistent normalization of alanine aminotransferase as compared to untreated patients. Recently, a large-scale randomized controlled trial, called the HALT-C study, showed no significant difference in the incidence of HCC between patients on maintenance interferon therapy and those without. The reason for the discrepant results in Japanese and USA studies needs further clarification, together with analysis of the difference in incidence rates of HCC among cirrhotic patients. There has also been progress in the treatment of HCC, and together with advances in diagnostics facilitating HCC detection at an early stage, tumor nodules can often be completely removed either by medical ablation or surgical resection. Nevertheless, recurrence of HCC after apparently curative treatment is extraordinarily frequent, since the remaining liver is still at a high risk of HCC. The prevention of the recurrence of HCC, or tertiary prevention, is currently one of the most challenging tasks in hepatology.

An updated follow-up of chronic hepatitis C after three decades of observation in pediatric patients cured of malignancy. Cesaro S, Bortolotti F, Petris MG, Brugiolo A, Guido M, Carli M. *Pediatr Blood Cancer*. 2010 Jul 15;55(1):108-12.

<http://www.ncbi.nlm.nih.gov/pubmed/20127849>

BACKGROUND: The aim of the study was to evaluate the clinical characteristics and the long-term outcome of chronic hepatitis C in a cohort of Caucasian children cured of pediatric malignancy. **PROCEDURE:** The study population included 83 consecutive patients, referred to our Center with a diagnosis of leukemia/lymphoma (50) or solid tumors (33) between 1977 and 1989 and infected with hepatitis C virus (HCV) during chemotherapy. **RESULTS:** At enrollment 77 subjects were HCV-RNA positive. After a median follow-up of 21 years (range 13-36), a sustained virological response (SVR) was obtained in 3 of 29 patients (10%) treated with interferon (IFN), in 1 of 3 patients (33%) treated with IFN and ribavirin, and in 5 of 11 patients (42%) treated with pegylated-IFN and ribavirin ($P = 0.03$). Forty-two patients remained untreated and only one (2.5%) cleared viremia. Four of 77 patients (5%) developed cirrhosis while other 4 patients died of causes not related to liver. At last follow-up, 72% of HCV-RNA positive patients had abnormal ALT. **CONCLUSIONS:** In patients cured of pediatric malignancy chronic hepatitis C tends to run an indolent course during childhood and adolescence but more than 70% of treated and more than 80% of untreated cases children maintained HCV viremia. Moreover, after 2-3 decades of observation, 60% of HCV-RNA positive patients had abnormal ALT and 5% had developed cirrhosis. Among treated patients, IFN or pegylated-IFN and ribavirin obtained the higher rate of HCV-RNA clearance.

Peginterferon alpha-2a and ribavirin treatment of patients with haemophilia and hepatitis C virus infection: a single-centre study of 367 cases. Alavian SM, Tabatabaei SV, Keshvari M, et al. *Liver Int.* 2010 Jul 8. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/20629950>

BACKGROUND/AIMS: Chronic hepatitis C virus infection (HCV) is a major comorbidity in patients with haemophilia. Peginterferon alpha and ribavirin is current standard anti-HCV therapy but there is little information about safety and efficacy of peginterferon alpha-2a and ribavirin combination therapy in these patients. **MATERIAL AND METHODS:** In an open-label single-treatment arm cohort study, 367 haemophilia patients seronegative for hepatitis B and human immunodeficiency virus markers and chronically infected with HCV (HCV RNA > 50 IU/ml for at least 6 months) received 180 µg of Pegasys((R)) and 800-1200 mg of ribavirin according to body weight. Genotypes 1 and 4, mixed and untypable infections were treated for 48 weeks, while genotypes 2 and 3 were treated for 24 weeks. The efficacy of therapy was expressed as sustained virological response (SVR). **RESULTS:** Two hundred and twenty-five subjects [61%, 95% confidence interval (CI) 56-66] achieved SVR, 66 patients relapsed and 30 subjects did not respond and nine patients developed breakthrough during treatment. In a multivariate logistic regression model, age < 24 odds ratio (OR) = 1.8 (95% CI 1.1-3.1), genotype non-1 OR = 1.8 (95% CI 1.1-3.2), BMI < 25 OR = 2.1 (95% CI 1.3-3.3) and HCV RNA < 600 000 IU/ml OR = 1.7 (95% CI 1.1-3.2) were independent predictors of SVR. Eight patients discontinued the treatment because of persistent neutropenia and 22 subjects were dropped out because of intractable side effects. Furthermore, two patients died during treatment and five were lost to follow-up after treatment cessation. **CONCLUSIONS:** Peginterferon alpha-2a in combination with weight-based ribavirin has SVR rate of 51% for genotype 1 and 71% for genotype non-1 infections in haemophilia patients. Age < 24, BMI < 25, viral load < 600 000 IU/ml and genotype non-1 are the major determinants of SVR achievement in these patients.

Hyperinsulinaemia reduces the 24-h virological response to PEG-interferon therapy in patients with chronic hepatitis C and insulin resistance. Bortoletto G, Scribano L, Realdon S, et al. *J Viral Hepat.* 2010 Jul;17(7):475-80.

<http://www.ncbi.nlm.nih.gov/pubmed/19878535>

Insulin resistance (IR) reduces response to pegylated-interferon (PEG-IFN)/ribavirin in chronic hepatitis C (CHC), but the mechanisms are still undefined. We examined the relationship between baseline insulin levels, the main component affecting homeostasis model of assessment - insulin resistance (HOMA-IR) for assessment of IR in non-diabetic patients, and the 'acute' virological response to PEG-IFN measured 24 h after the first injection and taken as correlate of intracellular interferon signalling. In 62 patients treated with PEG-IFN/Ribavirin, serum insulin and HOMA-IR were assessed at baseline, while hepatitis C virus (HCV)-RNA was measured at baseline and 24 h, 1, 2, 4 and 12 weeks after treatment initiation. Sustained virological response was examined 24 weeks after therapy discontinuation. Mean baseline insulin was 11.52 +/- 8.51 U/L and mean HOMA-IR was 2.65 +/- 2.01 both being significantly higher with advanced liver fibrosis. Hepatitis C virus-RNA decay observed 24 h after the first injection of PEG-IFN was significantly lower (0.7 +/- 0.8 log) in patients with HOMA > or = 3 compared with those with HOMA < 3 (1.7 +/- 0.8, P = 0.001). A highly significant (r = -0.42) inverse correlation was observed between baseline insulin levels and the 24-h HCV-RNA decay. The difference in early viral kinetics between patients with HOMA > or = 3 or < 3 resulted in a significant difference in the percentage of patients achieving rapid (week 4) and sustained virological response.

Multivariate analysis, inclusive of patient age, HCV genotype and fibrosis stage, identified baseline insulin levels as the main independent variable affecting the 24-h response to PEG-IFN. Hyperinsulinaemia reduces the cellular response to Pegylated-interferon in CHC with IR. Strategies to reduce insulin levels before initiation of treatment should be pursued to improve efficacy of anti-viral treatment.

Influence of alpha-1 antitrypsin heterozygosity on treatment efficacy of HCV combination therapy. Kok KF, van Soest H, van Herwaarden AE, et al. Eur J Gastroenterol Hepatol. 2010 Jul;22(7):808-12.

<http://www.ncbi.nlm.nih.gov/pubmed/19794310>

BACKGROUND: The role of heterozygosity for alpha-1 antitrypsin (A1AT) alleles in patients with chronic hepatitis C virus (HCV) is unclear. There is limited evidence to suggest that there is an increased prevalence of heterozygous A1AT carriers in HCV, but it is unclear how this affects treatment success. **AIM:** To investigate the (i) prevalence of A1AT heterozygosity among two HCV cohorts and (ii) its effect on treatment outcome. **METHODS:** We performed a retrospective cohort study using two different cohorts. Cohort 1 consisted of 678 German HCV patients, 507 of them were treated for HCV with standard therapy. Cohort 2 consisted of 370 Dutch HCV patients of which 252 were part of a clinical trial (treatment with amantadine or placebo, in combination with pegylated interferon alpha-2b and ribavirin) whereas 37 HCV patients received standard therapy. We analyzed A1AT status using direct sequencing of the A1AT gene (cohort 1) or isoelectric focusing of serum (cohort 2). In addition, we measured A1AT serum levels (cohort 2). **RESULTS:** In total, we included 1048 HCV patients; 986 (94%) were wildtype [protease inhibitor (Pi) MM], whereas 61 (6%) were heterozygous for a mutant A1AT allele (41 Pi MS, 20 Pi MZ). Mean A1AT serum levels (370 patients) were lower in A1AT heterozygous patients (1.68 vs. 1.36 g/l), ($P < 0.05$) compared with wildtypes. Sustained viral response (SVR) after treatment was equal between the wildtypes and heterozygotes (54 vs. 56%). **CONCLUSION:** We found a heterozygosity rate of 0.06, in line with healthy controls in other studies. Serum A1AT levels from A1AT heterozygous HCV patients are significantly lower compared with wildtype patients, although they do not discriminate on an individual level. Finally, SVR in A1AT wildtypes was not different from SVR in A1AT heterozygotes.

Is irritable bowel syndrome associated with chronic hepatitis C? Fouad YM, Makhoul MM, Khalaf H, et al. J Gastroenterol Hepatol. 2010 Jul;25(7):1285-8.

<http://www.ncbi.nlm.nih.gov/pubmed/20594257>

BACKGROUND AND AIM: Hepatitis C virus (HCV) is a common chronic infection that is widely associated with symptoms of fatigue and abdominal pain. The aim of the present study was to determine the prevalence of irritable bowel syndrome (IBS) among patients with hepatitis C compared to controls. **METHODS:** This study included 258 patients with chronic hepatitis C, 36 patients with chronic hepatitis B, and 160 healthy volunteers. Clinical and laboratory data were recorded for every patient. All patients and controls were administered a questionnaire of IBS according to Rome III criteria. **RESULTS:** The percentage of patients with IBS was significantly higher in patients with chronic HCV (66%, 170/258) than chronic hepatitis B virus (HBV; 22%, 8/36) and normal controls (18%, 28/160 patients; $P < 0.001$ and $P < 0.001$, respectively). There was no significant difference between chronic HBV and normal controls. In chronic HCV patients, IBS with constipation was the predominant type (51%, 86/170) followed by mixed IBS (73/170, 43%). In patients with chronic HCV, the percentage of females with IBS

(91%) was significantly higher than those without IBS (9%; $P < 0.001$), and the percentage of patients with a high fibrosis score (F2-3) was significantly higher in patients with IBS (45%) than in patients without IBS (6%; $P < 0.001$). There was no difference regarding age, alanine aminotransferase level, or HCV viremia. A multivariate regression analysis revealed a significant association between sex, fibrosis score, and IBS. **CONCLUSION:** IBS is more prevalent in patients with chronic hepatitis C. Female patients with chronic HCV and those with higher fibrosis scores are more likely to have IBS.

Reinfection with hepatitis C virus following sustained virological response in injection drug users. Grebely J, Knight E, Ngai T, et al. *J Gastroenterol Hepatol.* 2010 Jul;25(7):1281-4. <http://www.ncbi.nlm.nih.gov/pubmed/20594256>

BACKGROUND AND AIM: Despite that 60-90% of injection drug users (IDUs) are infected with hepatitis C virus (HCV) infection, IDUs are often denied therapy based on concerns of reinfection following treatment. However, there are little data in this regard. We evaluated HCV re-infection following sustained virologic response (SVR) among HCV-infected IDUs having received HCV treatment in a multidisciplinary program. **METHODS:** Following treatment, participants were encouraged to return at follow-up intervals of 1 year and illicit drug use histories were obtained. In those with SVR, HCV RNA testing by PCR was performed to determine if relapse or reinfection occurred. **RESULTS:** Among 58 receiving HCV treatment between January 2002 and December 2006, 60% (35 of 58) achieved an SVR. Patients were followed for a median of 2.0 years following SVR (range, 0.4-5.0 years), with ongoing illicit and injection drug use reported in 54% (19 of 35) and 46% (16 of 35). Of the 35 with SVR, 28 remained HCV RNA negative during follow-up (80%), with four lost to follow-up and one dying of hepatocellular carcinoma and two cases of reinfection were observed (2 of 35). The rates of reinfection were 3.2 per 100 p-y (95% CI:0.4, 11.5) overall and 5.3 per 100 p-y (95% CI:0.6, 19.0) among those reporting injecting following SVR ($n = 16$). One of two participants with HCV re-infection spontaneously cleared virus following reinfection. **CONCLUSION:** The rate of reinfection following treatment for HCV infection among current and former IDUs engaged in a multidisciplinary program is low.

High prevalence of late relapse and reinfection in prisoners treated for chronic hepatitis C. Bate JP, Colman AJ, Frost PJ, Shaw DR, Harley HA. *J Gastroenterol Hepatol.* 2010 Jul;25(7):1276-80.

<http://www.ncbi.nlm.nih.gov/pubmed/20594255>

BACKGROUND AND AIM: Prisoners have a high prevalence of injection drug use (IDU) and chronic hepatitis C (CHC) infection. Treatment of CHC in these patients is effective; however, their long-term outcomes following treatment are unknown. We determined the durability of a sustained virological response (SVR) in prisoners treated for CHC. **METHODS:** Patients were treated as part of routine clinical practice with interferon (IFN) and ribavirin. A retrospective review of medical records and a computerized pathology system was performed for clinical and laboratory information. **RESULTS:** Seventy-four prisoners (70 males, mean age 34 years, IDU in 55%) were evaluable for a SVR over a 12-year period to December 2008; the mean follow-up period was 1243 days. Genotype 1, 2, 3, and 6 infection was present in 18, three, 38 and three patients, respectively; the genotype was unknown in 12. Three out of 52 biopsied had cirrhosis. Standard IFN was administered to 25 (34%; 11 with ribavirin), and 49 received pegylated IFN and ribavirin; one did not complete treatment, and two had breakthrough relapses. The end-of-

treatment response was achieved in 57 and SVR in 53; 14 were non-responders. Five male patients, four with unknown genotypes and treated with standard IFN alone, relapsed late (following SVR, 9%). Five patients, all treated with pegylated IFN and ribavirin, were reinfected (one prior to and four following SVR). **CONCLUSIONS:** Prisoners are often successfully treated for CHC. However, this retrospective study indicates that there is a high (17%) prevalence of late recurrence of viremia that is likely a reflection of reinfection due to ongoing risk-taking behavior.

Randomized trial of albinterferon alfa-2b for the treatment of patients with chronic hepatitis C Virus Genotype 2 or 3. Nelson DR, Benhamou Y, Chuang WL, et al.

Gastroenterology. 2010 Jul 2. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/20600017>

BACKGROUND & AIMS: A phase 3 active-controlled study was conducted to assess the efficacy/safety of albinterferon alfa-2b (albIFN)-a novel, long-acting genetic fusion polypeptide of recombinant human albumin and interferon alfa-2b-in patients with chronic hepatitis C virus (HCV) genotype 2/3. **METHODS:** In all, 933 patients were randomized to open-label subcutaneous treatment with pegylated interferon alfa-2a (Peg-IFNalpha-2a) 180 mug qwk, or albIFN 900 or 1200 mug q2wk for 24 weeks, each administered with oral ribavirin 800 mg/d. Primary endpoint: sustained virologic response (SVR; HCV RNA <15 IU/mL at week 48). During the study, the data monitoring committee recommended dose modification for all patients receiving albIFN 1200 mug to 900 mug, impacting 38% of this treatment arm. **RESULTS:** By intention-to-treat analysis, SVR rates were 84.8% (95% confidence interval 80.4%-88.6%), 79.8% (74.9%-84.1%), and 80.0% (75.1%-84.3%) with Peg-IFNalpha-2a and albIFN 900 and 1200 mug, respectively. The primary hypothesis of noninferiority of SVR was established for albIFN 900 mug (P = .009) and 1200 mug (P = .006). Independent positive predictors of SVR by multivariate regression analysis were pretreatment HCV RNA <400,000 IU/mL, age <45 years, body mass index <30 kg/m², genotype 2, normal gamma-glutamyl transpeptidase and elevated alanine aminotransferase at baseline, fibrosis stage F0-2, no steatosis, and Asian geographic region (Peg-IFNalpha-2a only). The 3 treatment groups showed similar rates of serious (7%-8%) and severe (13%-16%) adverse events, and discontinuations due to adverse events (3.6%-5.5%). **CONCLUSION:** Albinterferon alfa-2b 900 mug q2wk provides an alternative efficacious treatment option in patients with chronic HCV genotype 2 or 3.

Randomized trial of albinterferon alfa-2b for the treatment of patients with chronic hepatitis c virus genotype 1. Zeuzem S, Sulkowski MS, Lawitz EJ, et al. Gastroenterology.

2010 Jul 2. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/20600013>

BACKGROUND & AIMS: The current standard of care for patients with chronic hepatitis C virus genotype 1 is once-weekly pegylated interferon-alpha (Peg-IFNalpha) plus daily ribavirin for 48 weeks. Objective: To evaluate the efficacy/safety of albinterferon alfa-2b (albIFN), a novel, long-acting, genetic fusion polypeptide of albumin and IFNalpha-2b. **METHODS:** In the phase 3 ACHIEVE-1 trial, 1331 patients were randomized equally to 3 open-label, 48-week treatment groups: Peg-IFNalpha-2a 180 mug qwk, or albIFN 900 or 1200 mug q2wk administered subcutaneously, with weight-based oral ribavirin 1000-1200 mg/d. During the study, the data monitoring committee recommended dose modification for all patients receiving albIFN 1200 mug to 900 mug due to increased pulmonary adverse events (AEs) in the 1200-mug

arms of both ACHIEVE studies. **MAIN OUTCOME MEASURE:** Sustained virologic response (SVR; undetectable serum HCV RNA at week 72). **RESULTS:** Intention-to-treat SVR rates: 51.0% (225/441), 48.2% (213/442), and 47.3% (208/440) with Peg-IFNalpha-2a, and albIFN 900 and 1200 mug, respectively. The primary objective of demonstrating noninferiority of albIFN 900 mug ($P < .001$) and 1200 mug ($P = .003$) vs Peg-IFNalpha-2a for SVR was achieved. Multivariate modeling indicated consistency of treatment effect across subgroups. Serious/severe AE rates: 23.1%, 24.0%, 28.2%; treatment discontinuation rates due to AEs: 4.1%, 10.4%, 10.0%; discontinuation rates due to respiratory AEs: 0%, 0.9%, 1.6%; with Peg-IFNalpha-2a, and albIFN 900 and 1200 mug, respectively. Hematological abnormality rates were comparable across the Peg-IFNalpha-2a and albIFN 900-mug groups. **CONCLUSIONS:** albIFN 900 mug q2wk demonstrated comparable efficacy, with similar serious/severe AE rates, although with a higher discontinuation rate, vs Peg-IFNalpha-2a in patients with chronic HCV genotype 1.

Meta-analysis shows extended therapy improves response of patients with chronic hepatitis C virus genotype 1 infection. Farnik H, Lange CM, Sarrazin C, et al. Clin Gastroenterol Hepatol. 2010 Jul 2. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/20601130>

BACKGROUND & AIMS: Clinical trials have provided conflicting results about whether extended duration of treatment with pegylated interferon-alfa (pegIFN-alfa) and ribavirin (more than 48 weeks) improves rates of sustained virologic response (SVR) in patients infected with hepatitis C virus (HCV) genotype 1 that have a slow virologic response. We performed a meta-analysis to determine the overall impact of extended treatment, compared to standard treatment, on virologic response rates in these patients. **METHODS:** We performed a literature search to identify randomized controlled trials (RCT) that included mono-infected, treatment-naive patients infected with HCV genotype 1; data were compared between slow responding patients treated with pegIFN-alfa-2a/b plus ribavirin for 48 weeks and those that received extended treatment (as much as 72 weeks). Endpoints included SVR rates, end-of-treatment response and relapse rates; they were calculated as meta-analysis of data with binary outcome according to the DerSimonian-Laird estimate. **RESULTS:** Six randomized controlled trials assessed the benefits of extended treatment with pegIFN-alfa-2a/b and ribavirin in treatment-naive patients with HCV genotype 1 that were slow responders ($n=669$). The extended treatment significantly improved SVR rates in slow responders, compared to the standard of care (14.7% increase in overall SVR, 95% confidence interval: 4%-25.5%, $P=0.0072$). Rates of viral relapse were significantly reduced by extended treatment but end-of-treatment response rates were similar. The frequency of voluntary treatment discontinuation, but not of serious adverse events, was significantly increased by extended therapy. **CONCLUSIONS:** Extending the duration of treatment with pegIFN-alfa-2a/b and ribavirin in patients with HCV genotype 1 and a slow response to therapy improves the rate of SVR.

BASIC AND APPLIED SCIENCE, PRE-CLINICAL STUDIES

Impairment of TLR7-dependent signaling in dendritic cells from chronic hepatitis C virus (HCV)-infected non-responders to interferon/ribavirin therapy. Simone O, Tortorella C, <http://www.ncbi.nlm.nih.gov/pubmed/20390327>

BACKGROUND AND AIM: Dendritic cell (DC) dysfunction has been suggested to play a role in the weak antiviral T-cell responsiveness observed during the course of chronic hepatitis C

virus (HCV) infection. This study was undertaken to evaluate whether changes in DC functions might be related to a different therapeutic outcome in HCV-infected patients. **METHODS:** Peripheral blood DCs (PBDCs) or monocyte-derived DCs (MoDCs) were obtained from chronic HCV-infected patients, sustained virologic responders (SVR) or non-responders (NR) to interferon/ribavirin therapy, and from healthy controls (HC). The frequency of BDCA-1+, BDCA-3+ or CD16+ myeloid DCs (mDCs) and BDCA-2+ plasmacytoid DCs (pDCs), as well as the expression of the costimulatory molecule CD86 in each PBDC subset, were evaluated by flow cytometry. MoDCs from single individuals were stimulated with TLR2, TLR3, TLR4, and TLR7 ligands and analyzed for CD86, CD83, CD40, CD80, and CD209 expression. Finally, mitogen-activated protein kinase (MAPK) phosphorylation of TLR7-triggered MoDCs was assessed by Western blotting. **RESULTS:** NR exhibited a reduced percentage of BDCA-1+ mDCs, as well as lower levels of CD86+ cells, in both BDCA-1+ mDCs and pDCs as compared to SVR and HC. Furthermore, MoDCs from NR displayed a defective CD86 and CD83 increase and ERK1/2 or p38-MAPK phosphorylation upon TLR7-cell triggering. **CONCLUSIONS:** Our data suggest that a TLR7-dependent impairment of costimulatory molecule expression caused by HCV persistence may affect DC activity in NR patients.

Safety and immunogenicity of HCV E1E2 vaccine adjuvanted with MF59 administered to healthy adults. Frey SE, Houghton M, Coates S, et al. *Vaccine*. 2010 Jul 6. [Epub ahead of print] Abrignani S, Chien D, Rosa D, et al. *Vaccine*. 2010 Jul 6. [Epub ahead of print]

BACKGROUND: Hepatitis C virus (HCV) causes chronic liver disease that often leads to cirrhosis and hepatocellular carcinoma. In animal studies, chimpanzees were protected against chronic infection following experimental challenge with either homologous or heterologous HCV genotype 1a strains which predominates in the USA and Canada. We describe first in humans clinical trial of this prophylactic HCV vaccine. **METHODS:** HCV E1E2 adjuvanted with MF59C.1 (an oil-in-water emulsion) was given at 3 different dosages on day 0 and weeks 4, 24 and 48 in a phase 1, placebo-controlled, dose escalation trial to healthy HCV-negative adults. **RESULTS:** There was no significant difference in the proportion of subjects reporting adverse events across the groups. Following vaccination subjects developed antibodies detectable by ELISA, CD81 neutralization and VSV/HCV pseudotype neutralization. There was no significant difference between vaccine groups in the number of responders and geometric mean titers for each of the three assays. All subjects developed lymphocyte proliferation responses to E1E2 and an inverse response to increasing amounts of antigen was noted. **CONCLUSIONS:** The vaccine was safe and generally well-tolerated at each of the 3 dosage levels and induced antibody and lymphoproliferative responses. A larger study to further evaluate safety and immunogenicity is warranted.

Ratio of HCV structural antigens in protein-based vaccine formulations is critical for functional immune response induction. Martínez-Donato G, Musacchio A, Alvarez-Lajonchere L, et al. *Biotechnol Appl Biochem*. 2010 Jul 9;56(3):111-8.

<http://www.ncbi.nlm.nih.gov/pubmed/20515441>

HCV (hepatitis C virus) infection is among the leading causes of chronic liver disease, but currently there is no vaccine available. Data have accumulated about the importance of targeting different HCV antigens in vaccine candidate preparations. Here, a surface response study to select the optimal ratio of recombinant HCV structural antigens in a vaccine preparation, capable of generating in vivo functional cellular immune response in mice, was performed. The

immunogenicity of the selected HCV structural protein mixture (Co-E1-E2) in mice and African green monkeys, after five doses of immunization, was also demonstrated. Specific T-cell proliferative response against HCV structural antigens was induced in vaccinated mice. Moreover, on challenge with recombinant HCV VV (vaccinia virus), all mice controlled the viraemia and 80% were protected. On the other hand, monkeys immunized with Co-E1-E2 developed antibodies, specifically directed to region 412-438 of E2 protein, that include an epitope implicated in HCV neutralization, in addition to a specific proliferative response against HCV Core and E2 proteins. These results indicated that the optimal amount and ratio of HCV recombinant proteins should be taken into account to elicit a successful immune response against HCV and therefore have important implications for vaccine design.

A polymorphism near IL28B is associated with spontaneous clearance, of acute hepatitis C virus and jaundice. Tillmann HL, Thompson AJ, Patel K, et al. *Gastroenterology*. 2010 Jul 13. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/20637200>

BACKGROUND & AIMS: A single nucleotide-polymorphism (SNP) upstream of the IL28B gene has been associated with response of patients with chronic hepatitis C to therapy with pegylated interferon and ribavirin, and also with spontaneous clearance of acute hepatitis C in a heterogeneous population. We analyzed the association between IL28B and the clinical presentation of acute hepatitis C virus (HCV) infection in a homogeneous population.

METHODS: We analyzed the SNP rs12979860 in 190 women from the German anti-D cohort (infected with HCV-genotype-1b via contaminated rhesus-prophylaxis) and its association with spontaneous clearance. Clinical data were available in 136 women with acute infection who were also evaluated for IL28B genotype. Based on results of a TaqMan PCR assay, the rs12979860 SNP genotypes studied were C/C, C/T or T/T. **RESULTS:** Spontaneous clearance was more common in patients with the C/C genotype (43/67; 64%) compared to C/T (22/90, 24%) or T/T (2/33, 6%) ($p < 0.001$). Jaundice during acute infection was more common among patients with C/C genotype (32.7%) than 'non-C/C patients' (with C/T or T/T) (16.1%; $p = 0.032$). In C/C patients, jaundice during acute infection was not associated with an increased chance of spontaneous clearance (56.3) compared to those without jaundice (60.6%). In contrast, in non-C/C patients, jaundice was associated with a higher likelihood of spontaneous clearance (42.9%) compared to those without jaundice (13.7%). **CONCLUSION:** The SNP rs12979860 upstream of IL28B is associated with spontaneous clearance of HCV. Women with the C/T or T/T genotype that did not develop jaundice had a lower chance of spontaneous clearance of HCV infection.

ITPA polymorphism affects ribavirin-induced anemia and outcome of therapy - a Genome-wide study of Japanese HCV patients. Ochi H, Maekawa T, Abe H, et al. *Gastroenterology*. 2010 Jul 13. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/20637204>

BACKGROUND & AIMS: Ribavirin-induced anemia is one of the major causes of discontinuation and dose reduction during anti-hepatitis C virus (HCV) therapy. Factors influencing this anemia, especially host genetic factors, are poorly understood. In this study we investigated predictive factors in HCV patients treated with combination therapy. **METHODS:** We performed a two-step genome-wide screening followed by replication analysis and fine mapping using a total of 923 Japanese HCV 1b-infected patients treated with pegylated-

interferon plus ribavirin. We also applied logistic regression analysis to search for possible independent associations of clinical parameters and genetic variants with treatment-induced hemoglobin (Hb) decline as well as treatment outcome. **RESULTS:** We identified a variant, located upstream of the inosine triphosphate pyrophosphatase (ITPA) gene on chromosome 20p13 that is significantly associated with treatment-induced anemia (combined $p=6.0 \times 10^{-14}$). Re-sequencing and fine mapping revealed several single nucleotide polymorphisms (SNPs) strongly associated with Hb decline, including the nonsynonymous SNP rs1127354 ($p=3.5 \times 10^{-44}$), which was recently reported for other ethnic groups. Another reported SNP, the splicing variant-related SNP rs7270101, was not polymorphic in the Japanese population. Stratified analysis based on rs1127354 genotype revealed that ITPA expression is not correlated with Hb decline, suggesting that rs1127354 is a direct causal variant in the Japanese population. Multivariate analysis demonstrated that age, baseline Hb, baseline platelet count, and rs1127354 were independently associated with severe anemia (Hb < 10g/dl). **CONCLUSIONS:** A missense substitution in ITPA gene affects ribavirin-induced anemia in HCV-infected Japanese patients.

Adaptation of hepatitis C virus to mouse CD81 permits infection of mouse cells in the absence of human entry factors. Bitzegeio J, Bankwitz D, Hueging K, et al. PLoS Pathog. 2010 Jul 1;6:e1000978.

<http://www.ncbi.nlm.nih.gov/pubmed/20617177>

Hepatitis C virus (HCV) naturally infects only humans and chimpanzees. The determinants responsible for this narrow species tropism are not well defined. Virus cell entry involves human scavenger receptor class B type I (SR-BI), CD81, claudin-1 and occludin. Among these, at least CD81 and occludin are utilized in a highly species-specific fashion, thus contributing to the narrow host range of HCV. We adapted HCV to mouse CD81 and identified three envelope glycoprotein mutations which together enhance infection of cells with mouse or other rodent receptors approximately 100-fold. These mutations enhanced interaction with human CD81 and increased exposure of the binding site for CD81 on the surface of virus particles. These changes were accompanied by augmented susceptibility of adapted HCV to neutralization by E2-specific antibodies indicative of major conformational changes of virus-resident E1/E2-complexes. Neutralization with CD81, SR-BI- and claudin-1-specific antibodies and knock down of occludin expression by siRNAs indicate that the adapted virus remains dependent on these host factors but apparently utilizes CD81, SR-BI and occludin with increased efficiency. Importantly, adapted E1/E2 complexes mediate HCV cell entry into mouse cells in the absence of human entry factors. These results further our knowledge of HCV receptor interactions and indicate that three glycoprotein mutations are sufficient to overcome the species-specific restriction of HCV cell entry into mouse cells. Moreover, these findings should contribute to the development of an immunocompetent small animal model fully permissive to HCV.

Heat shock protein 72 is associated with the hepatitis C virus replicase complex and enhances viral RNA replication. Chen YJ, Chen YH, Chow LP, et al. J Biol Chem. 2010 Jul 2. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/20601427>

The NS5A protein of the hepatitis C virus (HCV) is an integral component of the viral replicase. It also modulates cellular signaling and perturbs host interferon responses. The multifunctional characteristics of NS5A are mostly attributed to its ability to interact with various cellular proteins. This study aimed to identify the novel cellular factors that interact with NS5A and

decipher the significance of this interaction in viral replication. The NS5A-interacting proteins were purified by the tandem affinity purification (TAP) procedure from cells expressing NS5A and identified by mass spectrometry. The chaperone protein Hsp72 was identified herein. In vivo protein-protein interaction was verified by co-immunoprecipitation and an in situ proximity ligation assay. In addition to NS5A, Hsp72 was also associated with other members of the replicase complex, NS3 and NS5B, suggesting that it might be directly involved in the HCV replication complex. Hsp72 plays a positive regulatory role in HCV RNA replication by increasing levels of the replicase complex, which was attributed either to the increased stability of the viral proteins in the replicase complex or to the enhanced translational activity of the internal ribosome entry site of HCV. The fact that the host chaperone protein Hsp72 is involved in HCV RNA replication may represent a therapeutic target for controlling virus production.

HIV/HCV/HBV COINFECTION

Hepatitis C virus infection is associated with endothelial dysfunction in HIV/hepatitis C virus coinfecting patients. Castro IF, Micheloud D, Berenguer J, et al. AIDS. 2010 Jul 7. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/20616694>

OBJECTIVE: To quantify serum levels of intercellular adhesion molecule-1 (sICAM-1) and vascular cell adhesion molecule-1 (sVCAM-1) in HIV/HCV coinfecting patients to examine their association with several clinical and epidemiological characteristics and the therapeutic responsiveness to interferon (IFN)-alpha and ribavirin therapy (IFN-alpha + RBV). **DESIGN::** Retrospective study. **METHODS:** We carried out a cross-sectional study with 183 IFN-alpha-naive patients on HAART, and 24 healthy controls. We also analyzed 30 out of 183 patients on IFN-alpha + RBV for the duration of 48 weeks. **RESULTS:** HIV/HCV coinfecting patients had higher levels of sICAM-1 and sVCAM-1 than the healthy control group ($P < 0.05$). Patients with HCV-genotype 1, advanced fibrosis ($F \geq 3$) or moderate to severe activity grade ($A \geq 2$) had the highest values of sICAM-1 and sVCAM-1. When we carried out a multivariate analysis, we found a significant positive relationship between both HCV-genotype 1 and advanced fibrosis ($F \geq 3$) with sICAM-1 ($R = 0.549$; $P < 0.001$); and a significant positive relationship between HCV-genotype 1 and advanced fibrosis ($F \geq 3$) with sVCAM-1 ($R = 0.624$; $P < 0.001$). We also found a positive relationship of sICAM-1 or sVCAM-1 levels with transaminases and alkaline phosphatase circulation levels ($P < 0.05$). Nonresponder patients had higher sICAM-1 and sVCAM-1 serum levels, and patients with sustained virologic response had significantly lower levels of sICAM-1 ($P = 0.001$) and sVCAM-1 ($P = 0.019$). **CONCLUSION:** HIV and HCV coinfection induces alterations in sICAM-1 and sVCAM-1 serum levels, which were higher in patients with HCV-genotype 1 and advanced stage of HCV infection. However, response to IFN-alpha + RBV may reduce these cardiovascular risk markers.

Treatment of hepatitis C in HCV mono-infected and in HIV-HCV co-infected patients: an open-labelled comparison study. Gonvers JJ, Heim MH, Cavassini M, et al. Swiss Med Wkly. 2010 Jul 19;140:w13055. doi: 10.4414/smw.2010.13055.

<http://www.ncbi.nlm.nih.gov/pubmed/20648398>

BACKGROUND/AIMS: Treatment of chronic HCV infection has become a priority in HIV+ patients, given the faster progression to end-stage liver disease. The primary endpoint of this study was to evaluate and compare antiviral efficacy of Peginterferon alpha 2a plus ribavirin in

HIV-HCV co-infected and HCV mono-infected patients, and to examine whether 6 months of therapy would have the same efficacy in HIV patients with favourable genotypes 2 and 3 as in mono-infected patients, to minimise HCV-therapy-related toxicities. Secondary endpoints were to evaluate predictors of sustained virological response (SVR) and frequency of side-effects.

METHODS: Patients with genotypes 1 and 4 were treated for 48 weeks with Pegasys 180 microg/week plus Copegus 1000-1200 mg/day according to body weight; patients with genotypes 2 and 3 for 24 weeks with Pegasys 180 microg/week plus Copegus 800 mg/day.

RESULTS: 132 patients were enrolled in the study: 85 HCV mono-infected (38: genotypes 1 and 4; 47: genotypes 2 and 3), 47 HIV-HCV co-infected patients (23: genotypes 1 and 4; 24: genotypes 2 and 3). In an intention-to-treat analysis, SVR for genotypes 1 and 4 was observed in 58% of HCV mono-infected and in 13% of HIV-HCV co-infected patients ($P = 0.001$). For genotypes 2 and 3, SVR was observed in 70% of HCV mono-infected and in 67% of HIV-HCV co-infected patients ($P = 0.973$). Undetectable HCV-RNA at week 4 had a positive predictive value for SVR for mono-infected patients with genotypes 1 and 4 of 0.78 (95% CI: 0.54-0.93) and of 0.81 (95% CI: 0.64-0.92) for genotypes 2 and 3. For co-infected patients with genotypes 2 and 3, the positive predictive value of SVR of undetectable HCV-RNA at week 4 was 0.76 (95% CI, 0.50-0.93). Study not completed by 22 patients (36%): genotypes 1 and 4 and by 12 patients (17%): genotypes 2 and 3. **CONCLUSION:** Genotypes 2 or 3 predict the likelihood of SVR in HCV mono-infected and in HIV-HCV co-infected patients. A 6-month treatment with Peginterferon alpha 2a plus ribavirin has the same efficacy in HIV-HCV co-infected patients with genotypes 2 and 3 as in mono-infected patients. HCV-RNA negativity at 4 weeks has a positive predictive value for SVR. Aggressive treatment of adverse effects to avoid dose reduction, consent withdrawal or drop-out is crucial to increase the rate of SVR, especially when duration of treatment is 48 weeks. Sixty-one percent of HIV-HCV co-infected patients with genotypes 1 and 4 did not complete the study against 4% with genotypes 2 and 3.

HBsAg profiles in patients receiving peginterferon alfa-2a plus ribavirin for the treatment of dual chronic infection with hepatitis B and C viruses. Yu ML, Lee CM, Chuang WL, et al. *J Infect Dis.* 2010 Jul 1;202(1):86-92.

<http://www.ncbi.nlm.nih.gov/pubmed/20482252>

BACKGROUND: With use of peginterferon alfa-2a and ribavirin combination therapy in patients with dual chronic hepatitis B virus (HBV) and hepatitis C virus (HCV) infection, 11.2% of patients achieved clearance of hepatitis B surface antigen (HBsAg) at 6 months after treatment; however, reactivation of HBV DNA was observed in 36.3%. We investigated the predictive potential of HBsAg quantification. **METHODS:** HBsAg quantification was performed in 120 e antigen-negative patients dually infected with HBV and hepatitis C virus and treated with peginterferon alfa-2a/ribavirin for 48 weeks (HCV genotype 1; $n = 74$) or 24 weeks (HCV genotype 2/3; $n = 46$). HBsAg was quantified at baseline, week 4, week 12, end of treatment, and 24 weeks after treatment. **RESULTS:** The baseline median serum HBsAg level was 120 IU/mL and decreased gradually during treatment. Low baseline HBsAg was significantly associated with HBsAg clearance (40% for HBsAg level 20 IU/mL vs 2.2% for HBsAg level >20 IU/mL; $P < .05$). A decrease in HBsAg level from baseline to week 12 of 50% was associated with a reduced likelihood of HBV DNA reactivation in patients with baseline undetectable serum HBV DNA (positive predictive value, 89.5%). **CONCLUSIONS:** HBsAg quantification appears to be a useful indicator of posttreatment outcome in patients dually infected with HBV and hepatitis C virus.

Management of HIV and hepatitis virus coinfection. Mendes-Corrêa M, Núñez M. Expert Opin Pharmacother. 2010 Jul 14. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/20629586>

Liver disease related to infection with hepatitis C virus (HCV) and/or hepatitis B virus (HBV) is a frequent cause of morbidity and mortality in those infected with the human immunodeficiency virus (HIV) in this era of highly active antiretroviral therapy (HAART). Although progress has been made in the treatment of HBV and HCV in the setting of HIV-coinfection, there is a lack of data in certain areas and several aspects of the management are unclear at this time. Areas covered in this review: Available data on the treatment of HBV and HCV infections, especially in the HIV-coinfected patient, are presented. Practical aspects of the management of these patients are reviewed, including diagnosis, treatment indications, monitoring, and toxicities. The impact of HAART on liver disease, end-stage-liver disease, and new therapeutic approaches are also reviewed. What the reader will gain: There are two modalities for the treatment of chronic HBV infection: interferon and nucleos(t)ide reverse transcriptase inhibitors (NRTI). The latter is the mainstream of therapy for HIV-HBV-coinfected patients. The double antiviral activity of NRTI requires coordination and careful selection of treatment for both viruses to avoid selection of resistance mutations and toxicity. Combination of pegylated interferon and ribavirin, the current standard treatment for chronic hepatitis C, has significant toxicity and limited efficacy in HIV-HCV-coinfected individuals. Oral anti-HCV treatments are currently under development and need to be studied in the HIV-coinfected population. Liver transplantation has a better outcome in HBV- than in HCV-HIV-coinfected patients. HAART seems to have a positive impact on the liver disease of HBV- and/or HCV-coinfected subjects but the CD4 threshold above which the benefit might take place is unknown at this time. Take home message: Anti-HBV treatment in the HIV-coinfected patient relies on the available NRTIs with activity against both viruses. Whereas HBV suppression can be achieved with this approach, toxicities and the selection of HBV-resistant variants result in challenging clinical scenarios. Current anti-HCV treatment (pegylated interferon and ribavirin) has limited efficacy in the HIV-coinfected patient, and STAT-C drugs are eagerly awaited.

Hepatic steatosis in patients coinfecting with human immunodeficiency virus/hepatitis C virus: a meta-analysis of the risk factors. Machado MV, Oliveira AG, Cortez-Pinto H.

Hepatology. 2010 Jul;52(1):71-8.

<http://www.ncbi.nlm.nih.gov/pubmed/20578130>

Hepatic steatosis (HS) is frequent in patients with hepatitis C virus (HCV) infection, occurring in 40%-80%, associating with metabolic and virus-related factors, namely, genotype 3 and viral load. Human immunodeficiency virus (HIV) infection and antiretroviral treatment seem to be risk factors for HS. Several studies addressed this issue in coinfecting patients, with discrepant results. A meta-analysis was performed on the HS risk factors in coinfecting patients. Eligible studies were identified through structured keywords including coinfection, HCV, HIV, and steatosis in relevant databases including PubMed. Pooled odds ratios (ORs) and confidence limits (CIs) were obtained with the random-effects model and the DerSimonian-Laird method. Twelve studies, including 1,989 coinfecting patients, were selected. Twenty percent were infected with HCV genotype 3. The overall prevalence of HS was 50.8% (23%-72%). Four studies also included 1,540 HCV mono-infected patients, not showing an increased risk for HS in coinfecting patients (OR 1.61, 95% CI 0.84-3.10, $P = 0.151$). In coinfecting patients, HS was associated with higher body mass index (OR 1.13, 95% CI 1.07-1.19, $P < 0.001$), diabetes mellitus (OR 2.32,

95% CI 1.32-4.07, $P = 0.003$), elevated alanine aminotransferase levels (OR 1.28, 95% CI 1.02-1.61, $P = 0.035$), necroinflammatory activity (OR 1.72, 95% CI 1.11-2.67, $P = 0.016$), and fibrosis (OR 1.67, 95% CI 1.20-2.34, $P = 0.003$). No associations were found between HS and gender, other metabolic factors (dyslipidemia, glucose, metabolic syndrome), HCV-related factors (genotype, viral load), or HIV-related factors (viral load, CD4 count, antiretroviral therapy, and class of medication). **CONCLUSION:** In coinfecting patients, HS does not seem to be more frequent than in HCV mono-infected patients and is mostly associated with metabolic factors, such as increased weight, diabetes mellitus, and more severe liver disease. The fact that no associations with HCV factors were found may be due to the small percentage of genotype 3-infected patients.

Interobserver concordance in the assessment of liver fibrosis in HIV/HCV-coinfecting patients using transient elastometry. Neukam K, Recio E, Camacho A, et al. Eur J

Gastroenterol Hepatol. 2010 Jul;22(7):801-7.

<http://www.ncbi.nlm.nih.gov/pubmed/19773664>

OBJECTIVES: Although the reproducibility of transient elastometry (TE) in hepatitis C virus (HCV)-mono-infected patients seems to be high, this may not be the case in HIV/HCV-coinfecting patients because of different degrees of steatosis and/or inflammation. This study was aimed to determine the interobserver concordance of TE measurements in HIV/HCV-coinfecting patients.

METHODS: A total of 188 patients were evaluated in a cross-sectional, prospective study in two hospitals. The interobserver variability of TE results and the rate of unequal classification of significant fibrosis (cutoff value = 7.2 kPa) and cirrhosis (cutoff value = 14.6 kPa) for two observers were evaluated. **RESULTS:** The values of liver stiffness (LS) for two observers highly correlated [intra-class correlation index = 0.976; 95% confidence interval (CI): 0.968-0.982]. The kappa indexes for the concordance of patient classification were 0.60 for significant fibrosis and 0.89 for cirrhosis. Using two cutoff points to diagnose or rule out significant fibrosis ($LS \geq 9$ kPa or < 6 kPa) yielded a kappa index of 0.96, but 46% of patients were not classified.

Covariables that influenced the interobserver agreement were a high interquartile range in the determination (adjusted odd ratio: 0.189; 95% CI: 0.087-0.411; $P = 0.001$) and elevated levels of triglycerides (adjusted odd ratio: 1.004; 95% CI: 1.000-1.008; $P = 0.031$). **CONCLUSION:** TE measurement is an observer-independent method to evaluate LS in HIV/HCV coinfecting patients. The concordance of the classification of mild-to-severe fibrosis is good and for the diagnosis of cirrhosis is excellent. Lower interquartile ranges and triglyceride levels lead to a higher interobserver agreement.

Effect of control selection on sustained viral response rates in genotype 2/3 HCV mono-infected versus HIV/HCV co-infected patients. Nilsson J, Weiland O. Scand J Infect Dis. 2010 Jul;42(6-7):533-9.

<http://www.ncbi.nlm.nih.gov/pubmed/20214543>

Human immunodeficiency virus (HIV) and hepatitis C virus (HCV) co-infected patients have lower rates of sustained viral response (SVR) to treatment than HCV mono-infected patients. A rapid viral response (RVR) with negative HCV-RNA at week 4 predicts SVR in most patients. We evaluated the RVR for the prediction of SVR in mono- and co-infected patients, and the effect caused by the selection of mono-infected controls on SVR rates. Co-infected ($n = 13$) and mono-infected naïve patients ($n = 100$) with HCV genotype 2/3 were treated with 135 microg pegylated interferon alpha-2a weekly and weight-based ribavirin daily for 24 weeks. For each

co-infected patient, 2 mono-infected controls matched for genotype, baseline viral load, and age, were chosen. RVR was achieved in 6/13 (46%) co-infected, 16/26 (62%) matched controls, and 69/98 (70%) mono-infected patients. All co-infected, 14/16 (88%) matched controls, and 66/69 (96%) mono-infected patients with RVR achieved SVR. In total SVR was reached by 10/13 (77%) co-infected patients and 20/26 (77%) matched controls, somewhat lower than the 86/100 (86%) mono-infected patients (not significant). The ability of RVR to predict SVR was high both in co-infected and mono-infected patients with genotypes 2 and 3 chronic HCV, and the results indicate that co-infected patients with well controlled HIV (with CD4 T-cell counts above 300/microl) can be offered the same treatment as mono-infected patients.

Prevalence and correlates of co-infection with human immunodeficiency virus and hepatitis C virus in male injection drug users in Iran. Hosseini M, SeyedAlinaghi S, Kheirandish P, et al. Arch Iran Med. 2010 Jul;13(4):318-23.

<http://www.ncbi.nlm.nih.gov/pubmed/20597566>

OBJECTIVE: Aim of the study was to evaluate the HIV and hepatitis C virus (HCV) coinfection and associated risk behaviors among Injection Drug Users in Detention, Tehran, Iran. **METHODS:** A cross-sectional survey included 499 male Injection Drug Users arrested by police during a predetermined police sweep in Tehran (February, 2006). At the temporary detention center, they were screened using a urine test and a physical examination for injection marks. Those who were identified as injectors were sent to the rehabilitation center for 3 months. A questionnaire was filled out for each individual by interview. Blood specimens were collected for HIV and HCV testing. The variables associated with HIV/HCV coinfection at a significance level of $P < 0.10$ were considered in multivariate analysis. **RESULTS:** Of the 417 participants, 100 (24.0%) had HIV/HCV coinfection (95%CI 19.9 - 28.4). Factors independently associated with HIV/HCV coinfection included history of using opioid in jail, and age ($P < 0.05$). There were not any association between other demographic characteristics (marital status, birthplace, residence, and education), type and years of drug abuse, age of first injection, years of injection, sharing needles inside and outside of jail, injection in jail, history of tattooing, any sexual behavior, and history of sexually transmitted diseases with HIV/HCV coinfection ($P > 0.05$). **CONCLUSIONS:** This study supports that incarceration is contributing to the increased spread of HIV/HCV coinfection. So, there is urgent need for effective harm reduction programs, particularly among incarcerated Injection Drug Users.

Prevalence of hepatitis C virus and hepatitis B virus infections in HIV-positive Chinese patients. Yan YX, Gao YQ, Sun X, et al. Epidemiol Infect. 2010 Jul 2:1-7. [Epub ahead of print] Wang W, Huang XJ, Zhang T, Li M, Zang CP, Li ZC, Wu H.

<http://www.ncbi.nlm.nih.gov/pubmed/20598209>

To evaluate the prevalence of hepatitis C virus (HCV) and/or hepatitis B virus (HBV) infections in HIV-infected patients in China, an epidemiological serosurvey was conducted from May 2007 to September 2008 using a random cluster sampling design of infectious disease hospitals in seven high HIV-prevalent provinces (municipalities). Univariate analysis and logistic regression were used to study the determinants of HIV and HBV and/or HCV co-infection. The overall prevalence was 41.83% (95% CI 40.36-43.30) for anti-HCV and 12.49% (95% CI 11.50-13.48) for HBsAg, respectively. The prevalence of anti-HCV and HBsAg varied according to the route of HIV transmission. Compared to those with sexually acquired HIV infection, intravenous drug users and blood donors/recipients had the greatest risk of carrying anti-HCV. Needle sharing and

unprotected sexual exposures are important modes of transmission for HBV. Further interventions including health education and harm reduction strategies should be implemented in high-risk populations.

Impact of hepatitis C viral replication on CD4+ T-lymphocyte progression in HIV-HCV coinfection before and after antiretroviral therapy. Potter M, Oduyungbo A, Yang H, et al. AIDS. 2010 Jul 31;24(12):1857-65.

<http://www.ncbi.nlm.nih.gov/pubmed/20479633>

OBJECTIVE: HIV is known to have a negative impact on the progression of hepatitis C virus (HCV) infection, whereas the reverse remains unclear. We examined the impact of spontaneous clearance of HCV on CD4(+) T-lymphocyte count progression before and after initiation of antiretroviral therapy (ART) in HIV-HCV coinfecting adults. **METHODS:** Data were analysed from participants in a Canadian, multisite prospective cohort of HIV-infected adults with serologic evidence of HCV infection. The rate of CD4(+) T-lymphocyte change was determined using multivariate mixed linear regression comparing chronically HCV RNA+ with spontaneous clearers (persistently HCV RNA- without HCV therapy). **RESULTS:** Baseline characteristics of the 271 participants analysed did not differ between individuals whose HCV RNA cleared (n = 35) and those whose HCV RNA persisted (n = 236) except with respect to markers of liver disease. HCV RNA+ individuals had on average seven-times slower recovery of CD4(+) T-cells on chronic ART compared with HCV RNA-: (adjusted change in absolute CD4 cell T-lymphocyte count per year: 4 (95% confidence interval, -0.6 to 8) cells/microl vs. 26 (95% confidence interval, 12 to 41) cells/microl; P < 0.001. Analyses restricted to individuals initiating ART showed similar results. There was also a trend to greater CD4 decline prior to ART initiation among those HCV RNA+, although this did not reach statistical significance. **CONCLUSION:** We found that CD4 cell progression is negatively affected by the presence of ongoing HCV replication in coinfecting individuals initiating ART which persisted throughout stable ART suggesting active HCV infection affects immune restoration even after years of ART exposure.

Hepatitis C infection in HIV-1 natural viral suppressors. Sajadi MM, Shakeri N, Talwani R, Redfield RR. AIDS. 2010 Jul 17;24(11):1689-95.

<http://www.ncbi.nlm.nih.gov/pubmed/20467290>

OBJECTIVE: HIV-1 natural viral suppressors (NVSs) demonstrate an intrinsic ability to control HIV-1 replication in the absence of antiretroviral therapy. The objective of this study was to investigate whether HIV-infected NVSs also demonstrate enhanced ability to control hepatitis C virus (HCV) infection, and whether HCV infection in the NVSs affects the degree of HIV control. **DESIGN AND METHODS:** A cross-sectional study was undertaken to compare HCV-related parameters in the NVS to the two race-matched cohorts (HIV/HCV-coinfecting or HCV-monoinfecting patients). Within the NVS, HIV-related parameters were compared based on the presence or absence of chronic HCV. **RESULTS:** NVS patients had a significantly higher clearance rate of HCV at 23.3% (seven of 30), compared to the 6.5% (23 of 350) of HIV/HCV-coinfecting and 9.1% (32 of 350) of HCV-monoinfecting patients (P = 0.005 and P = 0.024, respectively). Apart from the HCV clearance rate, there was no significant difference in HCV-related parameters such as HCV viral load or liver histology in the NVS with chronic HCV compared to HCV/HIV-coinfecting patients or HCV-monoinfecting patients. However, NVS patients with chronic HCV infection had statistically significant lower CD4 cell count and

CD4%, and lower CD4/CD8 ratio compared to those NVSs without chronic HCV infection ($P = 0.029$, $P = 0.046$, and $P = 0.062$, respectively). **CONCLUSION:** It appears that some NVS patients have the ability to effectively control multiple agents that can cause chronic viral infections. In addition, it appears that the presence of chronic HCV infection within the NVS adversely affects immunological parameters.

IP-10 predicts the first phase decline of HCV RNA and overall viral response to therapy in patients co-infected with chronic hepatitis C virus infection and HIV. Falconer K, Askarieh G, Weis N, et al. *Scand J Infect Dis.* 2010 Jul 7. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/20608766>

The aim of this study was to investigate the utility of baseline plasma interferon-gamma inducible protein-10 (IP-10) levels in human immunodeficiency virus (HIV)-hepatitis C virus (HCV) co-infected patients. Baseline IP-10 was monitored during HCV combination therapy in 21 HIV-HCV co-infected patients (HCV genotype 1 ($n = 16$), 2 ($n = 2$), and 3 ($n = 3$)). Lower baseline IP-10 was significantly associated with a rapid decline in HCV RNA, in particular with the first phase reduction, and similar cut-off levels (<150 and >600 pg/ml) as in HCV mono-infected patients apply. **In conclusion**, baseline IP-10 <150 pg/ml is predictive of a favourable viral response to HCV therapy in HIV-HCV co-infected patients, and may thus be useful in encouraging such difficult-to-treat patients to initiate therapy.

Acute hepatitis C in HIV-infected men who have sex with men: an emerging sexually transmitted infection. van de Laar TJ, Matthews GV, Prins M, Danta M. *AIDS.* 2010 Jul 31;24(12):1799-812.

<http://www.ncbi.nlm.nih.gov/pubmed/20601854>

Since 2000 outbreaks of acute hepatitis C virus (HCV) among HIV-positive men who have sex with men (MSM) who denied injecting drug use have been reported from Europe, the United States, Canada and Australia. Given the burden of liver disease, in particular HCV, on the morbidity and mortality in HIV patients in the era of combination antiretroviral therapy, the rapid and significant rise in the incidence of HCV in the HIV-infected MSM population in high-income countries is alarming. This relates to a significant change in the epidemiology of HCV that has occurred, with HCV emerging as a sexually transmitted infection within this population. Work to date suggests that this permucosal HCV transmission results from high-risk sexual and noninjecting drug use behaviours, reopening the discussion on the importance of sexual transmission. Given this occurs almost exclusively in HIV-infected MSM, HIV probably has a critical role mediated either through behavioural and/or biological factors. Finally, the management of acute HCV in HIV infection is complicated by concomitant HIV infection and combination antiretroviral therapy. This review will synthesize the most recent epidemiological, immunological and management issues that have emerged as a result of the epidemic of acute HCV among HIV-infected MSM.

Cellular immune responses to HCV core increase and HCV RNA levels decrease during successful antiretroviral therapy. Rohrbach J, Robinson N, Harcourt G, et al. *Gut.* 2010 Jul 26. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/20660698>

BACKGROUND Hepatitis C virus (HCV) infection is a major cause of morbidity in HIV infected individuals. Coinfection with HIV is associated with diminished HCV-specific immune

responses and higher HCV RNA levels. **Aims** To investigate whether long-term combination antiretroviral therapy (cART) restores HCV-specific T cell responses and improves the control of HCV replication. **METHODS** T cell responses were evaluated longitudinally in 80 HIV/HCV coinfecting individuals by ex vivo interferon-gamma-ELISpot responses to HCV core peptides, that predominantly stimulate CD4(+) T cells. HCV RNA levels were assessed by real-time PCR in 114 individuals. **RESULTS** The proportion of individuals with detectable T cell responses to HCV core peptides was 19% before starting cART, 24% in the first year on cART and increased significantly to 45% and 49% after 33 and 70 months on cART ($p=0.001$). HCV-specific immune responses increased in individuals with chronic (+31%) and spontaneously cleared HCV infection (+30%). Median HCV RNA levels before starting cART were 6.5 log₁₀ IU/ml. During long-term cART, median HCV-RNA levels slightly decreased compared to pre-cART levels (-0.3 log₁₀ IU/ml, $p=0.02$). **CONCLUSIONS:** Successful cART is associated with increasing cellular immune responses to HCV core peptides and with a slight long-term decrease in HCV RNA levels. These findings are in line with the favourable clinical effects of cART on the natural history of hepatitis C and with the current recommendation to start cART earlier in HCV/HIV coinfecting individuals.

Changes in liver stiffness in patients with chronic hepatitis C with and without HIV co-infection treated with pegylated interferon plus ribavirin. Macías J, Del Valle J, Rivero A, et al. *J Antimicrob Chemother.* 2010 Jul 22. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/20656678>

OBJECTIVES: To evaluate the changes in liver stiffness measurement (LSM) in patients infected by hepatitis C virus (HCV) under pegylated interferon (Peg-IFN) plus ribavirin therapy. **METHODS:** One hundred and forty-three HCV-infected patients, of whom 97 (68%) were also carrying HIV, who started treatment with Peg-IFN/ribavirin were included in this prospective cohort study. The outcome variable of the study was the change in LSM between baseline and the scheduled date for evaluating sustained virological response (SVR). **RESULTS** The median (Q1-Q3) LSM values at baseline and at the SVR assessment date were 8.1 (6.2-11.6) kPa and 6.8 (5.2-9.8) kPa ($P < 0.001$), respectively. The median (Q1-Q3) decrease between both timepoints was -1 (-2.75, 0.3) kPa. The baseline LSM decreased $\geq 20\%$ in 37 (46%) patients with SVR and in 19 (30%) without SVR ($P = 0.05$). In the linear regression analysis, baseline LSM {beta [standard error (SE)] -0.712 (0.044), $P = 0.004$ }, alcohol intake ≥ 50 g/day [beta (SE) 0.202 (0.030), $P = 0.014$] and achievement of SVR [beta (SE) -0.238 (0.026), $P = 0.029$] were independently associated with changes in LSM. **CONCLUSIONS** LSM decreases significantly among patients with chronic HCV infection who achieve SVR with Peg-IFN/ribavirin. These patients show a higher frequency of LSM reduction $\geq 20\%$ at the date of SVR evaluation.

Hepatitis C transmission, prevention, and treatment knowledge among patients with HIV.

Proeschold-Bell RJ, Blouin R, Reif S, et al. *South Med J.* 2010 Jul;103(7):635-41.

<http://www.ncbi.nlm.nih.gov/pubmed/20531062>

OBJECTIVE: Liver disease associated with hepatitis C virus (HCV) is a serious cause of mortality among people living with human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) (PLWHA). Little is known about the HCV knowledge of PLWHA. **METHODS:** One hundred seventy-nine patients at an infectious disease clinic were interviewed on HCV knowledge and alcohol use. **RESULTS:** Sixty-six percent of participants indicated that HCV is transmitted through blood; 53% indicated that persons with HIV-HCV co-infection can

benefit from HCV treatment; and 79% and 74%, respectively, indicated that safer sex and safer injection techniques can prevent HCV transmission. Among PLWHA with self-reported HCV, 97% indicated that persons with HCV should not drink alcohol, but 32% reported using alcohol in the past 30 days. **CONCLUSIONS:** Health education is needed to prevent HCV infections and increase HCV treatment-seeking. Higher education levels were related to more accurate HCV knowledge, indicating the need for health promotion for PLWHA of lower education levels.

COMPLEMENTARY AND ALTERNATIVE MEDICINE

Vitamin D supplementation improves response to antiviral treatment for recurrent hepatitis C. Bitetto D, Fabris C, Fornasiere E, *Transpl Int.* 2010 Jul 22. [Epub ahead of print] <http://www.ncbi.nlm.nih.gov/pubmed/20649944>

In immune-competent patients, higher vitamin D levels predicted sustained viral response (SVR) following interferon (INF) and ribavirin therapy for chronic hepatitis C. This study aimed to verify the influence of vitamin D serum levels and/or vitamin D supplementation in predicting SVR rates for recurrent hepatitis C (RHC). Forty-two consecutive patients were treated for RHC with combination therapy with INF-alpha and ribavirin for 48 weeks. Vitamin D serum levels were measured in all patients before antiviral therapy. In 15 patients oral vitamin D3 supplementation was administered to avoid further bone loss. SVR was observed in 13 patients; it was achieved in 1/10 severely vitamin D deficient (≤ 10 ng/ml) patients, in 6/20 deficient (>10 and ≤ 20 ng/ml) and in 6/12 with near normal (>20 ng/ml) 25-OH vitamin D serum levels ($P < 0.05$). Cholecalciferol supplementation, in the presence of a normal or near normal baseline vitamin D concentration, (improvement of chi-square $P < 0.05$, odds ratio 2.22) and possessing a genotype other than 1 (improvement of chi-square $P < 0.05$, odds ratio 3.383) were the only variables independently associated to SVR. In conclusion, vitamin D deficiency predicts an unfavourable response to antiviral treatment of RHC. Vitamin D supplementation improves the probability of achieving a SVR following antiviral treatment.

DIAGNOSTICS, EPIDEMIOLOGY, AND MISCELLANEOUS WORKS

Determining rates of hepatitis C in a clozapine treated cohort. Sockalingam S, Shammi C, Powell V, Barker L, Remington G. *Schizophr Res.* 2010 Jul 5. [Epub ahead of print] <http://www.ncbi.nlm.nih.gov/pubmed/20605572>

OBJECTIVE: To determine the prevalence rates of hepatitis C in patients with schizophrenia and schizoaffective disorder being treated with clozapine. **METHODS:** Clozapine-treated outpatients and inpatients were recruited from the Centre for Addiction and Mental Health Schizophrenia Program in Toronto, Canada. All subjects had liver function tests, and positive HCV status was defined as a positive qualitative HCV RNA assay. Subjects completed a self-report questionnaire assessing HCV risk factors, past history of liver disease, previous diagnosis of human immunodeficiency virus (HIV), past hepatitis B virus (HBV) infection and current alcohol use. **RESULTS:** 110 subjects participated in the study and the HCV prevalence rate (antibody and viremia-positive) was 2.7%, compared to a 0.8% prevalence rate in Canada. All study subjects had established housing, none reported a history of HIV, and only one patient had a history of HBV infection. A total of 9% drank two or more drinks on a typical day drinking and 7% endorsed having six or more drinks on one occasion at least monthly. Two of 3HCV-viremia

positive subjects had HCV risk factors, specifically intravenous drug use and intranasal cocaine use. There was no difference between HCV infected and HCV negative subjects on liver function tests. **CONCLUSIONS:** Our study demonstrates elevated rates of HCV in clozapine-treated patients compared to the general population in Canada and are congruent with reports from United States centres. Our study highlights the importance of homelessness and patterns of high-risk behaviour when interpreting HCV prevalence rates in this sub-population of patients and should be explored in future studies.

Liver fibrosis in chronic hepatitis C virus infection: differentiating minimal from intermediate fibrosis with perfusion CT. Ronot M, Asselah T, Paradis V, et al. *Radiology*. 2010 Jul;256(1):135-42.

<http://www.ncbi.nlm.nih.gov/pubmed/20574090>

PURPOSE: To prospectively assess the utility of perfusion computed tomography (CT) for differentiating minimal from intermediate fibrosis in treatment-naïve patients with chronic hepatitis C virus (HCV) infection. **MATERIALS AND METHODS:** This study was approved by the Institutional Review Board, and informed consent was obtained. Fifty-two patients with treatment-naïve HCV infection underwent perfusion CT and percutaneous liver biopsy on the same day. Portal vein, arterial, and total liver perfusion; mean transit time; and distribution volumes for the right and left liver lobes were measured. Liver samples were scored for fibrosis, and fibrosis area was determined. Differences in quantitative perfusion parameters between patients with minimal fibrosis (score of F1) and those with intermediate fibrosis (score of F2 or F3) were tested. **RESULTS:** In patients with intermediate fibrosis (F2 and F3) compared with those with minimal fibrosis (F1), the portal venous perfusion ($87 \text{ mL min}^{-1} 100 \text{ mL}^{-1} \pm 27$ [standard deviation] vs $138 \text{ mL min}^{-1} 100 \text{ mL}^{-1} \pm 112$, $P = .042$) and total liver perfusion ($107 \text{ mL min}^{-1} 100 \text{ mL}^{-1} \pm 31$ vs $169 \text{ mL min}^{-1} 100 \text{ mL}^{-1} \pm 137$, $P = .02$) were significantly decreased, and the mean transit time was significantly increased ($16 \text{ seconds} \pm 4$ vs $13 \text{ seconds} \pm 5$, $P = .025$). At multivariate analysis, only the mean transit time was an independent factor (odds ratio, 1.18; 95% confidence interval: 1.02, 1.37; $P = .030$). Receiver operating characteristic curve analysis showed that a mean transit time threshold of 13.4 seconds allowed discrimination between minimal and intermediate fibrosis with a sensitivity of 71% and a specificity of 65%. **CONCLUSION:** The results of this study show that perfusion changes occur early during fibrosis in chronic HCV infection and can be detected with perfusion CT. Perfusion CT may help to discriminate minimal from intermediate fibrosis. Mean transit time appears to be the most promising perfusion parameter for differentiating between fibrosis stages, although the large amount of overlap in the measured parameters limits the clinical utility of this test at present.

Direct detection of unamplified hepatitis C virus RNA using unmodified gold nanoparticles. Shawky SM, Bald D, Azzazy HM. *Clin Biochem*. 2010 Jul 19. [Epub ahead of print] <http://www.ncbi.nlm.nih.gov/pubmed/20627095>

BACKGROUND: AuNPs exhibit a unique phenomenon known as Surface Plasmon Resonance, which is responsible for their intense red color. This color changes to blue upon aggregation of AuNPs. **OBJECTIVE:** This work aims to develop a rapid, simple and cheap assay for direct detection of unamplified HCV RNA extracted from clinical samples using unmodified AuNPs. **METHODS:** Serum samples were collected from healthy volunteers ($n=45$) and chronic HCV patients ($n=30$). Extracted RNA, hybridization buffer containing PBS, and a primer targeting the

5'UTR of HCV were mixed. The mixture was denatured, annealed, and then cooled to room temperature for 10min followed by addition of AuNPs. **RESULTS:** Salt, primer, AuNPs concentrations and annealing temperature and time were all optimized. In HCV positive specimens, the color of the solution changed from red to blue within 1min. The assay has a sensitivity of 92%, a specificity of 88.9%, and a detection limit of 50 copies/reaction. **CONCLUSIONS:** To our knowledge, this is the first assay that allows the detection of unamplified HCV RNA in clinical specimens using unmodified AuNPs. The developed assay is highly sensitive, has a turnaround time of 30min, and eliminates the need for thermal cycling and detection instruments.

Early viral and peripheral blood mononuclear cell responses to pegylated interferon and ribavirin treatment: the first 24 h. Devitt E, Lawless MW, Sadlier D, et al. *Eur J Gastroenterol Hepatol.* 2010 Jul 13. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/20631625>

OBJECTIVES: This study explored gene expression differences in predicting response to pegylated interferon (IFN-PEG) and ribavirin (RBV) in hepatitis C infection. Current treatment for hepatitis C virus (HCV) with IFN-PEG alpha-2a/b and RBV is an expensive regimen with frequent significant side-effects where less than 60% of patients ultimately achieve a sustained virological response. Responders and nonresponders may not be identified for up to 6 months post-treatment. This dichotomy may be because of differences in the molecular genetic response. **METHODS:** Peripheral blood mononuclear cell samples were obtained from a cohort of 31 infected individuals within the first 24 h of treatment and the extracted RNA was hybridized to genome expression microarrays. Hepatitis C viral kinetics was also examined in these patients. The ability of differentially regulated genes to predict response to therapy was assessed with treatment outcome. **RESULTS:** Distinct patterns of gene expression distinguished responders from nonresponders to HCV treatment. The ultimate response to treatment with IFN-PEG and RBV was observed within the first 24 h of treatment by a greater drop in viral load (mean HCV RNA decline of $1.92 \pm 1.26 \log_{10}$ IU/ml) in responders compared with nonresponders ($P < 0.007$). Induced genes achieved maximal response within 12 h of therapy which coincided with a rapid decline in HCV RNA between 12 and 24 h. This study revealed that peripheral blood mononuclear cell metallothionein 2A, CCRL2, tumour necrosis factor-alpha-induced protein 6 (TNFAIP6) and IFN-induced protein with tetratricopeptide repeats 2 expression predicted viral treatment response to therapy verified by quantitative real time polymerase chain reaction. **CONCLUSION:** This study has identified a noninvasive gene microarray pattern and a set of verified genes to be predictive of hepatitis C patient response to IFN-PEG and RBV treatment within the first 24 h. The potential of this noninvasive diagnostic approach and identified genes as biomarkers of response to treatment warrants further investigation.

Hepatic fibrosis in patients with chronic hepatitis C assessed by transient elastography: implications for determining the efficacy of antiviral therapy. Mendoza J, Trapero-Marugán M, González-Moreno L, et al. *Rev Esp Enferm Dig.* 2010 Jul;102(7):426-34.

<http://www.ncbi.nlm.nih.gov/pubmed/20617863>

BACKGROUND: The efficacy of combination therapy with peginterferon plus ribavirin to eradicate viral infection in patients with chronic hepatitis C (CHC) is well established; moreover, it is able to arrest or even reverse liver fibrosis. **AIMS:** To analyze the measurements of hepatic stiffness as an index of liver fibrosis using transient elastography (TE) in patients who underwent

a sustained virological response (SVR) during long-term follow-up; comparing the changes in the severity of fibrosis with non-responders patients. **MATERIAL AND METHODS:** After hepatic fibrosis was studied in three patients with CHC who underwent a SVR during long-term follow up, a prospective study was initiated in 24 patients with CHC who received combination therapy to compare the evolution of fibrosis in those with SVR and those who were non-responders. The genotype of hepatitis C virus (HCV) and the degree of viremia were determined. METAVIR scoring system was used for liver fibrosis. Hepatic stiffness was measured by TE. **RESULTS:** Of the initial three patients pre-treatment liver biopsies revealed active disease and fibrosis (stage 3) in two and mild fibrosis (stage 1) in one. After several years of follow up serum AST/ALT levels were normal and HCV RNA was undetectable in each case; in contrast to the baseline histological assessments of fibrosis, values for hepatic stiffness (3.4-6.9 KPa) were compatible with an absence of any appreciable hepatic fibrosis. In the prospective study, 8 patients underwent a SVR and 16 were non-responders. TE indicated that the severity of hepatic fibrosis in the SVR group improved in 7 (88%) patients, whereas in the non-responder it improved in only 4 (25%) ($p < 0.05$). The difference between development of severe fibrosis ($F \geq 3$) in responders and non-responders was not significant ($p = 0.23$), possibly due to the small sample size. **CONCLUSIONS:** Regression of hepatic fibrosis appears to be common in patients with CHC who undergo a SVR. TE is a simple non-invasive technique that enables multiple assessments of the severity of hepatic fibrosis to be made efficiently during long-term follow-up of patients with CHC who receive combination antiviral therapy.

MELD Era: Is this time to replace the original Child-Pugh score in patients with decompensated cirrhosis of liver. Shaikh S, Ghani H, Memon S, Baloch GH, Jaffery M, Shaikh K. J Coll Physicians Surg Pak. 2010 Jul;20(7):432-5.

<http://www.ncbi.nlm.nih.gov/pubmed/20642940>

OBJECTIVE: To compare the predictive value of MELD (Model of end stage liver disease) and Child-Pugh (CP) scores in patients with decompensated cirrhosis of liver. Study Design: Descriptive study. **PLACE AND DURATION OF STUDY:** Medical Department, Liaquat University of Medical and Health Sciences, Jamshoro/ Hyderabad, from August 2006 to October 2007. **METHODOLOGY:** This study included 110 consecutive patients with decompensated cirrhosis of liver diagnosed either clinically or radiologically were followed-up during hospital stay. Studied variables included demographic data, cirrhosis related complications and investigations. Patients were classified according to original CP classification into A, B and C. MELD score was estimated from serum bilirubin, serum creatinine and INR (International normalized ratio) of the patients. Duration of hospitalization and in-hospital mortality were made as the end points of the study. T-test and Chi-square test were done for continuous and categorical data. Original CP and MELD score were compared by the ROC curve. 0.05 was kept as the level of significance. **RESULTS:** There were 110 patients with decompensated cirrhosis of liver. Mean age was 46.76 ± 12.93 years. There were 72 (65%) male and 38 (35%) females patients. Hepatitis C was the most prevalent cause of cirrhosis of liver present in 60/110 (60%) cases. Ascites was present in 93/110 (83%) patients. The mean MELD scores were 2.23 ± 0.712 (95% CI 2.09 - 2.36) and for CTP 2.52 ± 0.586 (95%; CI 2.41-2.63). The outcome of the patients were 12 deaths (11%); 54 (49%) remained hospitalized for up to 14 days and 44 (40%) for > 14 days. The majority of deaths and prolong hospitalization were found in patients with MELD score > 15 as well as with Child-Pugh grade C. The c-statistic was 0.726 ($p=0.001$) for CP score,

and 0.642 for MELD score ($p=0.021$). **CONCLUSION:** The MELD score was not found to be superior to CTP score for short-term prognostication of patients with cirrhosis in this study.

Hepatitis C virus prevalence and clearance among US Blood Donors, 2006-2007: associations with birth cohort, multiple pregnancies, and body mass index. Murphy EL, Fang J, Tu Y, et al. J Infect Dis. 2010 Jul 9. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/20617929>

BACKGROUND: During the period 1992-1993, the prevalence of hepatitis C virus (HCV) antibodies (anti-HCV) among US blood donors was 0.36%, but contemporary data on the prevalence of antibody to HCV and the prevalence of HCV RNA are lacking. **METHODS:** We performed a large, cross-sectional study of blood donors at 6 US blood centers during 2006-2007. Anti-HCV was measured with enzyme-linked immunosorbent assay followed by immunoblot, and HCV RNA was measured with nucleic acid testing. Adjusted odds ratios (aORs) were derived using multivariable logistic regression. **RESULTS:** Of 959,281 donors, 695 had anti-HCV detected (prevalence, 0.072%). Of those with anti-HCV, 516 (74%) had test results positive for HCV RNA, and 179 (26%) had test results that were negative for HCV RNA. Compared with the prevalence during the period 1992-1993, prevalence during 2006-2007 was lower and peaked in older age groups. Anti-HCV was associated with a body mass index (BMI) >30 (aOR, 0.6; 95% confidence interval [CI], 0.5-0.8), and among women, it was associated with higher gravidity (aOR for 5 vs 0 pregnancies, 3.2; 95% CI, 1.9-5.4). HCV RNA negative status was associated with black race (aOR, 0.4; 95% CI, 0.2-0.7), having more than a high school education (aOR, 1.6; 95% CI, 1.1-2.4), and BMI >30 (aOR, 2.4; 95% CI, 1.4-3.9).

CONCLUSIONS: Decreasing HCV prevalence is most likely attributable to culling of seropositive donors and a birth cohort effect. We found new associations between anti-HCV prevalence and gravidity and obesity. Recently discovered genetic factors may underlie differences in HCV RNA clearance in black donors.

Alcohol and hepatitis C virus-interactions in immune dysfunctions and liver damage.

Szabo G, Wands JR, Eken A, et al. Alcohol Clin Exp Res. 2010 Jul 1. [Epub ahead of print]
<http://www.ncbi.nlm.nih.gov/pubmed/20608905>

Hepatitis C virus infection affects 170 million people worldwide, and the majority of individuals exposed to HCV develop chronic hepatitis leading to progressive liver damage, cirrhosis, and hepatocellular cancer. The natural history of HCV infection is influenced by genetic and environmental factors of which chronic alcohol use is an independent risk factor for cirrhosis in HCV-infected individuals. Both the hepatitis C virus and alcohol damage the liver and result in immune alterations contributing to both decreased viral clearance and liver injury. This review will capture the major components of the interactions between alcohol and HCV infection to provide better understanding for the molecular basis of the dangerous combination of alcohol use and HCV infection. Common targets of HCV and alcohol involve innate immune recognition and dendritic cells, the critical cell type in antigen presentation and antiviral immunity. In addition, both alcohol and HCV affect intracellular processes critical for hepatocyte and immune cell functions including mitochondrial and proteasomal activation. Finally, both chronic alcohol use and hepatitis C virus infection increase the risk of hepatocellular cancer. The common molecular mechanisms underlying the pathological interactions between alcohol and HCV include the modulation of cytokine production, lipopolysaccharide (LPS)-TLR4 signaling, and reactive oxygen species (ROS) production. LPS-induced chronic inflammation is not only a

major cause of progressive liver injury and fibrosis, but it can also contribute to modification of the tissue environment and stem cells to promote hepatocellular cancer development. Alteration of these processes by alcohol and HCV produces an environment of impaired antiviral immune response, greater hepatocellular injury, and activation of cell proliferation and dedifferentiation.

Emerging therapies for hepatitis C virus. Birerdinc A, Younossi ZM. *Expert Opin Emerg Drugs*. 2010 Jul 15. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/20629602>

Currently, 170 million people worldwide are affected by the HCV. Chronic HCV infection is amongst the leading causes of chronic liver disease and its complications such as cirrhosis and hepatocellular carcinoma, making it the most common reason for liver transplantation. The current standard of treatment for HCV is pegylated IFN-alpha plus ribavirin. This treatment, when administered for the standard duration, allows sustained virological response (SVR) in approximately 50% of patients infected with HCV and about 40% for HCV genotype 1, the most prevalent form of HCV in the US. SVR rates for populations with co-morbidities (patients with chronic renal disease) and certain ethnic backgrounds (African Americans and Hispanics) are lower. Given the high prevalence and relatively low cure rates of current antiviral therapy, the burden of HCV is enormous. Areas covered in this review: Faced with this urgent and growing medical need, research into novel therapeutic compounds for the treatment of HCV is a rapidly growing industry. Several novel compounds are in advanced stages of clinical development, such as HCV protease inhibitors (particularly those against NS3-4A protease), HCV polymerase inhibitors (including both nucleoside and non-nucleoside analogs) and cyclophilin inhibitors. What the reader will gain: HCV treatment has seen many advances in the last decade and the discovery process has been fraught with both successes and disappointments. Through a process of rigorous research, the current late stage novel HCV therapeutics seem to have overcome some of the obstacles met by their early predecessors and offer the promise of meeting the shortfalls of the current standard of treatment. Take home message: Data from clinical trials are encouraging and suggest that combination therapies of these novel agents may have the potential to shorten treatment duration and increase viral clearance when used in conjunction with pegylated IFN-alpha and ribavirin.

Direct economic burden of chronic hepatitis C virus in a United States managed care population. Davis KL, Mitra D, Medjedovic J, Beam C, Rustgi V. *J Clin Gastroenterol*. 2010 Jul 10. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/20628308>

GOALS AND BACKGROUND: To estimate all-cause and disease-related resource utilization and costs among managed care enrollees with chronic hepatitis C virus (HCV). **STUDY:** A large United States claims database was analyzed (1/1/2002 to 12/31/2006). Inclusion criteria were: diagnosis of chronic HCV; no hepatitis B diagnoses; ≥ 6 and ≥ 12 months of continuous plan enrollment prediagnosis and postdiagnosis, respectively. Use and costs of medical services and prescription drugs over a 12-month period postdiagnosis were evaluated. Outcomes were assessed in controls without HCV matched (1:1) on age, sex, and plan enrollment. All cost estimates were generated using multivariate generalized linear models to adjust for additional covariates and skewness common in health care cost data. **RESULTS:** Of the 20,662 patients who met all inclusion criteria, mean age was 49 years; 61% were male. Adjusted all-cause costs were \$20,961 per HCV patient, compared with \$5451 per control ($P < 0.0001$). Hospitalization

occurred in 24% of HCV patients compared with 7% of controls ($P < 0.0001$). Mean inpatient costs were \$5892 and \$1159 per patient, respectively ($P < 0.0001$). Patients with HCV had higher prescription costs compared with controls (\$6191 vs. \$1315; $P < 0.0001$). At \$6864 per patient, disease-related costs were nearly one-third of all costs in patients with HCV, which exceeded all-cause costs among controls by 26% ($P < 0.0001$). **CONCLUSIONS:** Chronic HCV is a costly disease to managed care organizations. Disease-related costs in HCV exceed all-cause costs in demographically matched controls. Increased efforts in HCV screening and early treatment, particularly before progression to liver cirrhosis, may lead to long-term cost savings in HCV management for managed care systems.

Viral pathogens. Ragni MV, Sherman KE, Jordan JA. *Haemophilia*. 2010 Jul;16 Suppl 5:40-6.

<http://www.ncbi.nlm.nih.gov/pubmed/20590855>

Despite continuous improvement in safety and purity of blood products for individuals with haemophilia, transmissible agents continue to affect individuals with haemophilia. This chapter addresses three viral pathogens with significant clinical impact: HIV, hepatitis C and parvovirus B19. Hepatitis C is the leading cause of chronic hepatitis and the major co-morbid complication of haemophilia treatment. Clinically, asymptomatic intermittent alanine aminotransferase elevation is typical, with biopsy evidence of advanced fibrosis currently in 25%. Current treatment is effective in up to 70%, and many new agents are in development. For those progressing to end-stage liver disease, liver transplantation outcomes are similar to those in non-haemophilia subjects, although pretransplant mortality is higher. HIV infection, the second leading co-morbid condition in haemophilia, is managed as a chronic infection with highly active antiretroviral therapy (HAART). HAART also slows hepatitis C virus (HCV) progression in those with HIV/HCV co-infection. Viral inactivation and recombinant technologies have effectively prevented transfusion-transmitted viral pathogens in haemophilia. Human parvovirus B19 infection, typically associated with anaemia or, rarely severe aplastic crisis, is a non-lipid enveloped virus, for which standard inactivation techniques are ineffective. Thus, nucleic acid testing (NAT) to screen the blood supply for B19 DNA is currently under consideration by the Food and Drug Administration. To the extent, viral inactivation, recombinant, and NAT technologies are available worldwide, and the lifespan for those with haemophilia is approaching that of the normal population. **The purpose of this chapter** is to provide an update on three clinically significant transfusion-transmitted viral pathogens.

Pharmacy participation in non-prescription syringe sales in Los Angeles and San Francisco Counties, 2007. Cooper EN, Dodson C, Stopka TJ, Riley ED, Garfein RS, Bluthenthal RN. *J Urban Health*. 2010 Jul;87(4):543-52.

<http://www.ncbi.nlm.nih.gov/pubmed/20549568>

Increasing sterile syringe access for injection drug users (IDUs) is one way to prevent HIV and hepatitis C virus (HCV) transmission in this population. In 2005, California Senate Bill 1159 allowed counties to adopt the Disease Prevention Demonstration Project (DPDP). Where enacted, the DPDP allows pharmacies that register with the county to sell up to ten syringes to adults without a prescription. In the current study, we describe pharmacy participation in nonprescription syringe sales (NPSS) in two counties in California and examine factors associated with NPSS. Telephone and in-person interviews were conducted in Los Angeles (LA) and San Francisco (SF) with 238 pharmacies in 2007 ($n = 67$ in SF; $n = 171$ in LA). Quantitative survey items captured pharmacy registration with the county, pharmacy policies/practices,

episodes and conditions of NPSS and refusals to sell, potential negative consequences of NPSS, and staff attitudes regarding HIV and HCV prevention for IDUs. Overall, 42% of pharmacies reported NPSS (28% in LA and 81% in SF), although only 34% had registered with the county (17% in LA and 76% in SF). Many pharmacies required proof of a medical condition (80% in LA and 30% in SF) and refused NPSS if the customer was a suspected IDU (74% in LA, 33% in SF). Few negative consequences of NPSS were reported. In multivariate logistic regression analysis, we found that the odds of NPSS were significantly higher among pharmacists who thought syringe access was important for preventing HIV among IDUs [adjusted odds ratio (AOR) = 2.95; 95% confidence interval (CI) = 1.10-7.92], were chain pharmacies (AOR = 12.5; 95% CI = 4.55-33.33), and were located in SF (AOR = 4.88; 95% CI = 1.94-12.28). These results suggest that NPSS were influenced by pharmacists' perception. NPSS might be increased through greater educational efforts directed at pharmacists, particularly those in non-chain pharmacies.

Population risk of syringe reuse: estimating the probability of transmitting bloodborne disease. Sikora C, Chandran AU, Joffe AM, Johnson D, Johnson M. *Infect Control Hosp Epidemiol.* 2010 Jul;31(7):748-54.

<http://www.ncbi.nlm.nih.gov/pubmed/20509761>

BACKGROUND: In 2008, the Medical Officer of Health at Alberta Health Services (Edmonton, Canada) was notified that, in some practice settings, a syringe was used to administer medication through the side port of an intravenous circuit and then the syringe, with residual drug, was used to administer medication to other patients in the same manner. This practice has been implicated in several outbreaks of bloodborne infection in hospital and clinic settings. **METHODS:** A risk assessment model was developed to predict the risk of a patient contracting a bloodborne viral infection from the practice. The risk of transmission was defined as the product of 5 factors: (1) the population prevalence of a specific bloodborne pathogen, (2) the probability of finding a viral bloodborne pathogen in an intravenous circuit, (3) the rate of syringe reuse, (4) the probability of causing disease given a bloodborne pathogen exposure, and (5) the susceptibility of the exposed person. **RESULTS:** The risk was modeled first with consistent use of the proximal port of the intravenous circuit. The risk of transmission of hepatitis B virus was approximately 12-53 transmission events per 1,000,000 exposure events for a range of practice probabilities (ie, frequency of the risk practice) from 20% to 80%, respectively. The risk of transmission of hepatitis C virus was approximately 1.0-4.3 transmission events per 1,000,000 exposure events for the same practice probability range, and the risk of transmission of human immunodeficiency virus was approximately 0.03-0.15 transmission events per 1,000,000 exposure events for the same practice probability range. The use of the distal port was associated with a 10-fold decrease in the risk. **CONCLUSIONS:** Practitioners must practice safe, aseptic injection techniques. The model presented here can be used to estimate the risk of disease transmission in situations where reuse has occurred and can serve as a framework for informing public health action.

Use of gloves and reduction of risk of injury caused by needles or sharp medical devices in healthcare workers: Results from a case-crossover study. Kinlin LM, Mittleman MA, Harris AD, Rubin MA, Fisman DN. *Infect Control Hosp Epidemiol.* 2010 Jul 26. [Epub ahead of print] <http://www.ncbi.nlm.nih.gov/pubmed/20658920>

OBJECTIVE: Standard precautions are advocated for reducing the number of injuries caused by needles and sharp medical devices ("sharps injuries"), but the effectiveness of gloves in preventing such injuries has not been established. We evaluated factors associated with gloving practices and identified associations between gloving practices and sharps-injury risk. **DESIGN:** Usual-frequency case-crossover study. Setting. Thirteen medical centers in the United States and Canada. **PARTICIPANTS:** Six hundred thirty-six healthcare workers who presented to employee health clinics after sharps injury. **METHODS.** Structured telephone questionnaires were administered to assess usual behaviors and circumstances at the time of injury. **RESULTS:** Of 636 injured healthcare workers, 195 were scrubbed in an operating room or procedure suite when injured, and 441 were injured elsewhere. Nonscrubbed individuals were more commonly gloved when treating patients who were perceived to have a high risk of human immunodeficiency virus, hepatitis B virus, or hepatitis C virus infection than when treating other patients (adjusted odds ratio [aOR], 2.53 [95% confidence interval {CI}, 1.30-4.91]). Nurses (aOR, 0.11 [95% CI, 0.04-0.32]) and other employees (aOR, 0.24 [95% CI, 0.07-0.77]) were less commonly gloved at injury than were physicians and physician trainees. Gloves reduced injury risk in case-crossover analyses (incidence rate ratio [IRR], 0.33 [95% CI, 0.22-0.50]). In scrubbed individuals, involvement in an orthopedic procedure was associated with double gloving at injury (aOR, 13.7 [95% CI, 4.55-41.3]); this gloving practice was associated with decreased injury risk (IRR, 0.20 [95% CI, 0.10-0.42]). **CONCLUSIONS:** Although the use of gloves reduces the risk of sharps injuries in health care, use among healthcare workers is inconsistent and may be influenced by risk perception and healthcare culture. Glove use should be emphasized as a key element of multimodal sharps-injury reduction programs.

Sex and age differences in lipid response to chronic infection with the hepatitis C virus in the United States National Health and Nutrition Examination Surveys.

Lao XQ, Thompson A, McHutchison JG, McCarthy JJ. J Viral Hepat. 2010 Jul 19. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/20642483>

SUMMARY: Low levels of serum lipids were reported in subjects chronically infected with the hepatitis C virus (HCV) and correlated with poorer clinical outcomes. Whether HCV 'hypo-lipidemia' is constant across age, sex and race has not been systematically explored. We therefore investigated the association between HCV infection and serum lipid levels in two independent National Health and Nutrition Examination Survey (NHANES) cohorts. HCV antibody status and serum lipid levels were obtained from 14 369 adults from NHANES 1999-2006 and 12 261 from NHANES III (enrolled in 1988-1994). In multivariable models, the prevalence of HCV-associated hypo-low density lipoprotein-cholesterol was highest among women >50 years of age in both NHANES 1999-2006 (OR: 10.51, 95% CI: 2.86, 38.62) and III (OR: 24.21, 95% CI: 6.17, 94.92), but among women <50 years of age, the odds ratios were 3.01 (95% CI: 1.00, 9.04) for NHANES 1999-2006 and 0.52 (95% CI: 0.14, 1.88) for III, respectively. HCV by age interaction among women was significant in both cohorts (P < 0.001 and P = 0.004, respectively). Among men, the odds ratios of HCV-associated hypo-LDL-cholesterol were 2.74 (95% CI: 1.55, 4.85) in NHANES 1999-2006 and 3.84 (95% CI: 1.66, 8.88) in III, respectively, with no significant age effects. Similar patterns were observed for total-cholesterol, but no significantly discernable patterns for high density lipoprotein-cholesterol and triglycerides.

Results show that HCV infection is associated with lower total- and LDL-cholesterol in two US

population-based cohorts, and this relationship varies significantly by age and sex, suggesting a possible influence of sex hormones on host lipid response to HCV infection.

Development of the hepatitis C self-management program. Groessl EJ, Weingart KR, Gifford AL, Asch SM, Ho SB. Patient Educ Couns. 2010 Jul 15. [Epub ahead of print]

<http://www.ncbi.nlm.nih.gov/pubmed/20638216>

OBJECTIVE: Chronic hepatitis C infection (HCV) is a major health problem that disproportionately affects people with limited resources. Many people with HCV are ineligible or refuse antiviral treatment, but less curative treatment options exist. These options include adhering to follow-up health visits, lifestyle changes, and avoiding hepatotoxins like alcohol. Herein, we describe a recently developed self-management program designed to assist HCV-infected patients with adherence and improve their health-related quality of life (HRQOL).

METHODS: The development of the Hepatitis C Self-Management Program (HCV-SMP) was informed by scientific literature, qualitative interviews with HCV-infected patients, self-management training, and feedback from HCV clinical experts. **RESULTS:** The Hepatitis C Self-Management Program (HCV-SMP) is a multi-faceted program that employs cognitive-behavioral principles and is designed to provide HCV-infected people with knowledge and skills for improving their HRQOL. The program consists of six 2-h workshop sessions which are held weekly. The sessions consist of a variety of group activities, including disease-specific information dissemination, action planning, and problem-solving. **CONCLUSION:** The intervention teaches skills for adhering to challenging treatment recommendations using a validated theoretical model. A randomized trial will test the efficacy of this novel HCV self-management program for improving HRQOL in a difficult to reach population.

Implications of hepatitis C virus infection for behavioral symptoms and activities of daily living. Posada C, Moore DJ, Woods SP, et al. J Clin Exp Neuropsychol. 2010 Jul;32(6):637-44.

<http://www.ncbi.nlm.nih.gov/pubmed/20603743>

Hepatitis C virus (HCV) is neurovirulent and has been shown to be associated with neuropsychological (NP) deficits in a subset of infected individuals. Despite these previous findings, little work has been done to examine neurobehavioral symptoms associated with HCV infection. We examined 34 HCV seropositive (HCV+) individuals and 35 healthy comparison participants (HCV-) with the self-rating form of the Frontal Systems Behavior Scale (FrSBe). Results showed that at the group level, only the FrSBe apathy subscale mean was clinically elevated (T score >65) among HCV+ persons; executive dysfunction, disinhibition, and total subscale means were not clinically elevated. At the individual level, a significantly higher proportion of HCV+ individuals than of HCV- individuals reported clinically elevated FrSBe T scores. Moreover, HCV+ individuals were nearly 3 times as likely to report clinically elevated FrSBe T scores of apathy, executive dysfunction, and disinhibition as compared to HCV- participants. A multiple regression that included substance use disorders, neuropsychological impairment, and age indicated that HCV status was an independent predictor of self-reported FrSBe total T scores. Across all participants, small, yet significant, correlations were found between elevated self-reported FrsBe T scores and dependence in activities of daily living. These results show that a subset of HCV-infected individuals report clinically elevated behavioral symptoms. Clinical implications for the assessment and management of elevated behavioral symptoms in HCV are discussed.