

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

Interferon induced retinopathy and its risk in patients with diabetes and hypertension undergoing treatment for chronic hepatitis C virus infection. D Panetta J, Gilani N. *Aliment Pharmacol Ther.* 2009 Jun 22. [Epub ahead of print]

http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=Search&Term=%22D%20Panetta%20J%22%5BAuthor%5D&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVAbstract

ABSTRACT BACKGROUND: Ocular complications are amongst many side-effects of interferon based therapy for hepatitis C virus (HCV) infection. Some suggest that diabetic and hypertensive patients are at increased risk of these complications. **AIM:** To determine the frequency of ophthalmologic complications related to interferon use. **Methods:** Retrospective analysis of patients undergoing HCV treatment with pegylated interferon alfa-2a, alfa-2b, or consensus interferon plus ribavirin between 2005 and 2007. All patients underwent a baseline eye examination and any visual complaints during treatment prompted a repeat examination. Data recorded included HCV genotype, treatment duration, interferon type, pretreatment and on treatment visual complaints, known ocular pathology, and retinal findings at baseline and at follow-up. **RESULTS:** Of 183 patients, 29 (16%) had diabetes and 85 (46%) had hypertension. Seventy-one (38%) received interferon alfa-2a, 100 (55%) alfa-2b, and 12 (7%) consensus interferon. Seven (3.8%) had retinal changes on follow-up and treatment was discontinued in 3 (1.6%). Of seven with ocular changes 2 had hypertension and 1 had both hypertension and diabetes. **CONCLUSION:** The incidence of symptomatic retinopathy in HCV patients undergoing interferon therapy appears low and treatment cessation is rarely needed. Furthermore, patients with hypertension and diabetes may not be at higher risk for interferon induced retinopathy.

Economic evaluation of early monotherapy versus delayed monotherapy or combination therapy in patients with acute hepatitis C in Germany. Dintsios CM, Haverkamp A, Wiegand J, et al. *Eur J Gastroenterol Hepatol.* 2009 Jun 22. [Epub ahead of print]

http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=Search&Term=%22Dintsios%20CM%22%5BAuthor%5D&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVAbstract

BACKGROUND: Antiviral treatment of acute hepatitis C virus (HCV) almost doubles the chance of sustained virological response (SVR) compared with that achievable by treating chronic HCV. **AIM:** To conduct a health economic evaluation comparing early and delayed therapies for acute HCV in Germany. **METHODS:** One hundred and thirty-three patients with acute HCV were evaluated in two early monotherapy (EMT) studies and 60 in a delayed therapy study. Efficacy was determined by SVR. In the EMT studies, patients were treated with either standard or pegylated

interferon for 24 weeks. In the delayed therapy study, patients with persisting infection were treated with interferon monotherapy or combination therapy with ribavirin for a median of 36 weeks. We conducted a cost-effectiveness analysis based on the study results and a linear simulation model based on current treatment recommendations. **RESULTS:** The SVR rate for the sex-adjusted on-treatment analysis between early and delayed therapies was not significantly different (92.7 vs. 90.9%; $P = 0.7$). Medication costs accounted for more than 90% in both treatment options. Direct medical costs of early therapy (euro7064/patient) were euro321 lower than those of delayed therapy ($P = 0.8$). The incremental cost-effectiveness ratio was -178 euro/SVR(%) (confidence interval: -224 to 360 euro/SVR(%)). Average modeled direct medical costs of delayed combination therapy were from euro6745 to euro8299 per patient (from approximately 7% less up to 15% higher than EMT). Spontaneous viral clearance and therapy duration were the most sensitive variables.

CONCLUSION: There was no significant efficacy and cost difference between therapy alternatives in base cases. However, in the majority of scenarios in the sensitivity analyses, EMT was a more cost-effective option in acute HCV therapy.

Extended treatment duration of peginterferon-alpha2b plus ribavirin for 72 and 96 weeks in hepatitis C genotype 1-infected late responders. Nagaki M, Shimizu M, Sugihara JI, et al.

Aliment Pharmacol Ther. 2009 May 26. [Epub ahead of print]

http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=Search&Term=%22Nagaki%20M%22%5BAuthor%5D&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVAbstract

SUMMARY BACKGROUND: Prolonged duration and dose of peginterferon or ribavirin after 48 weeks of treatment to maximize SVR in HCV genotype 1-infected patients remain to be understood. **AIM:** To investigate whether extended treatment longer than 72 weeks may be superior to 72-week treatment. **METHODS:** A total of 120 treatment-naïve or retreated patients with HCV genotype 1 were treated with peginterferon-alpha2b (1.5 mug/kg/week) plus weight-based ribavirin. We had 34 late responders, in whom HCV RNA first became undetectable at week 12-48, and randomized them into 3 groups receiving standard-dose peginterferon-alpha2b plus low-dose ribavirin (200 mg/day) for extended 24 weeks (group A), receiving low-dose peginterferon-alpha2b (0.75 mug/kg/week) plus low-dose ribavirin for extended 48 weeks (group B), or no extended treatment (group C) and evaluated the outcome according to their virologic response. **RESULTS:** Multivariate analysis showed that the treatment for 96 weeks was identified as a significant, independent factor associated with SVR in HCV genotype 1-infected late responders, in comparison with group A [odds ratio (OR), 10.002; $P = 0.080$] and group C (OR, 17.748; $P = 0.025$).

CONCLUSIONS: Extending the treatment duration from 48 weeks to 96 weeks improves SVR rates in genotype 1-infected patients with late virologic response to peginterferon-alpha2b and ribavirin.

A randomised trial of pegylated-interferon-alpha-2a plus ribavirin with or without amantadine in treatment-naïve or relapsing chronic hepatitis C patients. Langlet P, D'Heygere F, Henrion J, et al. Aliment Pharmacol Ther. 2009 May 26. [Epub ahead of print]

http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=Search&Term=%22Langlet%20P%22%5BAuthor%5D&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVAbstract

SUMMARY BACKGROUND: The combination therapy of pegylated-interferon-alpha2a plus ribavirin is considered as the standard of care for patients with chronic hepatitis C. A sustained viral response is obtained in 40-50% of naïve patients with genotype 1 and in around 80% of naïve patients with genotype 2 or 3. **AIM:** To assess whether amantadine, added to the conventional bi-therapy, could improve the treatment efficacy. **METHODS:** 630 patients (intent-to-treat population) with chronic hepatitis C were randomized into two groups: 316 patients (treatment

group) received pegylated-interferon-alpha2a (180µg once weekly) plus ribavirin (1000-1200mg/daily) with amantadine (200mg/daily); 314 patients (control group) received pegylated-interferon-alpha2a (180µg once weekly) plus ribavirin (1000-1200mg/daily) without amantadine. The duration of the treatment was 48 weeks for genotypes 1, 4, 5 and 6, and 24 weeks for genotypes 2 and 3. **RESULTS:** There was no statistically significant difference between treatments groups for any of the variables tested for. Subgroups of patients likely to take advantage of the addition of amantadine were not identified. **CONCLUSIONS** This large study definitely excludes the role of amantadine in addition of conventional bitherapy in the treatment of chronic hepatitis C patients.

Decline in male sexual desire, function, and satisfaction during and after antiviral therapy for chronic hepatitis C.

Dove LM, Rosen RC, Ramcharran D, Wahed AS, Belle SH, Brown RS, Hoofnagle JH; Virahep-C Study Group. Gastroenterology. 2009 Jun 12. [Epub ahead of print] http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=Search&Term=%22Dove%20LM%22%5BAuthor%5D&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVAbstract

BACKGROUND: The recommended therapy for chronic hepatitis C, peginterferon and ribavirin for 24 or 48 weeks, has many known adverse side-effects. **AIMS:** To evaluate the impact of antiviral therapy on male sexual health. **METHODS:** As part of the Study of Viral Resistance to Antiviral Therapy of Chronic Hepatitis C (Virahep-C), 260 men treated with peginterferon alfa-2a and ribavirin completed self-administered questionnaires concerning sexual desire, sexual function, including erectile and ejaculatory function, and sexual satisfaction before, during, and after treatment. **RESULTS:** Before therapy, 37% of men reported at least some degree of impairment in sexual desire, 44% reported dissatisfaction with their sexual life, while 22% reported impairment in erectile and 26% in ejaculatory function. During therapy, significant declines were observed in all components of sexual health compared to pre-treatment. At the end of therapy (24 or 48 weeks), an estimated 38% to 48% of men reported that overall sexual function was worse than before treatment. African Americans reported less impairment in sexual desire and satisfaction than Caucasians Americans during therapy. By 24 weeks after treatment, sexual desire, and satisfaction improved and were comparable to baseline levels. However, among men who received 48 weeks of therapy, the estimated percentage of men reporting post-treatment erectile or ejaculatory problems remained higher than baseline, though persistent erectile impairment was limited to Caucasian Americans. **CONCLUSIONS:** Sexual impairment is common among men with chronic hepatitis C undergoing therapy with peginterferon and ribavirin and should be considered as a potential side-effect of antiviral therapy.

Efficacy of peginterferon-alpha-2b plus ribavirin in patients aged 65 years and older with chronic hepatitis C.

Honda T, Katano Y, Shimizu J, et al. Liver Int. 2009 Jun 12. [Epub ahead of print] http://www.ncbi.nlm.nih.gov/pubmed/19523048?ordinalpos=2&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

ABSTRACT OBJECTIVES: The aim of this study was to evaluate the efficacy and indication of combination therapy with ribavirin plus peginterferon-alpha-2b in chronic hepatitis C virus (HCV) patients aged 65 years and older. **METHODS:** Five hundred and ninety-one consecutive HCV patients were treated with combination therapy. These patients were divided into elder patients (>/=65 years) (n=115) and younger patients (<65 years) (n=476). The clinical characteristics, sustained virological response (SVR) rates and discontinuation rates were compared between the two groups. **RESULTS:** Compared with younger patients, baseline haemoglobin levels and baseline platelet counts were significantly lower (P<0.0001, P=0.013 respectively) and fibrosis was more advanced in elderly patients (P=0.0310). Moreover, the SVR rate was significantly lower (37.4 vs.

51.5%; $P=0.0067$) while the combination therapy discontinuation rate was significantly higher (32.2 vs. 17.0%; $P=0.0003$) in elderly patients. A multivariate analysis revealed that HCV load and genotype were significantly associated with an SVR in elderly patients. An SVR was achieved in over 50% of elderly male patients with genotype 1 and HCV RNA concentrations under 2 000 000 IU/ml. In contrast, the SVR rate was under 30% in elderly male patients with genotype 1 and with HCV RNA concentrations over 2 000 000 IU/ml and in all elderly female patients with genotype 1. **CONCLUSIONS:** The SVR rate was lower in elderly patients than in younger patients. However, in elderly patients combination therapy was most beneficial for genotype 1 patients, male patients with HCV RNA concentrations $<2\ 000\ 000$ IU/ml and patients with genotype 2.

Impact of ribavirin plasma level on sustained virological response in patients treated with pegylated interferon and ribavirin for chronic hepatitis C. Breilh D, Foucher J, Castéra L, et al. *Aliment Pharmacol Ther.* 2009 Jun 11. [Epub ahead of print]

http://www.ncbi.nlm.nih.gov/pubmed/19523176?ordinalpos=2&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

ABSTRACT BACKGROUND: The main goal of therapy in hepatitis C virus (HCV) infection is to achieve a sustained virological response (SVR). However, the impact of the pharmacological properties of ribavirin on the SVR has not been fully investigated. The aim of this prospective study was to evaluate the association between ribavirin plasma level and SVR response in HCV patients treated with pegylated interferon and ribavirin. **PATIENTS AND METHODS:** Patients had plasmatic ribavirin dosage at week 4 and 12. **RESULTS:** At week 4, a strong correlation was found between HCV-RNA and C min of ribavirin plasma level ($r=-0.376$, $p=0.002$) and AUC(0-->12h) of ribavirin plasma level ($r=-0.277$, $p=0.018$). At week 12, a strong correlation was found between HCV-RNA and Cmin of ribavirin plasma level ($r=-0.384$, $p<0.0001$) and AUC(0-->12h) of ribavirin plasma level ($r=-0.257$, $p=0.002$). In genotype 1 patients, AUC(0-->12h) ribavirin and Cmin were significantly correlated with negative HCV-RNA at week 12 and SVR. In the multiple logistic regression model, the only factor independently associated with SVR in genotype 1 patients was negative HCV-RNA at week 12. **CONCLUSION:** Our study does not emphasize the relationship between plasmatic ribavirin level at week 12 and SVR in genotype 1 patients treated with PEG-IFN and ribavirin.

Factors associated with the progression of hepatic fibrosis in end-stage kidney disease patients with hepatitis C virus infection. Becker VR, Badiani RG, Lemos LB, et al. *Eur J Gastroenterol Hepatol.* 2009 Jun 11. [Epub ahead of print]

http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=Search&Term=%22Becker%20VR%22%5BAuthor%5D&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVAbstract

BACKGROUND: Few studies have evaluated the histological aspects of hepatitis C virus (HCV) infection in hemodialysis patients and the factors related to the progression of hepatic fibrosis in this population have not been defined. **AIM:** To evaluate the influence of host-related factors on the fibrosis progression in end-stage renal disease (ESRD) patients with HCV infection. **METHODS:** HCV-infected ESRD patients who submitted to liver biopsy were included. The fibrosis stages were classified according to METAVIR scoring system. For the identification of factors associated with more advanced liver fibrosis, the patients were classified into two groups: group 1, absence of septal fibrosis (F0-1) and group 2, presence of septal fibrosis (F2-4). Groups 1 and 2 were compared regarding demographic, epidemiological, and laboratory variables and logistic regression analysis was used to identify the variables that were independently associated with the presence of septal fibrosis. **RESULTS:** A total of 216 ESRD patients (63% men, 44+/-11 years) were included. In the histological analysis, the fibrosis stages were as follows: F0=36%, F1=41%, F2=12%, F3=7, and 4%

had cirrhosis (F4). In the logistic regression model, the variables that were independently associated with the presence of septal fibrosis were duration of infection, estimated age at infection, coinfection with HBV and aspartate aminotransferase levels. **CONCLUSION:** These findings support the importance of obtaining an adequate immune response to HBV vaccination and careful monitoring of liver disease in patients who become infected at an advanced age and/or those presenting elevated aspartate aminotransferase levels, as these are the main factors associated with the presence of septal fibrosis in ESRD patients.

Development of hepatocellular carcinoma in elderly patients with chronic hepatitis C with or without elevated aspartate and alanine aminotransferase levels. Kobayashi M, Suzuki F, Akuta N, et al. J Gastroenterol. 2009 Jun 11:1-9. [Epub ahead of print]

http://www.ncbi.nlm.nih.gov/pubmed/19521923?ordinalpos=5&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

OBJECTIVE: Hepatocellular carcinoma (HCC) in the elderly infected with hepatitis C virus (HCV) is expected to increase globally within the next two decades. The purpose of the study was to define the natural history of elderly patients with chronic hepatitis C needs in order to prevent HCC from arising in these patients. **MATERIAL AND METHODS:** Treatment-naive patients aged ≥ 65 years with platelet counts $>120 \times 10^3/\text{mm}^3$ were classified as 120 with aspartate and alanine aminotransferase (ASAT and ALAT) levels ≤ 40 IU/l (group A) and 212 with either or both levels ≥ 41 (group B) and followed-up for 3 years or longer without antiviral treatment.

RESULTS: Cirrhosis and HCC developed more frequently in group B than in group A ($p < 0.001$ for both). In particular, of the patients aged 65-69 years at entry, cirrhosis and HCC developed more frequently in group B than in group A ($p < 0.001$ and $p = 0.001$, respectively). Liver-related causes of death were more common in group B than in group A (20/34 (59%) versus 1/9 (11%), $p = 0.021$). HCC developed more frequently in men than in women ($p = 0.033$). **CONCLUSIONS:** In elderly patients with chronic hepatitis C, cirrhosis and HCC develop more frequently in those with elevated transaminase levels than in those without elevated transaminase levels. Therefore, transaminase levels need to be suppressed below ≤ 40 IU/l, using antiviral treatments or other agents, in order to prevent cirrhosis and HCC arising in these patients. In view of rare liver-related deaths, aggressive antiviral treatment would not be necessary in the elderly with chronic hepatitis C who have normal transaminase levels.

Response to hepatitis A and B vaccine alone or in combination in patients with chronic hepatitis C virus and advanced fibrosis. Kramer ES, Hofmann C, Smith PG, Shiffman ML, Sterling RK. Dig Dis Sci. 2009 Jun 11. [Epub ahead of print]

http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=Search&Term=%22Kramer%20ES%22%5BAuthor%5D&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVAbstract

Patients with advanced fibrosis are at increased risk of severe outcomes if they develop acute infection with hepatitis A (HAV) or hepatitis B (HBV) viruses. There are no data on the efficacy of combined HAV/HBV vaccination in patients with advanced fibrosis. Our aim was to evaluate the response to the HAV and HBV vaccine alone or in combination for patients with chronic hepatitis C (HCV) and advanced fibrosis and to evaluate the impact of administering the vaccine while patients were receiving peginterferon for treatment of chronic HCV. In this prospective study of patients with advanced fibrosis (Ishak 3-6), those without serologic evidence of prior exposure were vaccinated with either Havrix((R)) HAV, Engerix((R)) HBV, or the TWINRIX((R)) HAV/HBV combination vaccine as appropriate, and response was defined as the development of anti-HAV or anti-HBV surface antibodies. Of the 162 eligible patients, the prevalence of prior exposure to HAV and HBV was 30 and 18%, respectively. Of the 84 patients vaccinated, 38% received Havrix, 14%

Engerix, and 48% TWINRIX((R)). The response to the HAV vaccine was 75% in those receiving Havrix((R)) compared to 78% receiving TWINRIX((R)). In contrast, the response to HBV vaccination was 42% in patients receiving Engerix((R)) compared to 60% in those vaccinated with TWINRIX((R)) (difference 18.3%; OR 0.29; 95% CI: 0.57-7.79). The presence of diabetes was the only risk factor identified for reduced HBV response (P = 0.01). Responses to both HAV and HBV vaccines when administered alone or in combination were lower than expected in patients with HCV and advanced fibrosis, especially in those with diabetes. The observation that the decline in HBV vaccine response was somewhat lower when this was administered alone as opposed to the combination A/B vaccine suggests that the administration of a combination vaccine may enhance the vaccination response to HBV.

Hepatitis C virus infection and the risk of coronary disease. Butt AA, Xiaoqiang W, Budoff M, Leaf D, Kuller LH, Justice AC. Clin Infect Dis. 2009 Jul 15;49(2):225-32

http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=Search&Term=%22Butt%20AA%22%5BAuthor%5D&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVAbstract

BACKGROUND: The association between hepatitis C virus (HCV) infection and coronary artery disease (CAD) is controversial. We conducted this study to determine and quantify this association. **METHODS:** We used an established, national, observational cohort of all HCV-infected veterans receiving care at all Veterans Affairs facilities, the Electronically Retrieved Cohort of HCV Infected Veterans, to identify HCV-infected subjects and HCV-uninfected control subjects. We used the Cox proportional-hazards model to determine the risk of CAD among HCV-infected subjects and control subjects. **RESULTS:** We identified 82,083 HCV-infected and 89,582 HCV-uninfected subjects. HCV-infected subjects were less likely to have hypertension, hyperlipidemia, and diabetes but were more likely to abuse alcohol and drugs and to have renal failure and anemia. HCV-infected subjects had lower mean (+/- standard deviation) total plasma cholesterol (175 +/- 40.8 mg/dL vs. 198 +/- 41.0 mg/dL), low-density lipoprotein cholesterol (102 +/- 36.8 mg/dL vs. 119 +/- 38.2 mg/dL), and triglyceride (144 +/- 119 mg/dL vs. 179 +/- 151 mg/dL) levels, compared with HCV-uninfected subjects ([Formula: see text] for all comparisons). In multivariable analysis, HCV infection was associated with a higher risk of CAD (hazard ratio, 1.25; 95% confidence interval, 1.20-1.30). Traditional risk factors (age, hypertension, chronic obstructive pulmonary disease, diabetes, and hyperlipidemia) were associated with a higher risk of CAD in both groups, whereas minority race and female sex were associated with a lower risk of CAD. **CONCLUSIONS:** HCV-infected persons are younger and have lower lipid levels and a lower prevalence of hypertension. Despite a favorable risk profile, HCV infection is associated with a higher risk of CAD after adjustment for traditional risk factors.

Light and moderate alcohol consumption significantly reduces the prevalence of fatty liver in the Japanese male population. Gunji T, Matsushashi N, Sato H, et al. Am J Gastroenterol. 2009 Jun 23. [Epub ahead of print]

http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=Search&Term=%22Gunji%20T%22%5BAuthor%5D&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVAbstract

OBJECTIVES: The effect of alcohol consumption on the liver is controversial. Recent reports have suggested that moderate alcohol consumption decreases the prevalence of elevated alanine aminotransferase levels. The role of alcohol consumption in the development of fatty liver (FL), however, has not been studied definitively. The aim of this study was to examine the association between alcohol consumption and FL in a large Japanese population. **METHODS:** A total of 7,431 asymptomatic male subjects who underwent a complete medical survey in our institute between May 2007 and July 2008 were recruited. Cases positive for hepatitis B or C viruses, potential hepatotoxic

drug intake, or under treatment for metabolic disorders were excluded. FL was defined by ultrasonography. Visceral and subcutaneous adipose tissues (VAT and SAT) were measured by computed tomography. Independent and significant predictors associated with FL were determined by multiple logistic regression analysis. **RESULTS:** Of the initial study candidates, 130 (1.7%) were positive for hepatitis B and 66 (0.8%) were positive for hepatitis C. On the basis of the inclusion and exclusion criteria, 5,599 men (50.9+/-8.1 years) were studied cross-sectionally. Light (40-140 g/week) and moderate (140-280 g/week) alcohol consumption significantly and independently reduced the likelihood of FL (odds ratio=0.824 and 0.754, 95% confidence interval=0.683-0.994 and 0.612-0.928, P=0.044 and 0.008, respectively) by multivariate analysis after adjusting for potential confounding variables. VAT, SAT, low-density lipoprotein, triglycerides, and fasting blood glucose were significant predictors of the increased prevalence of FL, whereas age was a predictor of the decreased prevalence of FL. **CONCLUSIONS:** The prevalence of FL was significantly and independently decreased by light and moderate alcohol consumption in men of an asymptomatic Japanese population.

Quality of life, depression, and cytokine patterns in patients with chronic hepatitis C treated with antiviral therapy. Falasca K, Mancino P, Ucciferri C, et al. Clin Invest Med. 2009 Jun 1;32(3):E212-8.

http://www.ncbi.nlm.nih.gov/pubmed/19480737?ordinalpos=1&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

PURPOSE: To evaluate the effect of chronic hepatitis C and antiviral therapy on health-related quality of life (HRQoL), depression symptoms and cytokine patterns. **METHODS:** Twenty HCV+ patients treated with peginterferon plus ribavirin were enrolled in this cohort study and invited to complete SF-12 and BDI questionnaires prior to (T0) and at the end of the treatment (T1). HCV-RNA, serum levels of ALT, AST, haemoglobin, ferritin and IFN-gamma, TNF-alpha, IL-2, IL-4, IL-6 and IL-10 were evaluated at T0 and T1. The questionnaire results were correlated to biochemical and cytokine parameters. **RESULTS:** Two patients (1%) dropped out and 18 HCV patients composed the final sample (11 males (61.1%); mean age 42.5+/-11.9 yr; mean disease duration 9.7+/-6.9 yr). Between T0 and T1 ALT (p=0.02), AST (p=0.052) HCV-RNA (P=0.0002) and haemoglobin levels decreased (p=0.0003), whereas ferritin level increased (P=0.003). Also, at T1 all cytokine levels were augmented. Regarding depression status, at T0 10 patients (55.5%) scored above to the BDI questionnaire (suggesting clinically significant depression), whereas at T1 14 patients scored 10 or above (77.7%). At T1 the mean BDI score increased, but this difference was not significant. Regarding HRQoL, the majority of patients had T0 summary scores < or = 50. At T1 HRQoL changed and scores decreased in 66.7% of the patients. A correlation was observed between the T0 level of ferritin and the amount of change in BDI and SF-12 mental score between T0 and T1 (Spearman rho = -0.56 and +0.61, respectively) and IL-4 level at T0 and the change in BDI and SF-12 mental scores (Spearman rho = -0.49 and +0.45, respectively). **CONCLUSION:** BDI, SF-12, IL-4 and ferritin are good tools to predict the appearance of depressive symptoms and worsening of the quality of life in the HCV+ population.

Predictive values of amino acid sequences of the core and NS5A regions in antiviral therapy for hepatitis C: a Japanese multi-center study. Okanoue T, Itoh Y, Hashimoto H, et al J

Gastroenterol. 2009 Jun 11. [Epub ahead of print]

http://www.ncbi.nlm.nih.gov/pubmed/19517057?ordinalpos=1&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

BACKGROUND: Chronic hepatitis C (CHC) genotype 1b patients with high viral load are resistant to peginterferon (PEG-IFN) and ribavirin (RBV) combination therapy, especially older and female patients. **METHODS:** To elucidate the factors affecting early and sustained viral responses (EVR and SVR), 409 genotype 1b patients CHC with high viral loads who had received 48 weeks of PEG-IFN/RBV therapy were enrolled. The amino acid (aa) sequences of the HCV core at positions 70 and 91 and of the interferon sensitivity determining region (ISDR) were analyzed. Host factors, viral factors, and treatment-related factors were subjected to multivariate analysis. **RESULTS:** Male gender, low HCV RNA load, high platelet count, two or more aa mutations of ISDR, and wild type of core aa 70 were independent predictive factors for SVR. In patients with over 80% adherences to both PEG-IFN and RBV, male gender, mild fibrosis stage, and wild type of core aa 70 were independent predictors for SVR. **CONCLUSIONS:** Independent predictive factors for SVR were: no aa substitution at core aa 70, two or more aa mutations in the ISDR, low viral load, high values of platelet count, mild liver fibrosis and male gender.

Differences in viral kinetics between genotypes 1 and 2 of hepatitis C virus after single administration of standard interferon-alpha. Toyoda H, Kumada T, Kiriyaama S, et al. J Med

Virol. 2009 Jun 23;81(8):1354-1362. [Epub ahead of print]

http://www.ncbi.nlm.nih.gov/pubmed/19551828?ordinalpos=1&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

Hepatitis C virus (HCV) kinetics were determined after a single administration of standard interferon (IFN) according to the HCV genotype that affects the response to antiviral therapy with IFN/peginterferon. A total of 208 patients were investigated. All patients received a single administration of 6 megaunits of standard IFN-alpha. HCV RNA concentration was measured before, and at 24, 48, 72, and 120 hr after administration. Changes in HCV RNA concentration were compared between genotypes. The patient group consisted of 132 patients with genotype 1B, 58 with genotype 2A, and 18 with genotype 2B. In the comparison between genotypes 1 and 2, the reduction in HCV RNA concentration after a single IFN administration was less marked in patients with genotype 1B at both 24 and 48 hr after administration ($P < 0.0001$). In contrast, an increase in HCV RNA concentration during 24-48 or 24-72 hr after a single administration was comparable between genotypes 1 and 2. In the comparison between genotypes 2A and 2B, the reduction in HCV RNA concentration after a single administration was more marked in patients with genotype 2A, despite the similar rate of sustained virologic response to peginterferon and ribavirin combination therapy. **The results** of the study indicate that the rapid decrease in HCV RNA concentration observed during IFN or peginterferon therapy in patients with genotype 2 appeared to be due to the difference in sensitivity to IFN. Within genotype 2, HCV genotype 2A was more sensitive to IFN than genotype 2B.

Hepatitis C virus core, NS3, NS4B and NS5A are the major immunogenic proteins in humoral immunity in chronic HCV infection. Sillanpaa M, Melen K, Porkka P, et al. *Virology*. 2009 Jun 23;6(1):84. [Epub ahead of print]

http://www.ncbi.nlm.nih.gov/pubmed/19549310?ordinalpos=2&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

ABSTRACT: BACKGROUND: The viral genome of hepatitis C virus constitutes a 9.6-kb single-stranded positive-sense RNA which encodes altogether 11 viral proteins. In order to study the humoral immune responses against different HCV proteins in patients suffering from chronic HCV infection, we produced three structural (core, E1 and E2) and six nonstructural proteins (NS2, NS3, NS4A, NS4B, NS5A and NS5B) in Sf9 insect cells by using the baculovirus expression system.

RESULTS: The recombinant HCV core, E1, E2, NS2, NS3, NS4A, NS4B, NS5A and NS5B proteins were purified and used in Western blot analysis to determine antibody responses against individual HCV protein in 68 HCV RNA and antibody positive human sera that were obtained from patients suffering from genotype 1, 2, 3 or 4 infection. These sera were also analysed with INNO-LIA Score test for HCV antibodies against core, NS3, NS4AB and NS5A, and the results were similar to the ones obtained by Western blot method. Based on our Western blot analyses we found that the major immunogenic HCV antigens were the core, NS4B, NS3 and NS5A proteins which were recognized in 97%, 86%, 68% and 53% of patient sera, respectively. There were no major genotype specific differences in antibody responses to individual HCV proteins. A common feature within the studied sera was that all except two sera recognized the core protein in high titers, whereas none of the sera recognized NS2 protein and only three sera (from genotype 3) recognised NS5B. **CONCLUSIONS:** The data shows significant variation in the specificity in humoral immunity in chronic HCV patients.

Enhancement of the expression of HCV core gene does not enhance core-specific immune response in DNA immunization: advantages of the heterologous DNA prime, protein boost immunization regiment. Alekseeva E, Sominskaya I, Skrastina D, et al. *Genet Vaccines Ther*. 2009 Jun 8;7(1):7. [Epub ahead of print]

http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=Search&Term=%22Alekseeva%20E%22%5BAuthor%5D&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVAbstract

ABSTRACT BACKGROUND: Hepatitis C core protein is an attractive target for HCV vaccine aimed to exterminate HCV infected cells. However, although highly immunogenic in natural infection, core appears to have low immunogenicity in experimental settings. We aimed to design an HCV vaccine prototype based on core, and devise immunization regimens that would lead to potent anti-core immune responses which circumvent the immunogenicity limitations earlier observed. **METHODS:** Plasmids encoding core with no translation initiation signal (pCMVcore); with Kozak sequence (pCMVcoreKozak); and with HCV IRES (pCMVcoreIRES) were designed and expressed in a variety of eukaryotic cells. Polyproteins corresponding to HCV 1b amino acids (aa) 1-98 and 1-173 were expressed in *E. coli*. C57BL/6 mice were immunized with four 25-mug doses of pCMVcoreKozak, or pCMV (I). BALB/c mice were immunized with 100 mkg of either pCMVcore, or pCMVcoreKozak, or pCMVcoreIRES, or empty pCMV (II). Lastly, BALB/c mice were immunized with 20 mkg of core aa 1-98 in prime and boost, or with 100 mkg of pCMVcoreKozak in prime and 20 mkg of core aa 1-98 in boost (III). Antibody response, [³H]-T-incorporation, and cytokine secretion by core/core peptide-stimulated splenocytes were assessed after each immunization. **RESULTS:** Plasmids differed in core-expression capacity: mouse fibroblasts transfected with pCMVcore, pCMVcoreIRES and pCMVcoreKozak expressed 0.22+/-0.18, 0.83+/-0.5, and 13+/-5 ng core per cell, respectively. Single immunization with highly expressing pCMVcoreKozak induced specific IFN-gamma and IL-2, and weak antibody response.

Single immunization with plasmids directing low levels of core expression induced similar levels of cytokines, strong T-cell proliferation (pCMVcoreIRES), and antibodies in titer 1000 (pCMVcore). Boosting with pCMVcoreKozak induced low antibody response, core-specific T-cell proliferation and IFN-gamma secretion that subsided after the 3rd plasmid injection. The latter also led to a decrease in specific IL-2 secretion. The best was the heterologous pCMVcoreKozak prime/protein boost regiment that generated mixed Th1/Th2-cellular response with core-specific antibodies in titer [greater than or equal to]3000. **CONCLUSIONS:** Thus, administration of highly expressed HCV core gene, as one large dose or repeated injections of smaller doses, may suppress core-specific immune response. Instead, the latter is induced by a heterologous DNA prime/protein boost regiment that circumvents the negative effects of intracellular core expression.

Tight junction-associated protein occludin is required for a post-binding step in hepatitis C virus entry and infection. Benedicto I, Molina-Jiménez F, Bartosch B, et al. J Virol. 2009 Jun 10.

[Epub ahead of print]

http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=Search&Term=%22Benedicto%20I%22%5BAuthor%5D&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVAbstract

The precise mechanisms regulating hepatitis C virus (HCV) entry into hepatic cells remain unknown. However, several cell surface proteins have been identified as entry factors for this virus. Among these molecules, claudin-1, a tight junction (TJ) component, is considered as a co-receptor required for HCV entry. Recently, we have demonstrated that HCV envelope glycoproteins (HCVgp) promote structural and functional TJ alterations. Additionally, we have shown that the intracellular interaction between viral E2 glycoprotein and occludin, another TJ-associated protein, could be the cause of the mislocalization of TJ proteins. Herein we demonstrated, by using cell culture-derived HCV particles (HCVcc), that interference of occludin expression markedly reduced HCV infection. Furthermore, employing HCV pseudotyped particles (HCVpp), our results indicated that occludin but not other TJ-associated proteins such as Junctional adhesion molecule-A (JAM-A) or Zonula Occludens protein-1 (ZO-1), was required for HCV entry. Using HCVcc we demonstrated that occludin did not play an essential role in the initial attachment of HCV to target cells. Surface protein-labelling experiments showed that both expression levels and cell-surface localization of HCV (co)receptors CD81, scavenger receptor class B type I (SR-BI) and claudin-1 were not affected upon occludin knockdown. In addition, immunofluorescence confocal analysis showed that occludin interference did not affect subcellular distribution of the HCV (co)receptors analyzed. However, HCVgp fusion-associated events were altered after occludin silencing. In summary, we propose that occludin plays an essential role in HCV infection probably affecting late entry events. This observation may provide new insights into HCV infection and related pathogenesis.

Presence of HCV-RNA after ultracentrifugation of serum samples during the follow-up of chronic hepatitis C patients with a sustained virological response may predict reactivation of hepatitis C virus infection. Castillo I, Bartolomé J, Quiroga JA, Barril G, Carreño V. Aliment Pharmacol Ther. 2009 Jun 11. [Epub ahead of print]

http://www.ncbi.nlm.nih.gov/pubmed/19523175?ordinalpos=2&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

SUMMARY BACKGROUND: Concentration of viral particles by ultracentrifugation of serum prior to PCR allows detection of hepatitis C virus (HCV) RNA in patients with undetectable viral RNA by conventional PCR assays. **AIM:** To analyze if HCV-RNA is detected after serum ultracentrifugation in chronic hepatitis C patients with a sustained virological response to antiviral therapy (defined as serum HCV-RNA negativity by conventional assays 6 months after the end of therapy). **METHODS:** HCV-RNA was tested by real-time PCR in ultracentrifuged sera collected

during the post-treatment follow-up (mean: 42 +/- 27 months) in 57 sustained virological responders (SVR). **RESULTS:** After serum ultracentrifugation, HCV-RNA was detected on at least one occasion during the follow-up in 29/57 (51%) SVR. Thirteen (23%) of these 57 SVR suffered a reactivation 18 +/- 8 months after the end of therapy (reappearance of serum HCV-RNA detectable by conventional assays). Among reactivated patients, 11/13 (85%) had HCV-RNA in ultracentrifuged serum samples (detectable 10 +/- 5 months before reactivation), while HCV-RNA was positive after ultracentrifugation in 18/44 (41%) long-term SVR ($p=0.01$). Persistence of detectable HCV-RNA after serum ultracentrifugation was associated with reactivation ($p=0.001$). **CONCLUSIONS:** Serum ultracentrifugation prior to PCR allows detection of HCV-RNA in SVR and its persistence may predict late reactivation.

HIV/HCV COINFECTION

Long-term serologic follow-up of isolated hepatitis B core antibody in HIV-infected and HIV-uninfected women. French AL, Lin MY, Evans CT, et al. Clin Infect Dis. 2009 Jul 1;49(1):148-54.

http://www.ncbi.nlm.nih.gov/pubmed/19480573?ordinalpos=2&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

BACKGROUND: Isolated antibody to hepatitis B core antigen (anti-HBc) is a common serologic finding in persons infected with human immunodeficiency virus (HIV), but the outcome and clinical significance are uncertain. **METHODS:** We performed repeated hepatitis B virus (HBV) serologic tests on women who participated in the Women's Interagency HIV Study and who had isolated anti-HBc at study entry. **RESULTS:** Repeated serologic tests were performed for 322 women (282 HIV-infected and 40 HIV-uninfected) at a median of 7.5 years after study entry. Seventy-one percent of women retained isolated anti-HBc serologic status, 20% acquired antibody to hepatitis B surface antigen (anti-HBs), and 2% acquired hepatitis B surface antigen (HBsAg). In unadjusted analysis, increasing age, injection drug use, and hepatitis C viremia were negatively associated with acquisition of anti-HBs. For HIV-infected women, predictors of acquisition of anti-HBs were an increase in CD4 cell count and the use of highly active antiretroviral therapy (HAART). Receipt of drugs with activity against HBV and self-reported HBV vaccination did not predict anti-HBs acquisition. In the multivariable regression model, HAART use remained a significant predictor of anti-HBs acquisition, whereas women with hepatitis C viremia were more likely to retain isolated anti-HBc serologic status. **CONCLUSIONS:** Isolated anti-HBc status remained stable over time for the majority of women, especially women with chronic hepatitis C virus infection. Development of anti-HBs was predicted by HAART use and an increase in CD4 cell count. We conclude that a proportion of HIV-infected women with isolated anti-HBc have prior natural HBV infection with anti-HBs that is at an undetectable level because of immune dysfunction. Isolated anti-HBc in the presence of chronic hepatitis C virus infection may be attributable to a different phenomenon, such as dysfunctional antibody production.

Hepatitis C virus infections among HIV-infected men who have sex with men: an expanding epidemic. Urbanus AT, van de Laar TJ, Stolte IG, et al. AIDS. 2009 Jun 17. [Epub ahead of print]

http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=Search&Term=%22Urbanus%20AT%22%5BAuthor%5D&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVAbstract

BACKGROUND: Since 2000 outbreaks of sexually transmitted hepatitis C Virus (HCV) infections have been reported among HIV-infected men who have sex with men (MSM). We studied the

prevalence and determinants of HCV-infection among MSM attending a large sexually transmitted infection (STI) clinic in the Netherlands. **METHODS:** In 2007-2008, 3125 attendees of the STI clinic Amsterdam, including 689 MSM, participated in an anonymous biannual cross-sectional survey. Participants were interviewed and screened for HIV and HCV antibodies. Additionally, all anti-HCV positive and HIV-infected individuals were tested for HCV RNA. Using phylogenetic analysis, HCV strains of the STI clinic attendees were compared with those isolated from MSM with acute HCV in 2000-2007. Determinants of HCV-infection were analysed using logistic regression. **RESULTS:** Two of 532 (0.4%) HIV-negative MSM and 28 of 157 (17.8%) HIV-positive MSM were infected with HCV. Over the study period, HCV prevalence among HIV-infected MSM increased (14.6%-20.9%). Seven of 28 (25.0%) HIV/HCV coinfecting MSM had acute HCV infection. Only five of 28 (17.9%) HIV/HCV coinfecting MSM ever injected drugs (IDU). HIV-infection, IDU, fisting and gamma hydroxy butyrate (GHB)-use were significantly associated with HCV-infection. Phylogenetic analyses revealed a high degree of MSM-specific clustering. **CONCLUSION:** We found a high and increasing HCV prevalence in HIV-infected MSM. Though not statistically significant, this trend, and the relatively large proportion of acute infections suggest ongoing transmission of HCV in HIV-positive MSM. Regardless of IDU, rough sexual techniques and use of recreational drugs were associated with HCV-infection; phylogenetic analysis supported sexual transmission. Targeted prevention, like raising awareness and routine testing, is needed to stop the further spread among HIV-infected MSM, and to prevent possible spillover to HIV-negative MSM.

Liver stiffness as a predictor of esophageal varices requiring therapy in HIV/hepatitis C virus-coinfecting patients with cirrhosis. Pineda JA, Recio E, Camacho A, et al. *J Acquir Immune Defic Syndr.* 2009 May 28. [Epub ahead of print]

http://www.ncbi.nlm.nih.gov/pubmed/19487952?ordinalpos=2&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

BACKGROUND: Liver stiffness (LS) measured by transient elastometry is associated with portal pressure in hepatitis C virus (HCV)-monoinfected patients and could predict the presence of esophageal varices in these subjects. The aim of this study was to assess the ability of LS to predict esophageal varices requiring preventive therapy for bleeding in HIV/HCV-coinfecting patients.

METHODS: One hundred two HIV/HCV-coinfecting patients with liver cirrhosis (LS \geq 14 kPa) underwent an upper gastrointestinal endoscopy (UGE) examination. The diagnostic performance of LS for esophageal varices requiring therapy (\geq F2 or F1 with red signs or Child-Pugh-Turcotte class C) was assessed by receiver operating receptor characteristic curves.

RESULTS: Nineteen patients (19%) harbored varices requiring therapy. LS in patients with and without varices needing treatment was 48 (33-71) kPa and 32 (18-48) kPa ($P = 0.004$). The area under the receptor operating characteristic curve (95% confidence interval) of LS for the occurrence of varices that should be treated was 0.71 (0.60 to 0.82). There was no cutoff level of LS with good positive predictive value for the presence of varices requiring therapy, but LS of 21 kPa had a negative predictive value of 100%. Twenty-six percent of patients with LS measurement and UGE showed LS $<$ 21 kPa. **CONCLUSIONS:** LS is higher in HIV/HCV-coinfecting patients with cirrhosis who show esophageal varices requiring therapy than in those who do not. A cutoff value of LS of 21 kPa could be useful to identify patients with very low probability of varices at risk for bleeding. UGE for screening could be spared in these patients until LS increases above 21 kPa.

Human immunodeficiency virus and hepatitis C infections induce distinct immunologic imprints in peripheral mononuclear cells. Kottitil S, Yan MY, Reitano KN, et al. *Hepatology*. 2009 May 6;50(1):34-45. [Epub ahead of print]

http://www.ncbi.nlm.nih.gov/pubmed/19551908?ordinalpos=1&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

Coinfection with hepatitis C virus (HCV) is present in one-third of all human immunodeficiency virus (HIV)-infected individuals in the United States and is associated with rapid progression of liver fibrosis and poor response to pegylated interferon (IFN) and ribavirin. In this study we examined gene expression profiles in peripheral blood mononuclear cells (PBMCs) from different groups of individuals who are monoinfected or coinfecting with HIV and HCV. Data showed that HIV and HCV viremia up-regulate genes associated with immune activation and immunoregulatory pathways. HCV viremia is also associated with abnormalities in all peripheral immune cells, suggesting a global effect of HCV on the immune system. Interferon-alpha-induced genes were expressed at a higher level in PBMCs from HIV-infected individuals. HCV and HIV infections leave distinct profiles of gene expression of immune activation in PBMCs. HIV viremia induces an immune activated state; by comparison, HCV infection induces immunoregulatory and proinflammatory pathways that may contribute to progression of liver fibrosis. **CONCLUSION:** An aberrant type-I IFN response seen exclusively in HIV-infected individuals could be responsible for the poor therapeutic response experienced by HIV/HCV coinfecting individuals receiving interferon-alpha-based current standard of care.

Peginterferon plus ribavirin for chronic hepatitis C in patients with human immunodeficiency virus. Gluud LL, Marchesini E, Iorio A. *Am J Gastroenterol*. 2009 Jun 9. [Epub ahead of print]

http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=Search&Term=%22Gluud%20LL%22%5BAuthor%5D&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVAbstract

OBJECTIVES: The aim of this study was to assess the effects of peginterferon plus ribavirin for chronic hepatitis C in patients with human immunodeficiency virus (HIV). **METHODS:** Trials were identified through manual and electronic searches. Randomized trials comparing peginterferon plus ribavirin with other antiviral treatments for patients with chronic hepatitis C and HIV were included. The primary outcome measure was virological response at the end of treatment and after ≥ 6 months (sustained). Intention-to-treat meta-analyses including data on all patients who were randomized were carried out. **RESULTS:** Seven randomized trials were eligible for inclusion. The patients included had chronic hepatitis C and stable HIV and were not previously treated with interferon or ribavirin (treatment naive). The mean dosages were 180 or 1.5 mg/kg once weekly for peginterferon and 800 mg daily for ribavirin. The treatment duration ranged from 24 to 48 weeks. Peginterferon plus ribavirin increased the proportion of patients with an end-of-treatment or sustained virological response compared with interferon plus ribavirin or peginterferon alone. In subgroup analyses of trials comparing peginterferon plus ribavirin with interferon plus ribavirin, the proportion with a sustained virological response was 26% (109 of 423) for patients with genotype 1 or 4 and 57% (130 of 230) for genotype 2 or 3. Several adverse events occurred, including fatal lactic acidosis and liver failure, but there were no significant differences in mortality rates between treatment groups. **CONCLUSIONS:** Peginterferon plus ribavirin may be considered for treatment-naive patients with HIV and chronic hepatitis C. Adverse events should be monitored carefully.

Effect of coffee and green tea consumption on the risk of liver cancer: cohort analysis by hepatitis virus infection status. Inoue M, Kurahashi N, Iwasaki M, et al. *Cancer Epidemiol Biomarkers Prev.* 2009 Jun;18(6):1746-53.

http://www.ncbi.nlm.nih.gov/pubmed/19505908?ordinalpos=11&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

In spite of their anticarcinogenic potential, the effect of coffee and green tea consumption on the risk of liver cancer has not been clarified prospectively in consideration of hepatitis C (HCV) and B virus (HBV) infection. We examined whether coffee and green tea consumption was associated with a reduced risk of liver cancer by hepatitis virus infection status in the Japan Public Health Center-Based Prospective Study Cohort II. A total of 18,815 subjects ages 40 to 69 years participating in a questionnaire and health checkup survey in 1993 to 1994 were followed for the incidence of liver cancer through 2006. A total of 110 cases of liver cancer were newly documented. Hazard ratios for coffee and green tea consumption categories were calculated with a Cox proportional hazards model. Compared with almost never drinkers, increased coffee consumption was associated with a reduced risk of liver cancer in all subjects (hazard ratio for <1, 1-2, and ≥ 3 cups/d; $P(\text{trend}) = 0.67, 0.49, 0.54,$ and 0.025). A similar risk tendency was observed in those with either or both HCV and HBV infection. In contrast, no association was observed between green tea consumption and the risk of liver cancer in all subjects. Our results suggest that coffee consumption may reduce the risk of liver cancer regardless of HCV and HBV infection status, whereas green tea may not reduce this risk

Proanthocyanidin from blueberry leaves suppresses expression of subgenomic hepatitis C Virus RNA. Takeshita M, Ishida YI, Akamatsu E, et al. *J Biol Chem.* 2009 Jun 16. [Epub ahead of print]

http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=Search&Term=%22Takeshita%20M%22%5BAuthor%5D&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVAbstract

Hepatitis C virus (HCV) infection is a major cause of chronic liver disease such as chronic hepatitis, cirrhosis and hepatocellular carcinoma. While searching for new natural anti-HCV agents in agricultural products, we found a potent inhibitor of HCV-RNA expression in extracts of blueberry leaves when examined in an HCV subgenomic replicon cell culture system. This activity was observed in a methanol extract fraction of blueberry leaves, and was purified by repeated fractionations in reversed-phase high-performance liquid chromatography. The final purified fraction showed a 63-fold increase in specific activity compared with the initial methanol extracts, and was composed only of carbon, hydrogen and oxygen. Liquid chromatography/mass-ion trap-time of flight analysis and butanol-HCl hydrolysis analysis of the purified fraction revealed that the blueberry leaf-derived inhibitor was proanthocyanidin. Furthermore, structural analysis using acid thiolytic analysis indicated that the mean degree of polymerization of the purified proanthocyanidin was 7.7, consisting predominantly of epicatechin. Proanthocyanidin with a polymerization degree of 8 to 9 showed the greatest potency at inhibiting the expression of subgenomic HCV RNA. Purified proanthocyanidin showed dose-dependent inhibition of expression of the neomycin resistant gene and the NS-3 protein gene in the HCV subgenome in replicon cells. While characterizing the mechanism by which proanthocyanidin inhibited HCV subgenome expression, we found that heterogeneous nuclear ribonucleoprotein A2/B1 showed affinity to blueberry leaf-derived proanthocyanidin and was indispensable for HCV subgenome expression in replicon cells. These

data suggest that proanthocyanidin isolated from blueberry leaves may have potential usefulness as an anti-HCV compound by inhibiting viral replication.

EPIDEMIOLOGY, DIAGNOSTICS, AND MISCELLANEOUS WORKS

Liver biopsies for chronic hepatitis C: Should nonultrasound-guided biopsies be abandoned? Flemming JA, Hurlbut DJ, Mussari B, Hookey LC. *Can J Gastroenterol.* 2009 Jun;23(6):425-30.

http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=Search&Term=%22Flemming%20JA%22%5BAuthor%5D&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVAbstract

BACKGROUND/OBJECTIVE: Liver biopsy has been the gold standard for grading and staging chronic hepatitis C virus (HCV)- mediated liver injury. Traditionally, this has been performed by trained practitioners using a nonimage-guided percutaneous technique at the bedside. Recent literature suggests an expanding role for radiologists in obtaining biopsies using an ultrasound (US)-guided technique. The present study was undertaken to determine if the two techniques produced liver biopsy specimens of similar quality and hypothesized that at our institution, non-US-guided percutaneous liver biopsies for HCV would be of higher quality than US-guided specimens. **METHODS:** Liver biopsies from 100 patients with chronic HCV infection (50 consecutive US-guided and 50 consecutive non-US-guided), were retrospectively identified using a hospital histopathology database. All original biopsy slides were coded and prospectively reanalyzed by a single hepatopathologist who was blinded to the technique used in obtaining the biopsy. Additionally, all liver biopsies for chronic HCV infection completed at the centre from 1998 to 2007 were identified and the technique used was recorded. Biopsy quality was determined primarily by the number of complete portal tracts (CPTs) identifiable in the slides. The total length of specimen and the degree of fragmentation were secondary outcome measures. **RESULTS:** There was a slight difference observed between the US-guided and non-US-guided groups in mean age (46.3 years versus 42.5 years, respectively; $P=0.018$) but no differences in sex, presence of cirrhosis, bilirubin, creatinine, international normalized ratio, and grade or stage of disease. Biopsies obtained using the US-guided technique produced higher quality specimens than the non-US-guided technique based on our primary outcome of number of CPTs in the biopsy (11.8 versus 7.4; $P<0.001$). US-guided specimens also were longer (24.4 mm versus 19.7 mm; $P=0.001$), had less fragmentation ($P=0.016$), and a higher overall histopathological quality assessment ($P=0.026$) than the non-US-guided biopsies. However, there was no significant difference between the two groups in the ability to grade and stage the disease (96% US-guided versus 90% in non-US-guided ($P=0.20$)). Over a 10-year period, 763 biopsies for chronic HCV infection were identified with an obvious trend toward the increased use of US-guided technique observed at 2% in 1998 to 85% in 2007. **CONCLUSIONS:** US-guided liver biopsies for chronic HCV are the most common method of obtaining specimens at the Kingston General Hospital, Kingston, Ontario, and are of higher quality than non-US-guided specimens. However, there is no significant difference in the two techniques in the ability to grade and stage chronic HCV.

Validation of hepascore, compared with simple indices of fibrosis, in patients with chronic hepatitis C virus infection in United States. Becker L, Salameh W, Sferruzza A, et al. Zhang K, ng Chen R, Malik R, Reitz R, Nasser I, Afdhal NH. *Clin Gastroenterol Hepatol.* 2009 Jun;7(6):696-701.

http://www.ncbi.nlm.nih.gov/pubmed/19514117?ordinalpos=2&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

BACKGROUND & AIMS: Biomarkers are being developed as alternatives to liver biopsy for predicting liver fibrosis in patients with chronic hepatitis C. Hepascore uses noninvasive serum markers and has been validated in Australian and European populations for predicting different degrees of fibrosis. This study validated this test in a U.S. population. **METHODS:** Patients with chronic hepatitis C virus infection were assigned to training (n = 203) or validation (n = 188) sets. Liver fibrosis was staged according to the METAVIR scoring system. The Hepascore algorithm uses data on age, sex, as well as total bilirubin, gamma-glutamyl transferase, alpha2-macroglobulin, and hyaluronic acid levels. **RESULTS:** The ability of Hepascore to predict significant fibrosis (F2-4) as determined by the area under the receiver operating curve was similar in training (0.83) and validation sets (0.81) and was comparable to results seen in previous studies. A cutoff score of $> \text{or} = 0.55$ was best for predicting significant fibrosis, with a sensitivity and specificity of 82% and 65% and positive and negative predictive values of 70% and 78%. When compared with 2 simple indices, FIB-4 (age, platelets, AST, and ALT) and APRI (AST/platelet ratio index), Hepascore performed better at excluding advanced fibrosis by using a low cutoff score but worse at predicting fibrosis by using a high cutoff score. An algorithm with Hepascore followed by FIB-4 or APRI spared 103 of 391 individuals a liver biopsy and missed advanced fibrosis in only 1 patient. **CONCLUSIONS:** Hepascore accurately predicted likelihood of developing fibrosis and could alleviate the need for liver biopsy in a subset of patients.

Healthcare-associated hepatitis C virus transmission among patients in an abdominal organ transplant center. Thompson ND, Hellinger WC, Kay RS, et al. *Transpl Infect Dis.* 2009 May 26.

[Epub ahead of print]

http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=Search&Term=%22Thompson%20ND%22%5BAuthor%5D&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVAbstract

BACKGROUND: De novo hepatitis C virus (HCV) infection among transplant patients is rarely recognized but can have severe consequences. We investigated the scope, source, and mode of HCV transmission within a transplant center after incident HCV infection was identified in 2 patients who had liver transplantation in late 2006. **METHODS:** Patients were interviewed, and transplant logs, medical records, and staff practices were reviewed to identify opportunities for HCV transmission. Infection via receipt of blood or organs was evaluated. Molecular epidemiology was used to determine the relatedness between persons with incident and chronic HCV infection. **RESULTS:** HCV from infected blood or organ donors was ruled out. Among the 308 patients who underwent transplant in 2006, no additional incident HCV infections were identified. Eighty-five (28%) had pre-transplant chronic HCV infection; 13 were considered possible HCV source patients based upon shared days on the inpatient unit, nursing assignment, or invasive procedures in common with incident HCV case-patients. Viral isolates from 1 HCV source patient and 1 incident case-patient were found to be highly related by quasispecies analysis, confirming patient-to-patient HCV transmission. Possible modes of transmission identified were the improper use of multidose vials, sharing of blood-contaminated glucometers, and touch contamination. **CONCLUSION:** Sporadic transmission or endemic levels of HCV transmission might be overlooked in a setting with high HCV prevalence, such as liver transplant units, where multiple, repeated opportunities for patient-to-patient HCV transmission can occur. Surveillance through pre- and post-transplant screening is necessary to identify incident HCV infection in this setting. Constant, meticulous attention must be paid to maintaining aseptic technique and good infection control practices to eliminate HCV transmission opportunities.

Increasing public awareness about hepatitis C: development and validation of the brief hepatitis C knowledge scale. Balfour L, Kowal J, Corace KM, Tasca GA, Krysanski V, Cooper CL, Garber G. *Scand J Caring Sci.* 2009 Jun 5. [Epub ahead of print]

http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=Search&Term=%22Balfour%20L%22%5BAuthor%5D&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVAbstract

Hepatitis C virus (HCV) is silently becoming a major public health problem. Currently, no validated HCV knowledge measures exist. This study aimed to develop and validate a brief measure to assess general knowledge about HCV risk factors, modes of transmissions, and treatment options. A total of 406 individuals participated in this cross-sectional study. All participants completed the proposed 19-item Brief HCV Knowledge Scale. Participants were: HCV mono-infected patients (n = 83), HCV-human immunodeficiency virus (HIV) co-infected patients (n = 24), HIV mono-infected patients (n = 128) community healthcare workers (n = 89), and college students (n = 82). Two-week test-retest data were collected for the college student sample. Psychometric evaluation of the proposed scale demonstrated high levels of validity (content and construct validity) and reliability (internal consistency and retest stability). Factor analysis indicated a one-factor solution, which accounted for 49% of the variance. HCV knowledge was positively correlated with length of time since HCV diagnosis ($r = 0.29$, $p < 0.05$). HCV treatment-experienced patients obtained significantly higher HCV knowledge scores (82% correct) than HCV treatment-naïve patients (72% correct) ($p < 0.05$). HCV knowledge in College students (43% correct) and HIV patients (54% correct) was significantly lower than in HCV patients (77% correct) and community healthcare workers (80% correct) ($p < 0.001$). Community workers' HCV knowledge was positively correlated with years of HCV work experience ($r = 0.30$, $p < 0.01$). This self-administered Brief HCV Knowledge scale has high levels of validity and reliability across patient, healthcare provider and college student populations. It has valuable applications as a clinical teaching tool with patients and healthcare providers and could be used as an outcome indicator in novel HCV educational intervention studies.

Hepatitis C performance measure on hepatitis A and B vaccination: Missed opportunities?

Hernandez B, Hasson NK, Cheung R. *Am J Gastroenterol.* 2009 Jun 2. [Epub ahead of print]

http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=Search&Term=%22Hernandez%20B%22%5BAuthor%5D&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVAbstract

OBJECTIVES: Prevention of hepatitis A virus (HAV) and hepatitis B virus (HBV) infection in patients with chronic hepatitis C (CHC) through vaccination is endorsed by all major professional societies. This study was conducted to determine adherence to the recently adopted physician performance measure on HAV and HBV vaccination. **METHODS:** This was a retrospective study. Hepatitis A and B serology data and immunization records between 2000 and 2007 from CHC patients with detectable hepatitis C virus (HCV) RNA were analyzed. **RESULTS:** A total of 2,968 CHC patients were included in the study. Of these, 2,143 patients (72%) were tested for susceptibility to HAV, of which 53% had immunity. Of the non-immune patients, 746 (74%) were vaccinated as well as an additional 218 without prior testing. For HBV, 2,303 patients (78%) were tested for immunity and 782 (34%) were immune. Of the susceptible patients, 1,086 (71%) were vaccinated as well as an additional 197 patients without prior testing. The overall vaccination performance measure adherence rate was 71% for HAV, 70% for HBV, and 62% for both HAV and HBV. Random review of 176 charts found the major reasons for non-adherence were missed opportunity (41%), change of health care system (31%), and documented vaccination outside our health care system (22%). **CONCLUSIONS:** Our study found a high and improved adherence to the recommendations, but missed opportunity was still the main reason of non-adherence. This study also supported the strategy of selective vaccination in the veteran population.

Chronic liver disease mortality among male prison inmates in Texas, 1989-2003. Harzke AJ, Baillargeon J, Paar DP, Pulvino J, Murray OJ. *Am J Gastroenterol.* 2009 Jun;104(6):1412-9. Epub 2009 Apr 21.

http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=Search&Term=%22Harzke%20AJ%22%5BAuthor%5D&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVAbstract

OBJECTIVES: Alcohol abuse and chronic hepatitis B virus (HBV) and hepatitis C virus (HCV) infections are the major etiologic factors for chronic liver disease/cirrhosis (CLD) in the United States. These CLD risk factors are highly prevalent in US adult incarcerated populations, but CLD-related mortality data from these populations are lacking. The primary objective of this study was to assess CLD-related mortality over time and across categories of race-ethnicity from 1989 through 2003 among male inmates in the Texas state prison system. The secondary objective was to examine patterns of recorded underlying, intervening, and contributing causes of death for CLD-related deaths. **METHODS:** Prisoner decedent data were linked with Texas Vital Statistics multiple-cause-of-death data. Deaths were considered CLD-related if CLD or common sequelae were recorded as the underlying, intervening, or contributing causes of death. CLD-related crude annual death rates, 5-year average annual death rates, and average annual percentage changes were estimated.

RESULTS: Among male Texas prisoners from 1989 to 2003, CLD-related deaths accounted for 16% of deaths (688/4,316). CLD-related crude annual death rates were high and increased over the study period by an average of 4.5% annually, with similar rate increases across categories of race-ethnicity. CLD-related average annual death rates were higher among Hispanic prisoners than among black prisoners in each 5-year period, and were higher than those for white prisoners in the 1994-1998 and 1999-2003 periods. HBV or HCV was identified as a causal factor in more than a third (34%) of CLD-related deaths. **CONCLUSIONS:** From 1989 to 2003, CLD-related death rates among male Texas prisoners were high and increased over time, particularly among Hispanics. Targeted prevention, screening, and treatment of CLD risk factors, especially HCV, and early detection and treatment of CLD should be considered as priorities of the US prison healthcare systems.

Improving access to care by allowing self-referral to a hepatitis C clinic. Doucette KE, Robson V, Shafran S, Kunimoto D. *Can J Gastroenterol.* 2009 Jun;23(6):421-4.

http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=Search&Term=%22Doucette%20KE%22%5BAuthor%5D&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVAbstract

BACKGROUND: Estimates suggest that more than 250,000 Canadians are infected with hepatitis C virus (HCV), but less than 10% have been treated. Access to specialists in Canada is usually via health care professional (HCP) referral and, therefore, may be a barrier to HCV care. However, clinics that operate in conjunction with the Hepatitis Support Program, Edmonton, Alberta, allow self-referral. It is hypothesized that this improves access to care without increasing inappropriate referrals. **OBJECTIVE:** To compare the baseline characteristics and outcomes of HCV patients who self-referred with those who were HCP-referred. **METHODS:** Data were collected from the Hepatitis Support Program HCV database and chart reviews. **RESULTS:** Between December 17, 2002, and December 31, 2007, 1563 patients were referred including 336 self- (21.5%) and 1227 HCP-referrals (78.5%). Self- and HCP-referred patients were similar in terms of age (mean [+/- SD] 43.0+/-10.3 years versus 43.9+/-10.0 years, respectively; P=0.18), sex (56.8% versus 62.0% [men], respectively; P=0.08) and risk factors for HCV (P=0.3), with 49.7% and 52.6%, respectively, identifying injection drug use as the primary risk factor. The two groups had similar HCV genotype distributions and liver biopsy fibrosis scores with similar treatment rates (31.3% versus 33.2%; P=0.6). Treatment outcomes were excellent (sustained virological response 40.2% for genotype 1,

67% for genotypes 2 and 3) in patients completing therapy and were similar between the two groups. **CONCLUSION:** Self-referred patients comprised 21.5% of patients accessing care in the clinic. Self- and HCP-referred patients had similar characteristics, treatment rates and outcomes. Facilitating self-referral to an HCV clinic can improve access to care, including risk reduction education and HCV treatment.

Prevalence of problem alcohol use among patients attending primary care for methadone treatment. Ryder N, Cullen W, Barry J, Bury G, Keenan E, Smyth BP. BMC Fam Pract. 2009 Jun 11;10(1):42. [Epub ahead of print]

http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=Search&Term=%22Ryder%20N%22%5BAuthor%5D&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVAbstract

ABSTRACT: BACKGROUND: Problem alcohol use is associated with adverse health outcomes among current or former heroin users and primary care is providing methadone treatment for increasing numbers of this population. This study aimed to determine the prevalence of problem alcohol use among current or former heroin users attending primary care for methadone treatment and to describe the socio-demographic characteristics and health service utilisation characteristics associated with problem alcohol uses. **METHODS:** We conducted a cross sectional survey of patients sampled from a national database of patients attending general practice for methadone treatment. Participants were recruited by their general practitioner and data was collected using an interviewer-administered questionnaire, which included the Alcohol Use Disorders Identification Test ('AUDIT'), with a score of >7 considered abnormal (ie 'AUDIT positive cases') and socio-demographic, medical and substance use characteristics. **RESULTS:** We interviewed 196 patients (71% of those invited, 31% of those sampled, 11% of the national database). The median age was 32 years, 55% were hepatitis C positive, 79% had used illicit drugs in the previous month and 68% were male. Sixty-eight 'AUDIT positive' cases were identified (prevalence of 35%, 95% CI=28-41%) and these were more likely to have attended a local Emergency Department in the previous year ($p<0.05$) and less likely to have attended a hospital clinic in the previous year ($p<0.05$). Twenty-seven (14%) scored 20 or higher indicating possible alcohol dependence. **CONCLUSIONS:** Problem alcohol use has a high prevalence among current or former heroin users attending primary care for methadone treatment and interventions that address this issue should be explored as a priority. Interventions that address problem alcohol use in this population should be considered as a priority, although the complex medical and psychological needs of this population may make this challenging.

Prevalence and trends of human immunodeficiency virus, hepatitis B virus, and hepatitis C virus among blood donors in Iran, 2004 through 2007. Amini Kafi-Abad S, Rezvan H, Abolghasemi H, Talebian A. Transfusion. 2009 Jun 10. [Epub ahead of print]

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BACKGROUND: Evaluation and monitoring the prevalence of transfusion-transmissible viral infections in blood donors is a valuable index of donor selection and blood safety. This study analyzed the trends of blood-borne infections among Iranian blood donations during 4 years. **STUDY DESIGN AND METHODS:** Viral screening results of 6,499,851 allogeneic donations from 2004 through 2007 were analyzed. All donations were screened for hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV), and syphilis. The prevalence of HBV, HCV, and HIV infections per 100,000 donations and 95% confidence interval was calculated.

The p value was estimated by chi-square test. **RESULTS:** The prevalences of HBV, HCV, and HIV decreased during the 4-year study from 2004 through 2007. The overall prevalence was 0.56% for HBV, 0.004% for HIV, and 0.13% for HCV. There was a significant and impressive decrease in hepatitis B surface antigen prevalence from 0.73% in 2004 to 0.41% in 2007. The prevalence of HIV appeared to have decreased from 0.005% in 2004 to 0.004% in 2007 although the decrease was not significant. HCV prevalence showed a slight decline in blood donations from 0.14% in 2005 to 0.12% in 2007. **CONCLUSION:** The trends of transfusion-transmitted infection prevalence in Iranian blood donations suggest that most of the safety measures employed in recent years in Iran have been effective.

Effective use of FibroTest to generate decision trees in hepatitis C. Lau-Corona D, Pineda LA, Avilés HH, et al World J Gastroenterol. 2009 Jun 7;15(21):2617-22.

http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=Search&Term=%22Lau-Corona%20D%22%5BAuthor%5D&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVAbstract

AIM: To assess the usefulness of FibroTest to forecast scores by constructing decision trees in patients with chronic hepatitis C. **METHODS:** We used the C4.5 classification algorithm to construct decision trees with data from 261 patients with chronic hepatitis C without a liver biopsy. The FibroTest attributes of age, gender, bilirubin, apolipoprotein, haptoglobin, alpha2 macroglobulin, and gamma-glutamyl transpeptidase were used as predictors, and the FibroTest score as the target. For testing, a 10-fold cross validation was used. **RESULTS:** The overall classification error was 14.9% (accuracy 85.1%). FibroTest's cases with true scores of F0 and F4 were classified with very high accuracy (18/20 for F0, 9/9 for F0-1 and 92/96 for F4) and the largest confusion centered on F3. The algorithm produced a set of compound rules out of the ten classification trees and was used to classify the 261 patients. The rules for the classification of patients in F0 and F4 were effective in more than 75% of the cases in which they were tested. **CONCLUSION:** The recognition of clinical subgroups should help to enhance our ability to assess differences in fibrosis scores in clinical studies and improve our understanding of fibrosis progression.

Prevalence of human cytomegalovirus co-infection in patients with chronic viral hepatitis B and C: A comparison of clinical and histological aspects. Bayram A, Ozkur A, Erkilic S. J Clin Virol. 2009 Jun 2. [Epub ahead of print]

http://www.ncbi.nlm.nih.gov/pubmed/19497785?ordinalpos=2&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

BACKGROUND: Human cytomegalovirus (HCMV) is a common pathogen of severe disease in patients with impaired immune functions. Reactivation of HCMV in immunocompetent host is usually asymptomatic, but may deteriorate the prognosis of patient with chronic illness.

OBJECTIVES: This study was conducted to detect HCMV infection in patients with chronic hepatitis B virus (HBV) and chronic hepatitis C virus (HCV) infections and to point out the effects of HCMV-HBV and HCMV-HCV co-infections on liver histology. **STUDY DESIGN:** Expression of HCMV DNA was determined in liver tissue biopsies by real-time quantitative polymerase chain reaction (qPCR) method. There were 44 chronic HBV, and 25 chronic HCV patients within the study group. Control group consisted of 36 patients with hepatologic malignancies. **RESULTS:** HCMV infection was demonstrated in 52.3% of chronic HBV, and 36% of chronic HCV patients. Although alanine aminotransferase (ALT) levels of HCMV-infected HBV patients were decreased slightly, they were increased in HCV patients. Histologic activity scores (necroinflammation and fibrosis) of HCMV-positive patients were higher than that of HCMV-negatives in both HBV and HCV groups. Intrahepatic HBV DNA or HCV RNA loads of the corresponding study groups were

decreased in HCMV-infected patients. **CONCLUSION:** We conclude that HCMV infection is common in chronic HBV and HCV patients, who can be regarded as patients at high risk for HCMV disease. Though the histological changes were more marked in liver, replication of HBV and HCV were inhibited in HCMV-positive cases.