

IN THE NEWS

10% of Babies Infected with HCV Via Moms [Japan]

<http://www.hcvadvocate.org/news/newsRev/2005/NewsRev-83.html> About 10 percent of babies in the nation born to mothers who are suffering from hepatitis C are infected with the hepatitis C virus, according to the findings of a study by a health ministry team. For some time now, it has been known that HCV is transmitted from mothers to children, but this is the first time that the number of those infected has been established. The Health, Labor and Welfare Ministry research team, led by Kazuo Shiraki, professor emeritus of Tottori University, surveyed a total of 421 pregnant women suffering from hepatitis C at five medical institutions until fiscal 2003. Forty-one of their babies were found to have been infected with HCV. The infection rate ranged from 7.5 percent to 11.9 percent depending on the type of hospital, which included university hospitals. The average rate stood at 9.7 percent, researchers said.

A New Website Resource, www.Heplinks.Com was recently launched on the First Annual International Hepatitis C Awareness Day <http://www.hcvadvocate.org/news/newsRev/2005/NewsRev-85.html>

The web portal is a result of a cooperative initiative among hepatitis C and liver disease patient associations in Europe and the Middle East. It is supported by Roche. Information found on www.Heplinks.com includes: Facts about hepatitis C, frequently asked questions and answers, links to patient associations and liver organizations, information about relevant scientific or medical congresses and meetings, links to relevant journals and publications.

Altor BioScience Corporation Establishes Collaboration with Leading Massachusetts General Hospital Investigator to Develop TCR-based Agents to Detect and Treat HIV and HCV Infection

<http://www.hcvadvocate.org/news/newsRev/2005/NewsRev-84.html> Altor BioScience Corporation today announced that it has established a collaboration with Massachusetts General Hospital (MGH) and Howard Hughes Medical Institute to use viral specific T-cell receptors (TCR) for research, diagnosis and treatment of HIV and hepatitis C (HCV) infections. The collaboration brings together the leading HIV/HCV research program of Professor Bruce Walker, M.D., a Howard Hughes Medical Institute investigator at the Partners AIDS Research Center at MGH, characterizing immune responses in virally infected patients, and STAR(TM) technologies developed at Altor for soluble TCR-based targeting reagents. Hing Wong, Ph.D., CEO of Altor, stated, "We are very excited about having the opportunity to work with Dr. Walker and his colleagues at MGH. Dr. Walker is one of the foremost authorities on viral antigen expression and the resulting T-cell immune responses in HIV and HCV infected patients. His laboratory has generated a number of different T-cells that react against these viruses. We have found that T-cells reactive against tumor associated antigens could be used to generate soluble TCR-based reagents, capable of quantitatively detecting antigens on cancer cells and inhibiting growth of primary tumors in animal models. This collaboration will allow us to extend our strategies to viral diseases."

Bayer Wins US FDA Approval for Automated Hepatitis C Test UPDATE

<http://www.hcvadvocate.org/news/newsRev/2005/NewsRev-84.html> Bayer AG's HealthCare Diagnostics division said its automated hepatitis C test has been approved by the US Food and Drug Administration. The test is developed, manufactured and sold by Bayer Diagnostics for Ortho-Clinical Diagnostics, Inc, a subsidiary of Johnson & Johnson. A Bayer spokeswoman explained that the test has been developed for Bayer's ADVIA Centaur Immunoassay System, a fully automated invitro diagnostic testing-lab which can perform more than 100 blood tests per minute. John Nosenzo, senior vice president in North America for Bayer HealthCare Diagnostics said the test will make the testing of at-risk individuals a more routine and reliable (procedure), reducing errors often garnered through manual test methods. The ADVIA Centaur System can test other conditions, such as cancer, cardiovascular diseases, fertility and allergy. The automated hepatitis C test was

approved in Europe, Latin America and Asia Pacific in April 2003.

Coffee and caffeine consumption reduce the risk of elevated serum alanine aminotransferase activity in the United States http://www.hivandhepatitis.com/hep_c/news/2005/012105_a.html CE Ruhl, JE Everhart. *Gastroenterology* January 2005 · 128(1) 24-32. **Background & Aims:** Based on experimental and epidemiologic studies, we investigated whether coffee and caffeine consumption reduced the risk of elevated alanine aminotransferase (ALT) activity in persons at high risk for liver injury in a national, population-based study. **Methods:** Participants were 5944 adults in the Third US National Health and Nutrition Examination Survey, 1988-1994, with excessive alcohol consumption, viral hepatitis, iron overload, overweight, or impaired glucose metabolism. Liver injury was indicated by abnormal serum ALT activity (>43 U/L). **Results:** Elevated ALT activity was found in 8.7% of this high-risk population. In unadjusted analysis, lower ALT activity was associated with increasing consumption of coffee (P = .001) and caffeine (P = .001). Multivariate logistic regression analyses showed that the risk of elevated ALT activity declined with increasing intake of coffee (P for trend = .034) and caffeine (P < .001). Comparing persons who drank more than 2 cups per day with noncoffee drinkers, the odds ratio was .56 (95% confidence interval, .31-1.0). Comparing persons in the highest caffeine quintile with the lowest, the odds ratio was .31 (95% confidence interval, .16-.61). These relationships were consistent across subgroups at risk for liver injury and were relatively unchanged when analyses included the entire population or when limited to persons without impaired liver function or right upper quadrant pain. Fasting insulin concentrations did not mediate the effects. **Conclusions:** In this large, national, population-based study, among persons at high risk for liver injury, consumption of coffee and especially caffeine was associated with lower risk of elevated ALT activity.

Cosmetic Injections Are Linked to Spread of Variant CJD and Hepatitis [UK]

<http://www.hcvadvocate.org/news/newsRev/2005/NewsRev-85.html> Injection of "fillers" to plump up lips and smooth out wrinkles could spread infections such as variant CJD and hepatitis, the Government's chief medical officer warned yesterday. "Aesthetic fillers" injected under the skin, popular with celebrities to counter sagging features, use material from animals, birds and human corpses, Sir Liam Donaldson said. In a crackdown on rogue cosmetic surgery clinics, Sir Liam said: "We do have to look into the use of aesthetic fillers to establish if there is any risk of variant CJD, hepatitis and other blood-borne viruses. There is no evidence of outbreaks in relation to the use of products but this is something we need to look into." One of the most heavily used materials is collagen, which may contain bovine material carrying a potential risk of infection with BSE. The singer Kylie Minogue was reported this week to have had injections of a filler to enhance her lips. Many fillers fall outside any system of regulation because they use human tissue. There are an estimated 20,000 high street clinics offering cosmetic treatments from Botox injections, which paralyze muscles rather than fill out wrinkles and do not contain animal or human tissue, to facelifts with widely varying standards and varying skill of surgeons.

Counties Studying Law OK'ing Needle Sales <http://www.hcvadvocate.org/news/newsRev/2005/NewsRev-82.html> A new law that took effect Saturday will allow California pharmacies to sell needles without a prescription to help prevent HIV/AIDS and hepatitis C, but addicts can't head to their local drugstore for a clean fix just yet. Local governments must approve such sales and, so far, only Contra Costa County has given the go-ahead. Most Bay Area public health departments are still studying the issue. The legislation, introduced by state Sen. John Vasconcellos, D-San Jose, and signed into law last year by Gov. Arnold Schwarzenegger, permits pharmacists to sell up to 10 sterile syringes and needles at a time to people older than 18. Pharmacists must sign up to participate in a "demonstration" program that will be tracked by state health authorities for its usefulness in preventing disease. Pharmacists' participation is voluntary, and life won't change for diabetics and other patients who routinely get prescriptions to purchase syringes to inject insulin or other medications.

Depression Caused by Common Treatment for Hepatitis C May Affect Outcome Emory University Health Sciences Center <http://www.hcvadvocate.org/news/newsRev/2005/NewsRev-83.html> An article appearing in the January 2005 issue of *Brain, Behavior and Immunity* suggests that developing depression while on

interferon-alpha plus ribavirin may impact how well the medications work. In a study conducted in the Department of Psychiatry and Behavioral Sciences at Emory University School of Medicine, Charles L. Raison, MD, Andrew Miller, MD, and colleagues, observed that patients who develop depressive symptoms during interferon-alpha plus ribavirin therapy were significantly less likely to have cleared the hepatitis C virus from their blood following six months of treatment.

Drug Firms Offer Saving Card for U.S. Uninsured

<http://www.hcvadvocate.org/news/newsRev/2005/NewsRev-83.html> Top pharmaceutical companies launched a new prescription drug savings card on Tuesday in an attempt to help reduce costs for the roughly 45 million Americans without health insurance. The free card, called Together RX Access, gives patients access to discounts at pharmacies on brand-name and generic medicines starting next month for poorer patients who are too young for Medicare coverage. To qualify, individual patients without health insurance must earn no more than \$30,000 and be younger than 65 and a legal U.S. resident. Income requirements are adjusted based on family size; for example, a family of four must earn no more than \$60,000.

Experts Warn against Growth Of Hepatitis C on Long Island

<http://www.hcvadvocate.org/news/newsRev/2005/NewsRev-83.html> The growing prevalence of hepatitis C on Long Island could pose a greater threat than the emergence of HIV two decades ago, a health expert said Friday. Doctors, researchers, community activists and people with the blood-borne infection testified in Manhattan before members of two state Assembly committees asking legislators to take action. The disease can cause irrevocable liver damage. Experts predict an epidemic could overwhelm health systems and overload waiting lists for transplantable livers. "This is just the start of a tidal wave that is going to hit in 2015 to 2020," said Dr. Alain Litwin, an infectious disease expert from Albert Einstein School of Medicine in the Bronx.

Health Officials Probe Hepatitis C Cases

<http://www.hcvadvocate.org/news/newsRev/2005/NewsRev-82.html> A vial of a radioactive solution, 12 hepatitis C cases and one death so far are the elements of a mystery health officials are pondering. The cases were from a group of 16 people injected with the solution Oct. 15 for routine heart-stress testing, all from a single vial produced by a Timonium pharmacy run by Cardinal Health, the Dublin, Ohio-based company said. Among them was John Leto, 80, a Brooklyn Park man who died of pneumonia on Christmas Day after suffering from hepatitis, a disease of the liver. Investigators are now trying to learn how the 12 were infected, a probe that could take months to complete, said John Hammond, a spokesman for the state health department. Cardinal said the investigation is focusing on the way the doses were prepared and not on the pharmaceutical tracer contained in the doses. Prof. Fadia Shaya, who chairs the state council that evaluates the state's plan for monitoring and controlling hepatitis.

Hepatitis C Caring Ambassadors Program Releases New, 3rd Edition of Hepatitis C Choices

<http://www.hcvadvocate.org/news/newsRev/2005/NewsRev-83.html> The Hepatitis C Caring Ambassadors Program (HCCAP) proudly announces the Internet release of the newly updated 3rd edition of Hepatitis C Choices: Distinctive Viewpoints on Choices for Your Hepatitis C Journey. The book is authored by a team of 20 leading medical experts and patient advocates. Hepatitis C Choices presents an objective review of conventional and alternative treatment options for the more than four million Americans currently infected with the hepatitis C virus (HCV). It is the only book of its kind currently available.

Hersh & Hersh Files Lawsuit Against Drug Maker Valeant for Brain Injury Sustained by Plaintiff During Hepatitis C Clinical Drug Trial

<http://www.hcvadvocate.org/news/newsRev/2005/NewsRev-83.html> Product liability law firm Hersh & Hersh today announced that it has filed a lawsuit in San Francisco Superior Court on behalf of plaintiff Linda Iacovetta against Valeant, a Southern California drug company, and California Pacific Medical Center (CPMC) in San Francisco. Hersh & Hersh attorneys claim that as a result of participating in Valeant's clinical trial to test the effects of the combination of viramidine and pegylated interferon for treating hepatitis C, Iacovetta developed brain damage and has become permanently disabled. CPMC physicians

who conducted the clinical trials are denying they were agents of Valeant and are not culpable under product liability law. They have requested a hearing which will take place on Friday, January 14 in San Francisco Superior Court. The San Francisco medical lawsuit ties into the recent barrage of high-profile drug controversies ignited by the stunning discovery that Vioxx , Celebrex and even Aleve are now known to cause heart attacks and strokes. Drug companies have come under fire for over-marketing their products to doctors while withholding negative findings of their for-profit clinical trials to the U.S. Food & Drug Administration, and for paying doctors large sums of money to enlist their patients in these studies. According to Nancy Hersh of Hersh & Hersh, "It is widely known that drug companies turn to physicians for access to patient volunteers to participate in studies and that they in turn receive fees for each patient enrolled. We can show that the CPMC physicians involved in the hepatitis C drug treatment study did accept payment for providing patients while knowing their patients would be at risk of the drug combination's side effects. "Ms. Iacovetta has been rendered mentally incapacitated by the fraudulent actions of Valeant and the CPMC physicians. They are part of the latest scourge against the drug industry and medical community."

Interferon Slows Hep C Progression: Research Confirms Low-Dose Therapy Works for Long-Term Maintenance

<http://www.hcvadvocate.org/news/newsRev/2005/NewsRev-83.html> For the first time, a study confirms what many doctors thought was true: The progression of hepatitis C can be prevented or delayed by using pegylated interferon alfa-2b (PEG-Intron) as long-term maintenance therapy in patients who have not responded to full-dose interferon therapy. The study, led by Dr. Nezam Afdhal of the Beth Israel Deaconess Medical Centre here, is not yet complete, but the results are promising. The study includes 550 chronic hepatitis C patients with advanced fibrosis who have failed interferon therapy to eradicate the virus. The patients, enrolled in the COPILOT (Colchicine versus PEG-INTRON long-term) study, have completed two years of the four-year study. The study is testing low-dose PEG-interferon alpha-2b against colchicine, an anti-inflammatory and antifibrotic medication. Those patients receiving PEG-interferon alfa-2b have experienced a 50% reduced chance of reaching a clinical endpoint, such as liver failure or liver transplantation, compared with patients in the colchicine group.

Metabasis Therapeutics, Inc. Announces an Extension and Expansion of Its Existing Collaboration With Merck & Co., Inc. to Develop New Treatments for Hepatitis C

<http://www.hcvadvocate.org/news/newsRev/2005/NewsRev-85.htm> Metabasis Therapeutics, Inc. announced today that it has extended and expanded a hepatitis C collaboration that was established with Merck in December 2003. The companies will continue their joint efforts to identify novel small molecule therapeutics for the treatment of hepatitis C virus infections (HCV) for an additional twelve months, through December 2005.

Mouse to Help Fight Hepatitis-C

<http://www.hcvadvocate.org/news/newsRev/2005/NewsRev-82.html> A genetically engineered mouse will soon be used in a new initiative by Indian and German scientists to prevent hepatitis and other communicable diseases. Under an agreement to be signed in March by the German Research Centre for Biotechnology (GBF) and the Indian Council of Medical Research, scientists will develop a mouse that would be infected with the hepatitis-C virus, said Rudi Balling, GBF's director. "So far, it has been impossible to create a study model for the disease. But we are trying our best since a mouse in many cases behaves like humans," Balling told IANS on the sidelines of the Indian Science Congress here. The mouse would receive human immune cells derived from the umbilical cord of a foetus and be infected with the "hepatocides" that cause the Hepatitis-C disease. "It would help in our study to a great extent," said Balling, whose organization does a lot of work with "mouse genetics".

Needlestick Injuries in Healthcare Workers Still Occurring, UK

<http://www.hcvadvocate.org/news/newsRev/2005/NewsRev-85.htm> The latest Health Protection Agency report on the occupational exposure of healthcare workers (HCWs) to blood borne viruses (BBVs) shows that nine healthcare workers were infected with hepatitis C through needlestick injuries over the last six years, with seven reported between July 2003 and June 2004. Between 1996 and 2004, 2140 incidents of significant

occupational exposure to BBVs were reported to the Agency; 47% (997/2140) of these HCWs were exposed to hepatitis C and 26% (551/2140) to HIV. These figures, gathered through the Agency's monitoring programme, which looks at exposures to BBVs in healthcare settings, indicate that there are still too many exposures occurring. Although over half of the injuries looked at occurred during the procedure, over a third were after the procedure and during disposal of clinical waste, including exposures sustained while recapping needles or clearing clinical waste left by another worker.

New Director of the Division of Viral Hepatitis at CDC Appointed

http://www.hepfi.org/news/research_news.html Dr. John Ward has accepted the position of Director, Division of Viral Hepatitis (DVH). Dr. Ward most recently served as Editor of the Morbidity and Mortality Weekly Report (MMWR) and as Acting Director of the Division of Scientific Communications, in the proposed National Center for Health Marketing, National Coordinating Center for Health Information and Service. Dr. Ward received his M.D. from the University of Alabama School of Medicine in Birmingham and completed an internship and residency in internal medicine at the University of Alabama Hospitals. In addition to his EIS training, he received postgraduate training in tropical medicine at the London School of Tropical Medicine and Hygiene, in pediatric immunology at the Royal Children's Hospital in Melbourne, Australia, and in infectious diseases as a CDC assignee at the University of Washington Medical Center in Seattle. He joined CDC in 1984 as an EIS officer in the Epidemiology Section of what was then known as the AIDS Activity, NCID. He remained in CDC's evolving AIDS program through 1998, working on many high profile investigations and serving in various leadership positions including section chief and then later branch chief of the Surveillance Branch in the Division of HIV/AIDS, NCID. He became Editor of the MMWR in 1998. The recipient of numerous CDC and PHS awards, Dr. Ward is a member of the Emory University School of Medicine Clinical Faculty and is active on many public health planning and steering committees. He is the author or coauthor of more than 100 scientific publications and serves as a peer reviewer for numerous journals including the American Journal of Public Health, JAMA, and Annals of Internal Medicine.

New NIDDK Branch Focuses on Liver Disease http://www.hepfi.org/news/research_news.html A New Liver Disease Branch at the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) will focus research efforts on the critical areas of hepatitis B and hepatitis C, clinical liver disease, liver and biliary diseases and liver transplantation. Heading the new branch is Dr. Jay Hoofnagle, former director of the NIDDK's Division of Digestive Diseases and Nutrition (DDN) and one of the world's leading authorities in the field of liver disease. This is not just a shuffling of the deck chairs," says Dr. Hoofnagle, noting that the new branch is the result of "strong interest" from Congress and the lay community in raising the status of liver disease with the Institute. The new branch will function within the DDN division, but with its own branch chief, staff, and an exclusive focus on the liver and liver disease. "This will give the liver research its own home at the NIH," Dr. Hoofnagle says. Dr. Stephen James, former deputy director of the DDN, is now the division's director.

NIH Action Plan Charts Future Challenges for Liver Disease Research

<http://www.hcvadvocate.org/news/newsRev/2005/NewsRev-82.html> The National Institutes of Health (NIH) today released the trans-NIH Action Plan for Liver Disease Research, a comprehensive plan that addresses the burden of liver diseases in the United States and maps out challenges for future research. The Action Plan is available on-line at <http://liverplan.niddk.nih.gov>.

Organetix, Inc. Announces Hepatitis C Patients Continue to Progress and Plans to Commence a Double Blind Placebo Controlled Study in Second Quarter of 2005

<http://www.hcvadvocate.org/news/newsRev/2005/NewsRev-84.html> Organetix Inc. announced today that the Hepatitis C patients from the June 2004 study are continuing to use the Company's A4+L formula and continue to enjoy a significant improvement in their quality of life. Organetix intends to conduct a follow-up study by the end of March 2005. Organetix, Inc. also plans to commence a new double-blind study involving a larger sample size with a placebo control during the second Quarter of 2005. Current laboratory results are

continuing to support the safety and efficacy of the A4+L liver formula. These results will also support and strengthen all future patent applications.

Researcher cites "bias" toward Peg-Intron in trial <http://www.natap.org/> A lead researcher for a high-stakes trial comparing the world's top-selling drugs for hepatitis C said the study's design could "bias" results in favor of Schering-Plough Corp.'s product. "Unfortunately life is not perfect and this study is not perfect as well," Dr. John McHutchison, co-lead investigator of the Schering-Plough trial, told Reuters in an interview on Thursday. Schering-Plough's Peg-Intron and Roche Holding AG's more popular rival medicine, Pegasys, are both injectable forms of interferon. They are used in 48-week treatments with a pill called ribavirin that helps them eradicate the hepatitis C virus, the biggest cause of liver transplants. McHutchison, a Duke University researcher, said the study's design will probably allow more patients receiving Peg-Intron to stay on stronger doses of ribavirin than those taking Pegasys. "Maintaining the (highest tolerable) dose of ribavirin, regardless of which interferon is used, is very important for controlling the virus, particularly in the early part of treatment," McHutchison said. Schering-Plough in May launched the 2,880-patient U.S. trial, called IDEAL, and hopes to unveil results in 2007 that will prove Peg-Intron is superior. Should it triumph, Schering-Plough aims to use the data as a marketing weapon to stem lagging sales of its one-time blockbuster, and help the struggling drugmaker regain earnings growth. Peg-Intron and Schering-Plough's brand of ribavirin had combined third-quarter sales of \$184 million, a fraction of the \$703 million they boasted in the same quarter of 2002. McHutchison said Peg-Intron patients will take starting ribavirin doses of 800 milligrams to 1400 milligrams daily, vs 1,000 to 1,200 milligrams for Pegasys patients. But Peg-Intron patients who develop anemia or other side effects from ribavirin will have their daily dose of the pill reduced by 200 milligrams, with subsequent 200-milligram cuts if necessary. By contrast, Pegasys patients with side effects must have their ribavirin cut back to 600 milligrams in one fell swoop. "The dose reductions for ribavirin are not equivalent in the two arms of the study and could therefore introduce a potential bias" in favor of the Peg-Intron arm of the trial, McHutchison said. McHutchison said he expressed his concerns to Schering-Plough, which in turn relayed them to the U.S. Food and Drug Administration before the trial began. However, the FDA insisted that instructions on the Pegasys drug label be followed -- any ribavirin reductions must be to 600 milligrams. "The FDA wouldn't allow it (smaller cutbacks), and unfortunately that's the way it stands," McHutchison said. However, McHutchison said most doctors typically reduce ribavirin among Pegasys patients by 200 milligram increments. Despite the potential ribavirin dose advantage to Peg-Intron patients, McHutchison and Schering-Plough said the study is large enough to demonstrate the true superiority of either medicine.

CO-INFECTION

Correlation of insulin resistance with steatosis and fibrosis in hepatitis C and HIV co-infection: Cross-sectional analysis of 101 patients. Agarwal K, Fiel M, Uriel AJ Program and abstracts of the 55th Annual Meeting of the American Association for the Study of Liver Diseases; October 29 - November 2; Boston, Massachusetts. Abstract 978. <http://clinicaloptions.com/hep/conf/aasld2004/cs/978.asp>. **Summary of Key Conclusions** Multivariate analysis indicates that homeostasis model assessment-insulin resistance (HOMA-IR) and HCV genotype significantly correlated with steatosis For each increasing unit of IR, odds ratio of steatosis increases by 1.067 IR may play important role in histologic progression of disease.

Histologic findings and clinical characteristics associated with steatosis in HIV/HCV co-infected patients. Marks KM, Petrovic LM, Talal AH, et al. Program and abstracts of the 55th Annual Meeting of the American Association for the Study of Liver Diseases; October 29 - November 2; Boston, Massachusetts. Abstract 675. <http://clinicaloptions.com/hep/conf/aasld2004/cs/675.asp> **Summary of Key Conclusions** Hepatic steatosis common (55%), but generally mild, in patients coinfecting with hepatitis C virus (HCV) and HIV; Increased steatosis grade significantly associated with: Increased fibrosis stage; Increased body mass index (BMI); Increased lipodystrophy; Decreased high-density lipoprotein cholesterol (HDL-C) level; Use of antiretroviral therapies (duration or type) not associated with steatosis grade.

Predictors of anemia in a cohort of HIV/HCV infected patients on interferon and ribavirin include age and sex, but not CD4 count. Ginzburg L, Uriel AJ, Bodain C, Dieterich DT. Program and abstracts of the 55th Annual Meeting of the American Association for the Study of Liver Diseases; October 29 - November 2; Boston, Massachusetts. Abstract 397. <http://clinicaloptions.com/hep/conf/aasld2004/cs/397.asp> **Summary of Key Conclusions** In patients coinfecting with HIV and hepatitis C virus (HCV), women and those > 55 years may be at increased risk of developing anemia. Development of anemia not associated with baseline iron deficiency, CD4+ cell count < 200 cells/mm³, cirrhosis, ribavirin dose, or zidovudine.

Relationships between Hepatic Iron Content and Virologic Response in Chronic Hepatitis C Patients Treated with Interferon and Ribavirin. Rulyak SJ, Eng SC, Patel K, McHutchison JG, Gordon SC, Kowdley KV. *Am J Gastroenterol* 2005;100:1-6

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15667490&dopt=Abstract

OBJECTIVES: The aims of this study were to determine the effect of pretreatment hepatic iron concentration (HIC) on response to combination therapy with interferon and ribavirin, and to examine the change in HIC associated with this treatment. **METHODS:** Patients with hepatitis C who underwent liver biopsy before and after combination therapy were studied retrospectively. HIC was measured from paired pre- and posttreatment liver biopsy specimens, and histologic grade and stage were recorded. **RESULTS:** Sixty of 112 (54%) patients achieved sustained virologic response (SVR); response varied by genotype (genotype 1 (44%), genotype 2 or 3 (85%)). There was no difference in pretreatment median HIC between responders and nonresponders (404 mug/g and 394 mug/g, respectively; $p = 0.31$); patients with HIC ≥ 500 mug/g were not less likely to achieve SVR (OR = 1.1; 95% CI 0.5-2.3). In a multivariate analysis, factors associated with SVR included genotype 2 or 3 (OR = 12.2; 95% CI 3.1-47.8) and viral load < 2 million copies/ml (OR = 3.6; 95% CI 1.3-10.0). HIC ≥ 500 mug/g did not decrease the likelihood of SVR (OR = 0.8; 95% CI 0.3-2.1). There was no significant change in HIC after combination therapy (median increase in HIC = 29.5 mug/g), and the change in HIC did not differ between responders and nonresponders ($p = 0.73$). **CONCLUSIONS:** Pretreatment HIC is not an independent predictor of response to therapy with interferon and ribavirin. Combination therapy does not significantly change HIC regardless of baseline histology or virologic response.

The effect of antiretroviral therapy on liver disease among adults with HIV and hepatitis C coinfection. SH Mehta, et al. *HEPATOLOGY* 2005;41:123-131 Abstract

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15619237&dopt=Abstract

In the era of antiretroviral therapy (ART), liver disease has emerged as an important cause of death among persons with human immunodeficiency virus (HIV)/hepatitis C virus (HCV) coinfection. The objective of this study was to estimate the burden of liver disease and evaluate determinants of liver fibrosis and necroinflammatory activity among HIV/HCV coinfecting patients receiving ART. We studied 112 randomly selected and 98 referred HCV-infected patients undergoing care in the Johns Hopkins University HIV clinic. Liver disease was characterized clinically and histologically. Of the 210 individuals studied - 64% of whom had received ART within 2 years of liver disease assessment - 33% had no fibrosis (F0), and 26% had bridging fibrosis or cirrhosis (F3). The median necroinflammatory activity score was 3 (range, 0-9 of 18). ART was not associated with fibrosis; however, significantly less hepatic necroinflammatory activity was observed among persons who had received highly active antiretroviral therapy longer ($P = .02$) and more effectively (defined by HIV RNA suppression; $P < .01$). Twelve percent of individuals had previous ART-associated liver enzyme elevations (grades 3-4), but liver fibrosis was not more severe if the liver enzyme elevation resolved. On the other hand, liver fibrosis was more severe in persons with persistent liver enzyme elevations (grades 1-4). In conclusion, despite widespread exposure to ART and documented instances of ART-related hepatitis, we found no evidence that ART caused serious histological liver disease. Recognition of bridging fibrosis and cirrhosis in some but not most patients underscores the importance of identifying and treating liver disease in HIV/HCV coinfecting persons.

The effect of HIV coinfection on the risk of cirrhosis and hepatocellular carcinoma in U.S. veterans with hepatitis C. Kramer JR, Giordano TP, Soucek J, Richardson P, Hwang LY, El-Serag HB. *Am J Gastroenterol.* 2005 Jan;100(1):56-63.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15654781&dopt=Abstract

OBJECTIVES: This study was conducted to determine whether HIV coinfection increases the risk of cirrhosis in HCV-infected patients in the HAART and pre-HAART eras. Further, the risk of hepatocellular carcinoma was also examined. **METHODS:** This retrospective cohort study was conducted among HCV-infected veterans who were seen at one of the 172 Veterans Health Administration hospitals between October 1, 1991 and September 30, 2000. Patients with prerecorded advanced liver disease were excluded. Incidence rates, cumulative incidence, and Cox proportional hazard ratios were calculated. **RESULTS:** There were 26,641 patients with HCV-only and 4,761 patients with HCV-HIV coinfection. The unadjusted incidence rate of cirrhosis was lower in patients with coinfection than HCV-only ($p < 0.01$). After controlling for demographics and confounders (including alcoholism and chronic hepatitis B), coinfection was not significantly associated with cirrhosis. However, there was an increased risk of cirrhosis in patients with coinfection compared to HCV-only during the pre-HAART era (before October 1, 1996) (hazard ratio = 1.48, 1.06-2.07, $p = 0.02$), but not among patients who entered the cohort during the HAART era. The unadjusted incidence rate of hepatocellular carcinoma in patients with coinfection and HCV-only was 1.3 and 2/1,000 person-years, respectively ($p = 0.04$). In the multivariate model, coinfection was not associated with hepatocellular carcinoma (hazard ratio = 0.84, $p = 0.40$). **CONCLUSIONS:** Coinfection was a significant risk factor for cirrhosis only during the pre-HAART era and was not associated with hepatocellular carcinoma, irrespective of time period, with persistent liver enzyme elevations (grades 1-4). In conclusion, despite widespread exposure to ART and documented instances of ART-related hepatitis, we found no evidence that ART caused serious histological liver disease. Recognition of bridging fibrosis and cirrhosis in some but not most patients underscores the importance of identifying and treating liver disease in HIV/HCV coinfecting persons.

The magnitude and breadth of hepatitis C virus-specific CD8+ T cells depend on absolute CD4+ T-cell count in individuals coinfecting with HIV-1 Arthur Y. Kim, Georg M. Lauer, Kei Ouchi, et al. *Blood.* 2005; 105(3): p. 1170-1178

<http://www.bloodjournal.org/cgi/content/abstract/105/3/1170?ct> CD8+ T-cell responses are an essential antiviral host defense in persistent viral infections, and their sustained effectiveness is thought to be critically dependent on CD4+ T-helper cells. To determine the relationship between HIV-1-induced CD4+ T-cell depletion and hepatitis C virus (HCV)-specific CD8+ T-cell responses during viral persistence, we studied 103 persons positive for HCV, 74 coinfecting with HIV-1. CD8+ T-cell responses to the entire HCV polyprotein were determined by using an interferon- enzyme-linked immunospot (ELISpot) assay. Although HIV-1 infection by itself was not associated with a diminished HCV-specific response, HIV-1-associated CD4+ depletion was associated with significantly lower HCV-specific CD8+ T cells ($R = 0.48$, $P < .0001$). In contrast, declining CD4+ counts over the same range were not associated with diminished Epstein-Barr virus (EBV)- ($R = 0.19$, $P = .31$) or HIV-1-specific ($R = -0.13$, $P = .60$) CD8+ T-cell responses in persons infected with all viruses. These data indicate that frequencies of circulating HCV-specific CD8+ T-cell responses are sensitive to absolute CD4+ T-cell counts and provide a possible explanation for the accelerated HCV disease course in persons coinfecting with HIV-1 and HCV.

CLINICAL TRIALS, COHORT STUDIES

An exercise intervention to prevent hepatitis-related fatigue. Zucker D. Program and abstracts of the 55th Annual Meeting of the American Association for the Study of Liver Diseases; October 29 - November 2; Boston, Massachusetts. Abstract 796. <http://clinicaloptions.com/hep/conf/aasld2004/cs/796.asp> **Summary of Key Conclusions** Exercise intervention feasible for patients with chronic hepatitis C virus (HCV) infection. Less fatigue reported by patients in exercise intervention group Pilot tests for measuring fatigue and quality of life showed high reliability. Larger study needed to achieve adequate statistical power. Study should be replicated in patients undergoing treatment with peginterferon and ribavirin.

Anesthetist to patient transmission of hepatitis C virus associated with non exposure-prone procedures. Mawdsley J, Teo CG, Kyi M, Anderson M. J. Med. Virol. 75:399-401, 2005.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15648071&dopt=Abstract

A 44-year-old lady was diagnosed with acute hepatitis C virus (HCV) infection 8 weeks after hysterectomy at which the attending anesthetist was known to be hepatitis C seropositive. Comparative nucleotide sequence analysis and phylogenetic comparison proved that transmission had occurred from the anesthetist to the patient. The patient had received general anesthesia with endotracheal intubation and peripheral intravenous cannulation. No exposure-prone anesthetic procedures had been performed. This is the first case described in UK involving transmission from an anesthetist to a patient during anesthesia where no exposure prone procedures were carried out. It is the first example in which the anesthetist was known to be seropositive for hepatitis C prior to the operation.

Antiviral therapy decreases hepatic venous pressure gradient in patients with chronic hepatitis C and fibrosis stage 3 or 4. Rincon D, Bañares R, Ripoll C, et al. Program and abstracts of the 55th Annual Meeting of the American Association for the Study of Liver Diseases; October 29 - November 2, 2004; Boston, Massachusetts. Abstract 189. <http://clinicaloptions.com/hep/conf/aasld2004/cs/189.asp> **Summary of Key Conclusions** Antiviral therapy reduced hepatic venous pressure gradient in patients with chronic hepatitis C virus (HCV) infection and stage 3/4 fibrosis; Improved in both responders and nonresponders to therapy; Greater improvement in those with end-of-treatment response but not significantly different from nonresponders; A nonsignificant trend toward histologic and HVPg improvement suggests that the decrease in HVPg may be due to decreased inflammation and improved histologic outcomes; Decrease in HVPg after AT is clinically significant.

Antiviral Therapy for Cirrhotic Hepatitis C: Association with Reduced Hepatocellular Carcinoma Development and Improved Survival Y Shiratori, et al. Ann Intern Med. 2005; 142(2): p. 105-114

<http://www.annals.org/cgi/content/abstract/142/2/105?ct> **Background:** Although cirrhosis is a major risk factor for development of hepatocellular carcinoma, no definitive prospective analyses have assessed the long-term efficacy of antiviral therapy in cirrhotic patients. **Objective:** To elucidate the role of antiviral therapy in the suppression of liver tumors and survival over a long-term follow-up period. **Design:** Prospective cohort study. **Setting:** 25 clinical centers. **Patients:** 345 patients with chronic hepatitis C and cirrhosis enrolled in previous trials. **Intervention:** 271 patients received 6 to 9 million U of interferon 3 times weekly for 26 to 88 weeks; 74 received no treatment. **Measurements:** Blood tests and abdominal ultrasonography were done regularly to detect hepatocellular carcinoma. **Results:** Hepatocellular carcinoma was detected in 119 patients during a 6.8-year follow-up: 84 (31%) in the interferon-treated group and 35 (47%) in the untreated group. Cumulative incidence of hepatocellular carcinoma among interferon-treated patients was significantly lower than in untreated patients (Cox model: age-adjusted hazard ratio, 0.65 [95% CI, 0.43 to 0.97]; $P=0.03$), especially sustained virologic responders. A total of 69 patients died during follow-up: 45 (17%) in the treated group and 24 (32%) in the untreated group. Interferon-treated patients had a better chance of survival than the untreated group (Cox model: age-adjusted hazard ratio, 0.54 [CI, 0.33 to 0.89]; $P=0.02$). This was especially evident in sustained virologic responders. **Limitation:** This was not a randomized, controlled study. Patients enrolled in the control group had declined to receive interferon treatment even though they were eligible for treatment. **Conclusion:** Interferon therapy for cirrhotic patients with chronic hepatitis C, especially those in whom the infection had been cured, inhibited the development of hepatocellular carcinoma and improved survival.

Antiviral therapy decreases hepatic venous pressure gradient in patients with chronic hepatitis C and fibrosis stage 3 or 4. Rincon D, Bañares R, Ripoll C, et al. Program and abstracts of the 55th Annual Meeting of the American Association for the Study of Liver Diseases; October 29 - November 2, 2004; Boston, Massachusetts. Abstract 189. <http://clinicaloptions.com/hep/conf/aasld2004/cs/189.asp> **Summary of Key**

Conclusions Antiviral therapy reduced hepatic venous pressure gradient in patients with chronic hepatitis C virus (HCV) infection and stage 3/4 fibrosis. Improved in both responders and nonresponders to therapy. Greater improvement in those with end-of-treatment response but not significantly different from nonresponders. A nonsignificant trend toward histologic and HVPg improvement suggests that the decrease in HVPg may be due to decreased inflammation and improved histologic outcomes. Decrease in HVPg after AT is clinically significant.

Chronic hepatitis C and type II diabetes mellitus: a prospective cross-sectional study. Zein CO, Levy C, Basu A, Zein NN. *Am J Gastroenterol.* 2005 Jan;100(1):48-55.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15654780&dopt=Abstract

An epidemiologic link between chronic hepatitis C (HCV) and type II diabetes mellitus (DM) has been established. Our aims were to prospectively determine the prevalence of DM in interferon-naïve patients with HCV in comparison with the general population, and to determine the association between DM and impaired fasting glucose (IFG) with histological stage in patients with HCV. A consecutive sample of 179 patients was included in this prospective cross-sectional study. The crude percentage of DM for the cohort was 14.5%, different from the crude rate of 7.8% for the general population ($p = 0.0008$) and from the rate of 7.3% observed in a matched control group with non-HCV liver disease. The prevalence of DM and IFG (DM/IFG) was higher among HCV-infected patients with advanced versus those with early histological disease ($p = 0.0004$). Advanced histological disease predicted DM/IFG after controlling for other identified risk factors for DM. Family history was the only other independent predictor of DM/IFG in HCV-infected patients. In conclusion, patients with HCV had a higher prevalence of DM compared to the general population. The presence of advanced histological disease in genetically predisposed HCV-patients is associated with a higher prevalence of DM/IFG. DM and IFG were not associated with anthropomorphic markers of obesity in HCV patients, suggesting a unique multifactorial pathogenesis of DM in HCV.

Diagnostic Algorithm for Chronic Hepatitis C Virus Infection: Role of the New HCV-Core Antigen Assay. Tillmann HL, et al. *Z Gastroenterol.* 2005 Jan;43(1):11-6.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15650966&dopt=Abstract

BACKGROUND: The diagnosis of chronic hepatitis C virus infection is based on nucleic acid testing (NAT) for HCV-RNA. We evaluated whether total HCV core antigen testing could be a substitute for NAT testing.

PATIENTS AND METHODS: Samples from 192 untreated chronic HCV positive patients previously tested for HCV-RNA by four different commercially available assays (SuperQuant, Amplicor HCV Monitor v 1.0 and v 2.0, Quantiplex) were tested for total HCV core antigen using the Ortho trak-C assay (Ortho Clinical Diagnostics, Raritan, NJ, USA). Furthermore, 52 HCV-RNA positive paired serum and plasma samples were analysed. Finally, inter-assay coefficients of variation for core antigen were determined by repeated testing of 59 samples.

RESULTS: 172/192 (89.6 %) samples from untreated HCV patients showed positive results with the trak-C assay. Importantly, all but two trak-C positive samples were NAT positive. Only four of the twenty trak-C negative samples tested positive by two NAT assays with viral loads below 30,000 copies/mL. Moreover, HCV core antigen levels correlated significantly with HCV-RNA levels ($r > 0.72$; $p > 0.001$), gave consistent results in paired serum and plasma samples ($r = 0.991$), and showed a very low inter-assay variability ($r = 0.943$) independent of genotype. **CONCLUSION:** Based on the performance characteristics, easiness of use, and potential lower cost of the core Ag assay, we propose an alternative testing algorithm for establishing the diagnosis of chronic HCV infection in which the trak-C assay could substitute for NAT as the first choice for detection of HCV viraemia in anti-HCV positive individuals. NAT would only be necessary in rare cases with low viral load.

Effect of ondansetron, a 5-HT₃ receptor antagonist, on fatigue in chronic hepatitis C: a randomized double blind placebo controlled study. Piche T, Vanbiervliet G, Renou C, et al Program and abstracts of the 55th Annual Meeting of the American Association for the Study of Liver Diseases; October 29 - November 2; Boston, Massachusetts. Abstract 354. <http://clinicaloptions.com/hep/conf/aasld2004/cs/354.asp> **Summary of Key Conclusions** The 5-HT₃ serotonin receptor antagonist ondansetron significantly improved fatigue in

patients with untreated chronic hepatitis C virus (HCV) infection; Ondansetron also mitigated depression; Larger studies needed to determine contribution of placebo effect; Serotonergic pathways may be involved in HCV-related fatigue.

Elevated prevalence of hepatitis C infection in users of United States veterans medical centers

Jason A. Dominitz, Edward J. Boyko, Thomas D. Koepsell et al. HEPATOLOGY 2005;41:88-96.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15619249&dopt=Abstract

Several studies suggest veterans have a higher prevalence of hepatitis C virus infection than nonveterans, possibly because of military exposures. The purpose of this study was to estimate the prevalence of anti-hepatitis C antibody and evaluate factors associated with infection among users of Department of Veterans Affairs medical centers. Using a two-staged cluster sample, 1,288 of 3,863 randomly selected veterans completed a survey and underwent home-based phlebotomy for serological testing. Administrative and clinical data were used to correct the prevalence estimate for nonparticipation. The prevalence of anti-hepatitis C antibody among serology participants was 4.0% (95% CI, 2.6%-5.5%). The estimated prevalence in the population of Veterans Affairs medical center users was 5.4% (95% CI, 3.3%-7.5%) after correction for sociodemographic and clinical differences between participants and nonparticipants. Significant predictors of seropositivity included demographic factors, period of military service (e.g., Vietnam era), prior diagnoses, health care use, and lifestyle factors. At least one traditional risk factor (transfusion or intravenous drug use) was reported by 30.2% of all subjects. Among those testing positive for hepatitis C antibody, 78% either had a transfusion or had used injection drugs. Adjusting for injection drug use and nonparticipation, seropositivity was associated with tattoos and incarceration. Military-related exposures were not found to be associated with infection in the adjusted analysis. **In conclusion**, the prevalence of hepatitis C in these subjects exceeds the estimate from the general US population by more than 2-fold, likely reflecting more exposure to traditional risk factors among these veterans.

Erythropoietic response to anemia in chronic hepatitis C patients receiving combination pegylated

interferon/ribavirin. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15667486&dopt=Abstract Balan V, Schwartz D, et al. Am J Gastroenterol. 2005 Feb;100(2):299-307

OBJECTIVES: In hepatitis C virus (HCV)-infected patients receiving pegylated interferon (PEG-IFN)/ribavirin (RBV) combination therapy, anemia is a well-known side effect. The purpose of this study was to describe the time course and extent of hemoglobin (Hb) changes and the erythropoietic response to PEG-IFN/RBV-induced anemia. **METHODS:** In this multicenter, observational, 8-wk study, laboratory parameters were measured weekly for 8 wk or until early withdrawal. Primary endpoints included changes in Hb and serum erythropoietin (sEPO) from baseline to week 8; other measures were changes in reticulocytes and RBV dose. The predictive value of baseline factors for maximum Hb decline was assessed. **RESULTS:** In the 97 evaluable patients, mean Hb decreased from 14.4 +/- 1.4 g/dl (baseline) to 11.9 +/- 1.3 g/dl (week 8). Twenty-one percent of patients withdrew before week 8. The estimated erythropoietic response was lower than that seen in two historic control populations of iron deficiency anemia patients. Mean RBV dose decreased from 986 +/- 190 mg/day (baseline) to 913 +/- 228 mg/day (week 8). Fifty-seven out of 77 (74%) patients who completed the study maintained their initial prescribed RBV dose. Patients maintained on the initial dose of RBV who had a higher baseline Hb and viral load showed a trend toward larger Hb declines. Platelets and white blood cells (WBCs) also declined during the study. **CONCLUSIONS:** HCV-infected patients receiving PEG-IFN/RBV therapy have reductions in Hb, platelets, and WBCs, possibly due to bone marrow suppression. They also have diminished endogenous sEPO production for their degree of anemia.

Factors influencing the rate of fibrosis progression in chronic hepatitis C. Fernandez-Rodriguez CM, Gutierrez ML, Serrano PL, et al Dig Dis Sci. 2004 Nov-Dec;49(11-12):1971-6.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15628736&dopt=Abstract

Alcohol consumption, age at infection, and male gender have been identified as risk factors for faster fibrosis progression in patients with chronic hepatitis C (CHC). Yet the influence of liver steatosis, light to moderate

alcohol consumption, or iron overload on this progression remains controversial. To analyze the effect of individual risk factors and their interaction on fibrosis progression in a group of patients with CHC and a definite date of infection, we studied 133 consecutive untreated patients. Covariates included were age, body mass index (BMI), gender, age at infection, alcohol intake, serum lipids, glycemia, serum ALT, AST, GGT, iron, and ferritin, grade and stage (METAVIR and Scheuer), and hepatic stainable iron (Perl's stain). The rate of fibrosis progression was inferred from the METAVIR score. By logistic regression analysis, hepatic steatosis (odds ratio [OR], 3.035; 95% confidence interval [CI], 1.16-7.93), serum ferritin levels higher than 290 ng/ml (OR, 5.5; 1.6-18.65), and light to moderate ethanol intake (1-50 g/day) (OR, 5.22; 1.5-17.67) were independently associated with faster fibrosis progression. There was no effect of interaction between these variables on the rate of fibrosis progression. Liver steatosis, serum ferritin levels, and light to moderate alcohol intake are associated with faster fibrosis progression in chronic hepatitis C. Combination of these factors did not further accelerate this progression. The impact of modification of these factors on progression should be tested in longitudinal studies.

Hepatitis C virus RNA in the skin eruption from patients with prurigo and chronic hepatitis C.

B Podanyi, A Kiss, P Kaposi Novak, et al. Orv Hetil 21 Nov 2004 145(47): p.2371.

<http://highwire.stanford.edu/cgi/medline/pmid:15641669> Hepatitis C virus RNA in the skin eruption from patients with prurigo and chronic hepatitis C. Since the discovery of hepatitis C virus (HCV) in 1989, many cutaneous disorders have been observed in patients suffering from chronic HCV infection. The relationship between HCV infection and cryoglobulinemia and porphyria cutanea tarda is clearly established, however, the link between HCV and other skin diseases is still controversial. **AIM:** Two patients with intense pruritus and secondary prurigo in chronic C hepatitis have been presented. **METHODS:** The chronic hepatitis C of the patients were proved by elevated ALT and AST level, anti HCV (ELISA), HCV-PCR serological examination and liver biopsy. The skin lesions were accompanied by severe itching. According to clinical symptoms the patients suffered from prurigo simplex. **RESULTS:** HCV RNA in the skin specimen from the biopsy of the skin lesion was detected by RT-PCR method, but the non affected skin specimen from the patients was HCV RNA negative. **CONCLUSIONS:** This report is a case of prurigo simplex with chronic C hepatitis proving a direct relation between the HCV infection and prurigo.

High-dose ribavirin in combination with standard dose peginterferon for treatment of patients with chronic hepatitis C.

Lindahl K, Stahle L, Bruchfeld A, Schvarcz R. HEPATOLOGY 2005;41:275-279.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15660393&dopt=Abstract Improved treatment regimens for patients with chronic hepatitis C, genotype 1 and high viral load are needed. Increasing the dose of ribavirin has increased the response rate, but experience with doses of more than 1,200 mg/day is limited. The aim of this study was to investigate the safety and tolerance to treatment with a high and individualized dose of ribavirin in combination with peginterferon. Ten patients with chronic hepatitis C, genotype 1 and high viral load were treated with peginterferon alfa-2a and ribavirin for 48 weeks in a prospective trial. The initial ribavirin dose was individualized and calculated from a pharmacokinetic formula based mainly on renal function. Ribavirin plasma concentrations were monitored, and the dose was adjusted to reach the target concentration. Hemoglobin was monitored, and patients were treated with erythropoietin and blood transfusions when indicated. After dose adjustments, the mean dose of ribavirin was 2,540 mg/day (range, 1,600-3,600) at week 24. The main side effect was anemia, which was controlled with erythropoietin. Two patients required blood transfusions. One patient was withdrawn at week 24 because of a lack of viral response, and one patient at week 39 because of side effects, primarily interferon associated. At follow-up (>=24 weeks posttreatment), nine of ten patients had undetectable HCV RNA and thus were cured by standard definitions. **In conclusion,** a high dose of ribavirin according to an individualized schedule is feasible but associated with more frequent and serious side effects such as anemia. The viral response merits further evaluation.

Impact of steatosis on progression of fibrosis in patients with mild hepatitis C Laetitia Fartoux , Olivier Chazouillères , Dominique Wendum et al. HEPATOLOGY 2005;41:82-87

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15617096&dopt=Abstract

Background: In patients with mild hepatitis C, the usefulness of antiviral therapy is subject of debate, as a low risk for progression of fibrosis is assumed. Several studies have shown that steatosis is a strong and independent predictor of the severity as well as the progression of fibrosis in chronic hepatitis C. Therefore, this study assessed the impact of steatosis on the progression of fibrosis between paired liver biopsies in untreated patients with mild hepatitis on index biopsy. **Methods:** One hundred thirty-five untreated patients (mean age, 38 years; M/F sex ratio, 1.43) with one known risk factor of infection (68 transfusions, 67 injecting drug use) had 2 liver biopsies after a median interval of 61 months (18-158). All had METAVIR score of A1F1 or lower at first liver biopsy. Unequivocal progression of fibrosis was considered if patients had a fibrosis score of 3 or 4 at the second liver biopsy. The probability of progression of fibrosis was estimated by using the Kaplan-Meier method. **Results:** During follow-up, progression of fibrosis occurred in 21 patients (16%) after a median delay of 65 months. Cumulative probabilities of the progression of fibrosis at 4 and 6 years were 5.2% and 19.8%, respectively. In multivariate analysis, steatosis was the only independent factor predictive of progression of fibrosis (RR, 4.8; CI, 1.3-18.3). Probability of progression of fibrosis was significantly related to the percentage of hepatocytes with steatosis. **Conclusions:** In conclusion, steatosis is a major determinant of the progression of fibrosis in mild hepatitis C, regardless of the genotype. Our results argue for antiviral treatment in the subgroup of patients with mild hepatitis and steatosis

Insulin resistance is associated with liver fibrosis in non-diabetic chronic hepatitis C patients Journal of Hepatology 42(1):41-46 Alba Muzzi, Gioacchino Leandro, Laura Rubbia-Brandt, et al. (see attachment - Muzzi article)

Background/Aims: Liver steatosis is a frequent finding in chronic hepatitis C. An association has been suggested between steatosis and fibrosis progression rate, but the pathogenetic mechanisms linking fatty infiltration and collagen deposition are unknown. **Methods** We measured the levels of insulin resistance (as HOMA score) and leptin in 221 non-diabetic chronic hepatitis C patients, to assess their impact on liver steatosis and fibrosis, relative to other factors, using a multivariable logistic regression. **Results** When all 221 patients were considered, steatosis was associated with excessive alcohol intake, genotype 3, and serum HCV RNA level, whereas fibrosis was associated with HOMA score and age. In 152 patients infected with genotype non-3, steatosis was associated with alcohol abuse and HCV RNA level, and fibrosis with HOMA score and age. In the 69 patients with genotype 3, steatosis and fibrosis were associated with each other. The association between fibrosis and HOMA score held also when 22 obese patients were excluded from the analysis. Levels of insulin resistance were not correlated with the presence of steatosis. **Conclusions** Thus, insulin resistance (but not leptin) may play a role in fibrogenesis in chronic hepatitis C patients infected with genotype non-3.

Liver steatosis is an independent risk factor for treatment failure in patients with chronic hepatitis

C. Thomopoulos KC, et al. Eur J Gastroenterol Hepatol. 2005 Feb;17(2):149-53.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15674091&dopt=Abstract

OBJECTIVES: Hepatic steatosis is a common feature of chronic hepatitis C. The purpose of this study was to determine factors related to the presence of steatosis and to define the role of steatosis in the response to antiviral treatment in chronic hepatitis C patients. **METHODS:** We retrospectively analysed all patients with chronic hepatitis C treated in a 5 year period in our department. Patients were included in the study only if a pretreatment liver biopsy specimen was available for evaluation. All patients treated either with interferon in combination with ribavirin, or with pegylated interferon in combination with ribavirin were included irrespectively of their response (early, end of treatment and/or sustained) to antiviral therapy. **RESULTS:** A total of 116 patients with chronic hepatitis C were included in the study with a mean age of 45.5+/-14.1 years. Steatosis was present in 52 patients (44.8%). On univariate analysis age, P=0.04 and body mass index ≥ 25 , P=0.004 were correlated with the presence of steatosis and on multivariate analysis only body mass index ≥ 25 , P=0.032. Advanced fibrosis was not found associated with steatosis. Sixty patients out of 116 (51.7%) had sustained virological response (SVR). In particular 42 out of 64 patients with no steatosis (65.6%) had SVR compared to 20 out of 52 patients (38.4%) with any degree of steatosis (P=0.009). Patients with

genotype 2 or 3 had a more favourable outcome compared to patients with 1 or 4 genotypes, 63.2% vs 49.2%, $P=0.032$. Also increased age ($P=0.0001$), gamma glutamyltransferase (GGT) ($P=0.029$), no history of intravenous drugs use ($P=0.001$) and advanced fibrosis on pretreatment biopsy ($P=0.046$) were correlated with treatment failure. On multivariate analysis significant independent association with SVR was found with the presence of steatosis on pretreatment biopsy ($P=0.004$), increased GGT ($P=0.005$) and genotype ($P=0.017$). **CONCLUSION:** Steatosis in the liver biopsy performed before the beginning of antiviral treatment was found to be associated only to the body mass index of the patients and to be a strong independent factor for treatment failure.

Long-Term Effects of Antiviral Treatment for Hepatitis C Ann Intern Med. 2005; 142(2): p. I-51
<http://www.annals.org/cgi/content/full/142/2/I-51?ct> **Background:** Hepatitis C is inflammation of the liver caused by hepatitis C virus (HCV). HCV is transmitted primarily by blood-to-blood contact through needlestick accidents, intravenous drug use, body piercing, and tattooing. Most people do not rid their body of HCV on their own. More than 80% keep the virus in their blood for longer than 6 months and develop chronic hepatitis C. Chronic hepatitis C progresses slowly over 10 to 30 years. It causes inflammation and severe scarring of the liver (cirrhosis). If untreated, it can lead to liver failure and liver cancer. Treatment with antiviral drugs, such as interferon, clears HCV from the blood and helps prevent some liver damage. Few studies, however, show whether treatment can prevent liver cancer in patients who already have severe scarring or cirrhosis. **Aims:** To see whether antiviral therapy prevents liver tumors and improves long-term survival in patients with chronic hepatitis C and cirrhosis. **Methods:** 345 adults with chronic hepatitis C and cirrhosis: 74 had declined to receive antiviral treatment and 271 had received interferon injections. In the early 1990s, the researchers conducted 2 trials of interferon therapy in patients with chronic hepatitis C and liver scarring. Patients in the trials received interferon injections 3 times a week for 26 to 88 weeks. For several years, the researchers followed these patients, as well as patients who declined antiviral therapy (median follow-up, 6.8 years). Every few months, the researchers tested the patients' blood for HCV and signs of liver inflammation, and they did liver ultrasonography to check for tumors. Additional tests, such as computed tomography and liver biopsies, were done to see whether any tumors were cancer. The researchers then compared outcomes among people who had and had not received antiviral treatment. **Results:** Liver cancer occurred in 47% of the patients who declined treatment compared with 31% of those treated with interferon. In addition, more patients who declined treatment died than did those who got interferon (32% vs. 17%). **Limitations:** The study was not a randomized, controlled trial. Factors other than the interferon treatment might have contributed to the differences between groups. The study did not assess effects of different types of treatments for hepatitis C. **Conclusions:** Antiviral treatment with interferon might prevent liver cancer and improve survival in some patients with chronic hepatitis C and cirrhosis.

Longer treatment duration with peginterferon alfa-2a (40KD) (Pegasys) and ribavirin (Copegus) in naïve patients with chronic hepatitis C and detectable HCV RNA by week 4 of therapy: final results of the randomized, multicenter TERAVID-4 Study. Sanchez-Tapias JM, Escartin P, Enriquez J, et al. Program and abstracts of the 55th Annual Meeting of the AASLD Oct-Nov 2004; Boston, Massachusetts. Abstract 126. <http://clinicaloptions.com/hep/conf/aasld2004/cs/126.asp> **Summary of Key Conclusions** In patients with hepatitis C virus (HCV) infection, extending peginterferon alfa-2a plus ribavirin from 48 to 72 weeks in patients who did not have a rapid virologic response by Week 4: Increased sustained virologic response (SVR) rate; Reduced relapse rate; Extending duration of therapy did not increase the incidence of adverse effects; But led to higher rate of treatment discontinuation.

Management of hepatitis C patients: a French population-based study. C Hatem, A Minello, L Martin, et al. Gastroenterol Clin Biol 1 Nov 2004 28(11): p. 1101. <http://highwire.stanford.edu/cgi/medline/pmid;15657533> **AIMS:** Our aim was to assess the proportion of patients in a well-defined population reaching specialized medical care after hepatitis C diagnosis. **METHODS:** Hepatitis C-positive patients recorded in the population-based registry of Cote-d'Or, an administrative district in France, constituted the study population. **RESULTS:** Between 1994 and 1999, new hepatitis C-positive serology was diagnosed in 847 patients, of whom 690 were eligible for this study. A total of 135 patients had not been given specialized medical care after diagnosis;

among them, 50.4% had a normal serum alanine transferase level at diagnosis, 62.2% had risk factors related to lifestyle (drug addiction, sexual risk...), and 26.7% were current alcoholics. The 555 other patients were involved in specialized medical care after diagnosis: 42.7% had a liver biopsy and 27.0% were treated. Treatment was carried out more often in males than in females (OR: 1.67; $P < 0.005$), and in patients less than 65 years old (OR: 2.94; $P < 0.0002$). Nearly 30.5% of patients with a Metavir score greater than A1F1 did not undergo treatment. **CONCLUSION:** This study shows that in a general population at least one patient out of five with hepatitis C infection remains outside the health care system. It also reveals that management practices vary with gender.

Noninvasive assessment of liver fibrosis by measurement of stiffness in patients with chronic hepatitis C
Marianne Ziol , Adriana Handra-Luca , Adrien Kettaneh ,et al. HEPATOLOGY 2005;41:48-54.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15617083&dopt=Abstract

Liver fibrosis is the main predictor of the progression of chronic hepatitis C, and its assessment by liver biopsy (LB) can help determine therapy. However, biopsy is an invasive procedure with several limitations. A new, noninvasive medical device based on transient elastography has been designed to measure liver stiffness. The aim of this study was to investigate the use of liver stiffness measurement (LSM) in the evaluation of liver fibrosis in patients with chronic hepatitis C. We prospectively enrolled 327 patients with chronic hepatitis C in a multicenter study. Patients underwent LB and LSM. METAVIR liver fibrosis stages were assessed on biopsy specimens by 2 pathologists. LSM was performed by transient elastography. Efficiency of LSM and optimal cutoff values for fibrosis stage assessment were determined by a receiver-operating characteristics (ROC) curve analysis and cross-validated by the jack-knife method. LSM was well correlated with fibrosis stage (Kendall correlation coefficient: 0.55; $P < .0001$). The areas under ROC curves were 0.79 (95% CI, 0.73-0.84) for F 2, 0.91 (0.87-0.96) for F 3, and 0.97 (0.93-1) for F = 4; for larger biopsies, these values were, respectively, 0.81, 0.95, and 0.99. Optimal stiffness cutoff values of 8.7 and 14.5 kPa showed F 2 and F = 4, respectively. **In conclusion**, noninvasive assessment of liver stiffness with transient elastography appears as a reliable tool to detect significant fibrosis or cirrhosis in patients with chronic hepatitis C.

Neurocognitive changes in patients with hepatitis C receiving interferon alfa-2b and ribavirin.

MR Kraus, A Schafer, S Wissmann, P Reimer, and M Scheurlen Clin Pharmacol Ther 1 Jan 2005 77(1): p. 90.

<http://highwire.stanford.edu/cgi/medline/pmid;15637534> **BACKGROUND:** During antiviral therapy of chronic hepatitis C, patients frequently report impairment of concentration or memory. Therefore we prospectively investigated neurocognitive performance in patients receiving interferon alfa and ribavirin. **METHODS:**

Repeated computer-based testing of neurocognitive function was performed in 70 patients with chronic hepatitis C receiving interferon alfa-2b (pegylated or conventional) and ribavirin. In addition, depression scores were obtained (Hospital Anxiety and Depression Scale). **RESULTS:** Reaction times were significantly increased during treatment (mean reaction time increase after 3 months of therapy: alertness, 46.76 ms [95% confidence interval (CI)], 26.86-66.66 ms), $P < .001$; divided attention, 47.04 ms [95% CI, 26.44-67.64 ms], $P < .001$; vigilance, 60.78 ms [95% CI, 29.24-92.32 ms], $P < .001$; and working memory, 38.53 ms [95% CI, 1.22-75.83], $P = .34$). Accuracy measures (number of false reactions) were affected for the working-memory task exclusively. Cognitive performance returned to pretreatment values after the end of therapy. Cognitive impairment was not significantly correlated with the degree of concomitant depression ($0.04 < r$ [absolute value] < 0.10 , $P > .390$). **CONCLUSIONS:** Interferon-based combination therapy of chronic hepatitis C causes significant but reversible impairment of neurocognitive performance. Consequences for the requirements of an active life in patients with chronic hepatitis C receiving antiviral therapy need to be assessed.

Patient concerns regarding chronic hepatitis C infections. Minuk GY, Gutkin A, Wong SG, Kaita KD. J Viral Hepat. 2005 Jan;12(1):51-7.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15655048&dopt=Abstract

Summary. Counselling of patients with chronic hepatitis C infections is often limited to discussions regarding how the virus is transmitted and what can be done to decrease the risk of transmission to others. The purpose of the present study was to document the principal concerns of newly diagnosed and follow-up patients with

chronic hepatitis C, and thereby enhance counselling strategies and content. Seventy newly diagnosed and 115 follow-up patients with chronic hepatitis C virus (HCV) infection were initially asked in an open-ended manner (volunteered concerns) and then to prioritize from a prepared list of seven potential concerns (prioritized concerns), to identify those concerns that were of utmost importance to them. The most common volunteered concerns of newly diagnosed patients in decreasing order were: disease progression (27%), premature death (19%), infecting family members (13%), side-effects of treatment (11%) and miscellaneous others. In decreasing order, prioritized concerns included: infecting family members, development of liver cancer, infecting others, development of cirrhosis, social stigma of having liver disease, need for liver transplant and loss of employment. The principal volunteered and prioritized concerns of follow-up patients were similar to those of newly diagnosed patients. Volunteered and prioritized concerns were relatively consistent across the different genders, age groups, ethnic backgrounds, education level, marital status, employment, modes of viral acquisition and in the case of follow-up patients, duration of follow-up. These results indicate that health care providers who focus counselling efforts exclusively on viral transmission are unlikely to address other important concerns of newly diagnosed and follow-up patients with chronic HCV infection.

Peginterferon alfa-2a for hepatitis C after liver transplantation: Two randomized, controlled trials.

Chalasan N, et al. *HEPATOLOGY* 2005;41:289-298..

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15660392&dopt=Abstract

There is currently no effective treatment for recurrent hepatitis C after orthotopic liver transplantation (OLT). We therefore performed two randomized, controlled trials—a prophylaxis trial and a treatment trial—to evaluate the safety and efficacy of peginterferon alfa-2a in patients who had undergone OLT. The prophylaxis trial enrolled 54 patients within 3 weeks after OLT, and the treatment trial enrolled 67 patients 6 to 60 months after OLT. In each trial, patients were randomized to treatment with once weekly injections of 180 mug peginterferon alfa-2a or no antiviral treatment for 48 weeks and were followed up for 24 weeks thereafter. Peginterferon alfa-2a treated patients had significantly lower hepatitis C virus RNA levels and more favorable changes in hepatic histological features compared with untreated controls. However, only 2 treated patients in the prophylaxis trial (8%) and 3 in the treatment trial (12%) achieved a sustained virological response. In the prophylaxis trial, 8 patients (31%) in the peginterferon alfa-2a group and 9 (32%) in the untreated group were withdrawn prematurely; whereas in the treatment trial, 10 patients (30%) in the peginterferon alfa-2a group and 6 (19%) in the untreated group were withdrawn prematurely. The incidence of acute rejection was similar in the treated and untreated groups in both the prophylaxis (12% vs. 21%; $P = .5$) and treatment (12% vs. 0%; $P = .1$) trials. **In conclusion**, peginterferon alfa-2a treatment for 48 weeks is safe and tolerable and offers some efficacy in the post-OLT setting. Randomized controlled studies are needed to establish the efficacy of pegylated interferon and ribavirin in patients who have undergone OLT

Persistence of hepatitis C virus in patients successfully treated for chronic hepatitis C

Marek Radkowski, Juan F. Gallegos-Orozco, Joanna Jablonska et al. *HEPATOLOGY* 2005;41:106-114

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15619235&dopt=Abstract

Abstract It is unclear whether the current antiviral treatment for chronic hepatitis C virus (HCV) infection results in complete elimination of the virus, or whether small quantities of virus persist. Our study group comprised 17 patients with chronic HCV who had sustained virological response (SVR) after interferon/ribavirin treatment. Serum and peripheral blood mononuclear cells were collected 2 to 3 times at 3- to 6-month intervals starting 40 to 109 months (mean, 64.2 ± 18.5 months) after the end of therapy. In addition, lymphocyte and macrophage cultures were established at each point. In 11 patients, frozen liver tissue samples were available from follow-up biopsies performed 41 to 98 months (mean, 63.6 ± 16.7 months) after therapy. Presence of HCV RNA was determined by sensitive reverse-transcriptase polymerase chain reaction, and concentration of positive and negative strands was determined by a novel quantitative real-time reverse transcriptase polymerase chain reaction. Only 2 of 17 patients remained consistently HCV RNA negative in all analyzed compartments. HCV RNA was detected in macrophages from 11 patients (65%) and in lymphocytes from 7 patients (41%). Viral sequences were also detected in 3 of 11 livers and in sera from 4 patients. Viral replicative forms were found in lymphocytes from 2 and in macrophages from 4 patients. **In**

conclusion, our results suggest that in patients with SVR after therapy, small quantities of HCV RNA may persist in liver or macrophages and lymphocytes for up to 9 years. This continuous viral presence could result in persistence of humoral and cellular immunity for many years after therapy and could present a potential risk for infection reactivation

Predicting progressive hepatic fibrosis stage on subsequent liver biopsy in chronic hepatitis C virus infection. Collier JD, Woodall T, Wight DG, et al. *J Viral Hepat.* 2005 Jan;12(1):74-80.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15655051&dopt=Abstract

Summary. Retrospective cross-sectional studies indicate that 20% with chronic hepatitis C virus (HCV) infection become cirrhotic within 20 years. Known risk factors for advanced hepatic fibrosis include age at time of infection, male sex, excess alcohol consumption and cytokine polymorphisms. Prospective study to assess and identify factors predictive of change in hepatic fibrosis stage in chronic HCV infection by interval protocol liver biopsy was performed. One hundred and five patients with paired liver biopsy specimens separated by a mean 41 months were recruited from a cohort of 823 HCV carriers. Five per cent developed worsening hepatic fibrosis by more than two stages. In 43% there was no change in fibrosis stage. Excessive alcohol intake currently ($P = 0.037$) or previously ($P = 0.07$) predicted progression. In contrast, always having a normal alanine transaminase ($P = 0.038$) and always being negative in serum for HCV RNA ($P = 0.067$) predicted no progression. Three models were developed to predict outcome. Progressive fibrosis was predicted by baseline fibrosis ($P = 0.018$), steatosis ($P = 0.02$) and age ($P = 0.017$). The rate of progressive fibrosis was predicted by baseline fibrosis ($P = 0.0002$), steatosis ($P = 0.039$) and lobular inflammation ($P = 0.09$). Fibrosis stage on the second biopsy was predicted by baseline fibrosis alone ($P = 0.01$). The rate of progression varies widely. Alcohol misuse is an important co-factor. Progressive fibrosis can be predicted at first liver biopsy, where baseline fibrosis is most critical, allowing targeted therapy for those with early disease and a significant risk of progression.

Reasons for non-treatment of hepatitis C in veterans in care. Butt AA, Wagener M, Shakil AO, Ahmad J. *J Viral Hepat.* 2005 Jan;12(1):81-5.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15655052&dopt=Abstract

Summary. We prospectively studied 354 patients with hepatitis C virus (HCV) infection who were referred to a hepatology specialty clinic to find the reasons for non-treatment of HCV. The median age was 48 years (range 27-77 years), 98.5% were male and 71% were white. Seventy per cent of the patients were not treated. The most common reasons for non-treatment were non-adherence to follow-up visit (24%), normal liver enzymes (14%), concurrent medical problems (11%), alcohol and drug use (9%), psychiatric problems (7%), advanced liver disease (7%), referral for transplant evaluation (6.4%) and patient refusal, transfer of care to another facility and non-detectable HCV RNA levels (5% each). The reason was not recorded for 5% of the patients and was treatment deferred in 2.4% while waiting for pegylated interferon approval. Non-treatment was more likely in patients with less than 12 years of education and a history of incarceration. Patients who were lost to follow-up and refused treatment were more likely to have current alcohol and drug use and a history of incarceration.

Spontaneous resolution of chronic hepatitis C virus infection after antiviral treatment and relapse. Andrej Potthoff, Jasmin Sarhaddar, Johannes Wiegand, et al. *Hepatology* 1 Jan 2005 31(1): p. 18.

<http://highwire.stanford.edu/cgi/medline/pmid;15652466>

Clearance of acute hepatitis C virus (HCV) infection is associated with strong and multi-specific cellular immune responses which are often weak in chronic hepatitis C. We here report a case of spontaneous and sustained resolution of chronic hepatitis C virus infection in the absence of apparent HCV-specific immunity. The patient received standard antiviral therapy for chronic HCV infection and was HCV-RNA negative at the end of treatment but relapsed between follow-up week 4 and 12. Surprisingly, from follow-up week 28 on, he persistently was HCV-RNA negative in serum, even when being tested with the highly sensitive TMA-assay (cut-off 5-10IU/ml). ALT levels were within the normal range throughout follow-up. Virus-specific CD4+ T cell responses were prospectively analysed during the relapse period and during spontaneous resolution by interferon-gamma ELISPOT assays. Importantly, no HCV-

specific cellular immune responses were detectable at any time-point. The patient suffered from an acute respiratory tract infection before HCV clearance and serum IL-8 levels were significantly increased during this period. Thus, spontaneous resolution of hepatitis C after antiviral treatment and relapse may occur even in the absence of hepatitis flares and apparent HCV-specific immune responses in single cases. The role of heterologous infections for HCV clearance requires further investigation.

T-cell responses and previous exposure to hepatitis C virus in indeterminate blood donors.

Semmo N, Barnes E, Taylor C, et al. *Lancet*. 2005 Jan 22;365(9456):327-9. **(See Semmo article attached)**
Blood donors are routinely screened for hepatitis C virus infection. Some individuals have weak or restricted virus-specific antibody responses, and are classed as indeterminate. Such donors are almost always negative for viral RNA in blood. We postulated that previous transient virus exposure might account for some of these cases. With sensitive ex-vivo analyses of T-cell responses, we identified virus-specific responses in 15 of 30 indeterminate blood donors tested, compared with none in controls ($p=0.0013$). Additionally, these responses were typically focused on core-derived peptides. These findings suggest previous exposure to the virus in many indeterminate blood donors.

The effect of adherence to therapy on sustained response in daily or three times a week interferon alpha-2b plus ribavirin treatment of naive and nonresponder chronic hepatitis C patients. Raptopoulou M, Tsantoulas D, Vafiadi I, et al. *J Viral Hepat*. 2005 Jan;12(1):91-5.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15655054&dopt=Abstract
Summary. The aim was to demonstrate adherence to treatment has been suggested to enhance rates of sustained response in patients with hepatitis C. In this study, we evaluated the effect of drug dosage reduction or the duration of the expected therapy in patients treated with interferon (IFN)-alpha2b plus ribavirin. Virologic response rates were re-analysed according to compliance to therapy in (i) 301 naive and (ii) 142 nonresponders to previous IFN therapy treated with either IFN 5 MU TIW for 8 weeks followed by IFN 3 MU TIW for 40 weeks plus ribavirin or IFN 3 MU QD for 16 weeks followed by IFN 3 MU TIW for 24 weeks plus ribavirin. Patients were separated into those who adhered to $\geq 80\%$ of their intended treatment schedule (dose of both drugs and duration) and those who did not. Compliance to treatment resulted in significantly higher response rates in both groups of patients: 43.93% compared with 6.90% of noncompliant naive patients and 30.77% compared with 10.53% of nonresponder patients. Compliance to treatment was found to have a similar effect when the results were analysed according to HCV genotype. Our findings suggest that compliance to treatment for $\geq 80\%$ of the intended treatment schedule results in significantly higher sustained response rates in both naive and nonresponder patients. Consequently, every effort should be made to improve patient adherence to therapy.

The rate of treatment of chronic hepatitis C in patients co-infected with HIV in an urban medical centre. Restrepo A, et al. *J Viral Hepat*. 2005 Jan;12(1):86-90

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15655053&dopt=Abstract
Summary. Hepatitis C virus (HCV) and human immunodeficiency virus (HIV) co-infection is common. HIV co-infection results in a higher rate of histologic progression and shorter interval to HCV-related cirrhosis. Successful treatment of HCV with interferon-based therapy reduces the morbidity and mortality of patients. Significant factors may limit the availability of treatment in co-infected patients. The rate of treatment of HCV and limiting factors to treatment in a co-infected population in an urban setting were determined. A retrospective review of co-infected patients was conducted at our liver and gastrointestinal (GI) clinics for treatment of HCV from July 2001 to June 2002. Treatment of HCV and reasons for nontreatment were recorded. A total of 104 HCV/HIV co-infected patients were identified. Seventy-two per cent were males. Mean age was 47.2 years (32-72). Seventy-four of the 82 (90%) with identifiable risk factors for HCV infection had a history of intravenous drug use (IVDU). Twenty per cent (21/104) of the total underwent a liver biopsy. Sixty-seven per cent who had a liver biopsy were treated. Overall, sixteen patients were treated. Eighty-eight (85%) patients were not treated for the following reasons: 13 refused treatment, and 75 were ineligible. Of the ineligible patients, 40% were noncompliant with visits, 15% were active substance abusers,

13% had decompensated cirrhosis, 8% had significant active psychiatric conditions and 24% had significant co-morbid disease. A majority of patients co-infected with HCV/HIV had a IVDU history. Most co-infected patients were not eligible for HCV treatment. A majority of noncandidates had potentially modifiable psychosocial factors leading to nontreatment.

The role of core antigen detection in management of hepatitis C: a critical review. K Seme, M Poljak, DZ Babic, T Mocilnik, and A Vince J Clin Virol, February 1, 2005; 32(2): 92-101.

<http://highwire.stanford.edu/cgi/medline/pmid;156534> Several assays in research format and two commercial assays for the detection of hepatitis C virus (HCV) core protein or HCV core antigen have been developed in recent years. In order to elucidate the role and significance of HCV core antigen detection in the diagnosis and management of hepatitis C, we reviewed 56 studies published in peer-reviewed journals until September 2004. Evaluations in transfusion settings showed that the HCV core antigen assay detects HCV infection, similarly as nucleic acid techniques (NAT), between 40 and 50 days earlier than the current third generation HCV antibody screening assays. HCV core antigen levels closely track HCV RNA dynamics, and allow clinical monitoring of a patient's therapy, independently of HCV genotype, however, mainly in the samples with HCV RNA levels above 20,000IU/ml. Considering the lower sensitivity of HCV core antigen detection in comparison to NAT, the HCV core antigen assay is not practical for the determination of the end of treatment response and sustained viral response, but could be useful for the determination of early viral response in the pegylated interferon-alpha and ribavirin treated patients infected with HCV genotype 1. The HCV core antigen detection is a viable tool for study of hepatitis C pathogenesis. The HCV core antigen can be used as a marker of HCV replication in anti-HCV positive individuals in the areas of the world that cannot afford NAT and/or in the settings that are not equipped or competent to perform HCV RNA testing. Because the manufacturer of HCV core antigen assays recently stopped an active marketing of these assays in several countries, it will, unfortunately and probably, never be possible to determine the actual potential and usefulness of HCV core antigen testing in the management of hepatitis C.

The spectrum of chronic hepatitis C virus infection in the Virginia correctional system: development of a strategy for the evaluation and treatment of inmates with HCV. Sterling RK, Brown RS Jr, Hofmann CM, et al Am J Gastroenterol 2005;100:313-321.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15667488&dopt=Abstract

BACKGROUND AND OBJECTIVE: Chronic hepatitis C virus (HCV) is common in the inmate population of the United States. Long-standing HCV can progress to cirrhosis, which can contribute to significant morbidity and mortality. However, those inmates with histologically mild disease are unlikely to develop liver-related morbidity or mortality during their period of incarceration. Our objective was to develop an economic strategy for evaluation and treatment of inmates with chronic HCV. **METHODS AND MEASURES:** A retrospective cohort analysis of 302 inmates within the Virginia Department of Corrections (VDOC) who underwent liver biopsy for chronic HCV at the Virginia Commonwealth University Health System between 1998 and 2002 was performed. The data from this analysis was utilized to develop a cost model for treatment of chronic HCV in this population based upon biochemical or histologic criteria. We used the perspective of the VDOC using actual costs paid to providers, hospitals, and pharmacies. The primary endpoint was cost-effectiveness of HCV treatment. **RESULTS:** Eighty percent of inmates with chronic HCV were genotype 1, 49% had a normal value for serum ALT at the time of evaluation, 30% had no fibrosis, and 24% had bridging fibrosis or cirrhosis. The cost to evaluate and treat 100 consecutive inmates with peginterferon and ribavirin regardless of serum ALT and liver histology was calculated to be \$1,775,900 or \$35,500 per sustained virologic response (SVR). Although the cost declined by 50% if only those patients with an elevated serum ALT were treated, 45% of those inmates with varying degrees of fibrosis, and 21% with cirrhosis would not have received therapy utilizing this scenario. In contrast, the cost of performing liver biopsy and treating only those patients with any degree of fibrosis was \$1,367,043; a savings of slightly more than \$400,000 per 100 patients evaluated. The overall cost of treatment was most influenced by the price of peginterferon and ribavirin, which declined as the histologic criteria utilized for treatment increased. **CONCLUSIONS:** A strategy in which inmates with chronic HCV are evaluated and a decision regarding treatment is based upon either biochemical or histologic

criteria, which appears to balance both the health-care rights of the inmate and the impact of treating this disease on the financial and other resources of the correctional system.

Therapeutic modalities in hepatitis C: challenges and development. Moreno-Otero R. *J Viral Hepat.* 2005 Jan;12(1):10-9.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15655043&dopt=Abstract

Summary. Our understanding of the pathogenicity of hepatitis C virus (HCV) is based on patients infected chronically for >20 years. The lack of a suitable animal model, the narrow host range of the virus, and the protracted onset of liver disease induced by HCV have hampered advances in treatment. In spite of these problems, we identified patient and viral characteristics that predict responses to current therapies, including HCV genotype, viral load, body weight, age, liver histology, co-infection with HIV and treatment adherence and tolerance. Interferon (IFN) alpha was the first therapy for chronic HCV infection. The combination of IFN plus ribavirin increases sustained virological response rates compared with IFN alone. Two pegylated IFNs have been developed and are widely approved for the treatment of chronic hepatitis C: peginterferon alpha-2a (40 KD), and pegylated IFN alpha-2b (12 KD). These products have reduced systemic clearance, prolonged half-lives and reduced antigenicity compared with conventional IFN. The reduced clearance results in sustained plasma levels of the drug and allows for once-weekly dosing. Pegylated IFN alpha-2b (12 KD) has a small, linear polyethylene glycol (PEG) moiety and has an intermediate duration of activity; peginterferon alpha-2a (40 KD) incorporates a large, branched-chain PEG moiety and has a longer half-life than both conventional IFN alpha and pegylated IFN alpha-2b (12 KD). The combination of a pegylated IFN plus ribavirin significantly increases sustained virological response rates compared with conventional IFN plus ribavirin in patients with chronic hepatitis C and is now recognized as the standard of care for these patients.

Treatment of histologically mild hepatitis C virus infection with interferon and ribavirin: a multicentre randomized controlled trial. Wright M, Forton D, Main J, et al. *J Viral Hepat.* 2005 Jan;12(1):58-66.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15655049&dopt=Abstract

Summary. Current guidelines advocate no treatment for patients with histologically mild hepatitis C virus (HCV) infection. This was a UK multicentre randomized controlled trial comparing alpha-interferon (3 MU thrice weekly) + ribavirin (1000-1200 mg/day) for 48 weeks with no treatment in treatment naive, adult patients with histologically mild chronic HCV infection. The aim was to compare benefits, safety and efficacy of combination therapy with alpha-interferon 2b and ribavirin for 48 weeks with no treatment (current standard management) in this patient group. In the treatment group 32 of 98 (33%) patients achieved a sustained virological response (SVR). Patients infected with genotype 1 had a lower SVR than those infected with genotype non-1 (18% vs 49% $P = 0.02$). No patients who failed to achieve a 2-log drop in viral load at 12 weeks achieved SVR. Improvements in quality of life 24 weeks post cessation of therapy compared with baseline using the SF-36 questionnaire measures were observed in the treated group. For patients with mild HCV infection with viral genotype non-1, the results are sufficiently good to suggest that therapeutic decisions should no longer be biopsy-driven. For patients infected with genotype 1, a liver biopsy is still indicated as the low chance of SVR is outweighed by an unacceptable burden of side-effects. Patients who fail to respond by 12 weeks of therapy should have their treatment curtailed early.

Usefulness of a new immuno-radiometric assay to detect hepatitis C core antigen in a community-based population. Hayashi K, Hasuike S, Kusumoto K, Ido et al. *J Viral Hepat.* 2005 Jan;12(1):106-10.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15655057&dopt=Abstract

Summary. A new immuno-radiometric assay (IRMA) to detect hepatitis C virus (HCV) core antigen (HCVcAg) has been developed. The aim of the present study was to investigate the sensitivity and specificity of this IRMA to measure HCV antigenemia, based on the detection of HCV RNA as the gold standard, and to assess the utility of the IRMA in a community-based population. Anti-HCV positive residents in a hyperendemic area of HCV infection in Japan were studied. Serum levels of HCVcAg were measured using IRMA, and the presence of HCV RNA was determined by a qualitative reverse transcription-polymerase chain reaction (RT-PCR) assay. The sensitivity and the specificity of the IRMA were 96.4 and 100%, respectively. The sensitivity of the

IRMA was similar between serological HCV group I (HCV genotypes 1a and 1b) (97.6%) and group II (HCV genotypes 2a and 2b) (94.0%). There was a strong correlation between serum HCVcAg level and HCV-RNA measured by a quantitative RT-PCR ($r = 0.832$, $P < 0.0001$). There also was a very strong correlation of HCVcAg level between IRMA measurements performed on serum and those performed on plasma ($r = 0.984$, $P < 0.0001$). **In conclusion**, this new IRMA is useful for the detection of HCV core antigen in a community-based population.

CAM THERAPIES

Hypericin--the facts about a controversial agent. Kubin A, Wierrani F, Burner U, Alth G, Grunberger W. *Curr Pharm Des.* 2005;11(2):233-53

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=15638760

Hypericin is a naturally occurring substance found in the common St. John's Wort (*Hypericum* species) and can also be synthesized from the anthraquinone derivative emodin. As the main component of *Hypericum perforatum*, it has traditionally been used throughout the history of folk medicine. In the last three decades, hypericin has also become the subject of intensive biochemical research and is proving to be a multifunctional agent in drug and medicinal applications. Recent studies report antidepressive, antineoplastic, antitumor and antiviral (human immunodeficiency and hepatitis C virus) activities of hypericin; intriguing information even if confirmation of data is incomplete and mechanisms of these activities still remain largely unexplained. In other contemporary studies, screening hypericin for inhibitory effects on various pharmaceutically important enzymes such as MAO (monoaminoxidase), PKC (protein kinase C), dopamine-beta-hydroxylase, reverse transcriptase, telomerase and CYP (cytochrome P450), has yielded results supporting therapeutic potential. Research of hypericin and its effect on GABA-activated (gamma amino butyric acid) currents and NMDA (N-methyl-D-aspartat) receptors also indicate the therapeutic potential of this substance whereby new insights in stroke research (apoplexy) are expected. Also in the relatively newly established fields of medical photochemistry and photobiology, intensive research reveals hypericin to be a promising novel therapeutic and diagnostic agent in treatment and detection of cancer (photodynamic activation of free radical production). Hypericin is not new to the research community, but it is achieving a new and promising status as an effective agent in medical diagnostic and therapeutic applications. New, although controversial data, over the recent years dictate further research, re-evaluation and discussion of this substance. Our up-to-date summary of hypericin, its activities and potentials, is aimed to contribute to this process.

Korean medicinal plant extracts exhibit antiviral potency against viral hepatitis.

Jacob JR, Korba BE, You JE, Tennant BC, Kim YH. *J Altern Complement Med.* 2004 Dec;10(6):1019-26.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=15673997

Objectives: Investigation of natural ethnopharmacologic extracts exhibiting antiviral potential may lead to the discovery of new therapeutics for the treatment of chronic viral hepatitis infections. Traditional Korean medicinal herbs have been identified that exhibit potency against hepatitis B virus (HBV) and hepatitis C virus (HCV) infections. Research on the antiviral potential of naturally derived extracts is facilitated through the use of appropriate animal and liver cell culture models for these hepatotropic pathogens. Objectives of this study were to demonstrate antiviral activity of an aqueous extract of herbal formulation KYH-1 in surrogate in vitro assays for HBV and HCV and identify mechanisms of action. **Methods:** Antiviral potency of KYH-1 was measured in tissue culture systems that support replication of the woodchuck hepatitis virus (WHV), and the bovine viral diarrhea virus (BVDV). These assays serve as surrogate models for HBV and HCV, respectively. A recombinant HBV polymerase gene expression assay was used to define a molecular target. **Results:** KYH-1 exhibited potent antiviral activity against WHV and to a lesser extent against BVDV. KYH-1 and its constituent components inhibited HBV polymerase priming in vitro. Additionally, KYH-1 suppressed HBV replication in a human hepatoblastoma cell line. **Conclusion:** Evaluation of naturally derived products for antiviral activity against HBV and HCV in standardized surrogate assays provides a scientific basis for potential use as complementary or alternative medicines. This study provides significant results justifying preclinical evaluation of KYH-1 as an antiviral therapy for HBV infections.

Licorice compounds, glycyrrhizin and 18beta -glycyrrhetic acid, are potent modulators of bile acid-induced cytotoxicity in rat hepatocytes. Gumpricht E, Dahl R, Devereaux MW, Sokol RJ. J Biol Chem. 2005 Jan 10;

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=15642733

The accumulation of hydrophobic bile acids results in cholestatic liver injury by increasing oxidative stress, mitochondrial dysfunction and activation of cell signaling pathways. Licorice root and its constituents have been utilized as anti-hepatotoxic agents against hepatitis C. The purpose of this study was to evaluate the potential modulation by a primary component of licorice root, glycyrrhizin (GL), and its metabolite, 18beta-glycyrrhetic acid (GA) in a hepatocyte model of cholestatic liver injury. Preincubation of fresh rat hepatocyte suspensions with GL or GA reduced glycochenodeoxycholic acid (GCDC)-dependent reactive oxygen species (ROS) generation, with GA more potent than GL. Interestingly, GL and GA had opposing effects toward GCDC-induced cytotoxicity: GA prevented both necrosis and apoptosis, whereas GL enhanced apoptosis. GCDC promoted activation of caspase 10, caspase 3, and PARP; all were inhibited by GA, but not GL. Induction of apoptosis by GCDC was also associated with activation of JNK, which was prevented by GA. Activation of caspase 9 and dissipation of mitochondrial membrane potential were prevented by GA, but not GL. In liver mitochondrial studies, GL and GA were both potent inhibitors of the mitochondrial permeability transition, ROS generation, and cytochrome c release at submicromolar concentrations. **Results from this study suggest** that GL exhibits pro-apoptotic properties, whereas GA is a potent inhibitor of bile acid-induced apoptosis and necrosis in a manner consistent with its antioxidative effect.

Ursodiol Use Is Possibly Associated with Lower Incidence of Hepatocellular Carcinoma in Hepatitis C Virus-Associated Liver Cirrhosis Kazuo Tarao, et al. Cancer Epidemiol. Biomarkers Prev. 2005; 14(1): p. 164-169 <http://cebp.aacrjournals.org/cgi/content/abstract/14/1/164?ct>

In a previous study of patients with hepatitis C virus (HCV)-associated liver cirrhosis (HCV-LC), we showed that increased liver inflammation, as assessed by higher serum alanine aminotransferase (ALT), was associated with increased risk for the development of hepatocellular carcinoma (HCC). This suggested that suppression of inflammation might inhibit HCC development in HCV-LC. Several agents have been suggested to possess chemopreventive potential against the development of HCC in chronic HCV-associated liver disease, including herbal medicines, such as Stronger-Neo-Minophagen C (glycyrrhizin) and Sho-saiko-to (TJ-9). Ursodiol [ursodeoxycholic acid (UDCA)], a bile acid widely used to treat cholestatic liver diseases, also possesses anti-inflammatory properties in liver disease. We hypothesized that suppression of liver inflammation, as assessed by decreases in serum ALT, might inhibit HCC occurrence in patients with HCV-LC. In this study, the preventive effect of UDCA on HCC was examined in patients with early-stage HCV-LC. One hundred two patients with HCV-LC (Child stage A) were treated with anti-inflammatory drugs, Stronger-Neo-Minophagen C, Sho-saiko-to, or UDCA, with the goal of lowering the average serum ALT level to <80 IU. If the average ALT level did not remain <80 IU after treatment with one agent, multiagent therapy was initiated. The patients were followed up for >5 years and were retrospectively subdivided into two groups: 56 UDCA users (group A) and 46 UDCA nonusers (group B). The mean \pm SD dosage of UDCA administered in group A was 473.7 ± 183.0 mg/d. The average duration of UDCA administration in group A was 37.3 ± 15.9 months over the 5-year study period. The cumulative incidence of HCC was recorded. The 5-year incidence of HCC in group A was 17.9% (10 of 56) and was significantly lower than that in group B (39.1%, 18 of 46; $P = 0.025$). The risk for HCC incidence, calculated by a logistic regression model, showed that the administration of UDCA significantly decreased hepatocarcinogenesis ($P = 0.036$). The herbal medicines used were comparable in dosage and treatment duration in the UDCA and non-UDCA groups. **In conclusion**, UDCA might prevent HCC development in HCV-LC. Interestingly, because the serum ALT trends over time were nearly the same in both groups, the chemopreventive effectiveness of UDCA was not accompanied by greater reductions in ALT compared with the UDCA nonusers.

OTHER RESEARCH

Major depressive disorder with psychotic features induced by interferon- α treatment for hepatitis C in a polydrug abuser O. Ayhan Kalyoncu, et al. *J Psychopharmacol.* 2005; 19(1): p. 102-105

<http://jop.sagepub.com/cgi/content/abstract/19/1/102?ct> Infectious diseases, especially hepatitis C, are prevalent among drug abusers. Interferon-alpha (IFN-) is the pharmacological treatment of choice for this condition. Patients being treated with IFN- can be expected to experience such psychiatric side-effects as development of depression, mania, irritability, changes in personality, hallucinations or delirium. In addition, certain patients are considered to be at greater risk of developing neuropsychiatric side-effects. Individuals meeting the following criteria are particularly vulnerable: over 40 years of age; having central nervous system abnormalities; a previous neurological or psychiatric history; a past familial psychiatric history; use of narcotics or having alcohol or substance use disorders; being HIV-positive; coadministration of other cytokines; receiving high doses of IFN- (> 6 million units). We report the case of a 29-year-old patient with chronic non-active hepatitis C, a previous psychiatric history of polydrug abuse (cannabis, heroin and illegal use of the psychotropic drug biperiden) and anxiety disorder. Two weeks after the initiation of IFN- treatment, he developed fatigue, sleeplessness and persecutory delusions. The patient responded partially to the discontinuation of the IFN- treatment. Due to the presence of three risk factors in this patient, he was considered to belong to the group of patients being 'at high risk' of developing neuropsychiatric side-effects. This is the first case report of major depressive disorder with psychotic features in such a 'high-risk patient'. This case report may prompt other research by showing the importance of the close monitoring, and the prevention of the progression of IFN--related psychiatric disorders in 'a high-risk patient'.

Prophylactic SSRI during interferon alpha re-therapy in patients with chronic hepatitis C and a history of interferon-induced depression. *J Viral Hepat* 1 Jan 2005 12(1): p. 96.

<http://highwire.stanford.edu/cgi/medline/pmid:15655055> **Summary.** Only limited data are available on selective serotonin re-uptake inhibitor (SSRI) prophylaxis for antiviral re-treatment in hepatitis C patients with previous interferon-induced major depressive episodes. Therefore, we investigated the efficacy and safety of secondary SSRI prophylaxis in these patients. In a prospective and longitudinal study, repeated psychometric testing (Hospital Anxiety and Depression Scale) was performed before, during, and after antiviral re-treatment. Chronic hepatitis C virus (HCV)-infected patients, who had been psychometrically monitored during an unsuccessful previous antiviral therapy, and had developed major depression were included. Interferon re-therapy with SSRI prophylaxis was started (n = 8). The reference group was comprised of HCV patients without a history of interferon-associated depression and also a group who were previously unsuccessfully treated with interferon and were re-treated without SSRI prophylaxis (n = 9). All patients receiving SSRI prophylaxis were able to complete interferon re-therapy as scheduled. As in the first therapeutic course, depression scores were significantly elevated during re-treatment also (P < 0.001). Depression scores were significantly lower (P = 0.036) during interferon re-therapy with SSRI prophylaxis. Reference group subjects showed similar depression scores during first therapy and re-therapy (P > 0.05). **In conclusion,** hepatitis C patients with a history of interferon-induced major depression can be successfully re-treated with peginterferon/ribavirin and concomitant SSRI prophylaxis. In these patients, SSRI prophylaxis is safe and efficacious and should be considered, if antiviral re-therapy is indicated.

Psychosocial Factors Associated With Perceived Disease Severity in Patients With Chronic Hepatitis C: Relationship With Information Sources and Attentional Coping Styles Aymery Constant, et al. *Psychosomatics.* 2005; 46(1): p. 25-33

<http://psy.psychiatryonline.org/cgi/content/abstract/46/1/25?ct> The aim of this study was to investigate psychosocial factors associated with perceived disease severity, with emphasis on informational processing, in 185 consecutive patients with chronic hepatitis C. Medical data, information sources regarding chronic hepatitis C, and attentional coping styles were assessed. The patients considered their hepatitis C a severe disease and gave it a mean rating of 74 (SD=19) on a 100-mm visual analogue scale, but this perception was not related to liver histological severity. In multivariate analysis, age, coping styles (monitoring, blunting), and having a hepatologist as an information source accounted for 23% of

the variance of perceived severity. These results suggest that information processing and psychological features play a key role in the way patients with chronic hepatitis C perceive their disease.