

Caring Ambassadors Hepatitis C Program Newsletter  
www.HepCChallenge.org  
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**IN THE NEWS**

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**Legendary heavy-metal DJ Tawn Mastrey—the disease that took her life**

<http://www.citypages.com/2009-04-01/music/legendary-heavy-metal-dj-tawn-mastrey-mdash-the-disease-that-took-her-life/>

“Best known locally for her work with heavy-rock station 93X, DJ Tawn Mastrey led the kind of life that is usually reserved for fiction. After hitchhiking to California at the age of 17, she put herself through broadcasting school and landed gigs as a DJ in the Bay Area and then Los Angeles, interviewing rock stars and becoming close friends with people like Slash, Ozzy Osborne, and Sammy Hagar.

Tawn Mastrey, a.k.a. the Leather Nun During the '80s, Mastrey was credited with popularizing then-unknown bands like Mötley Crüe and Poison, pushing hair bands and heavy rock onto the commercial airwaves. Her Wikipedia page credits her for "breaking" AC/DC and the Police single "Roxanne." Mastrey's radio shows and interviews were soon picked up for national syndication. Dubbed the "Leather Nun," she was renowned by rock lovers everywhere for being a sassy, strong woman in a field traditionally reserved for egomaniacal men.

Throughout her career as a DJ, Mastrey followed a steady upward trajectory. She moved back to her home state of Minnesota and worked as a DJ on the heavy-metal-friendly station 93X during the late '90s, then took a national gig at Sirius Satellite Radio as the host of Hair Nation. But things took a dramatic turn around the time she started working for Sirius. In the early 2000s, Mastrey began to feel sick, as if she had contracted a flu that she just couldn't shake.

"She became ill and she didn't know why," says Mastrey's younger sister Cara, seated at the dining room table in her bohemian south Minneapolis apartment, surrounded by photos of Tawn. "They did all sorts of tests, and finally it came out that she had the hepatitis C virus. She didn't even know what that was." [truncated]

**Increase in STDs a concern of new health commissioner**

<http://www.salemnews.net/page/content.detail/id/512014.html?nav=5007&showlayout=0>

“Unprotected sex and intravenous drug use can be blamed for causing 50 percent of the infectious diseases reported in Columbiana County, but one local health official said it doesn't have to be that way. "If everybody engaged in safe sexual activities and didn't engage in illicit drug use, our disease burden would be cut in half," public health epidemiologist Michael Ruta said.

Ruta serves as epidemiologist for Columbiana, Carroll and Tuscarawas counties and prepared the 2008 End-Of-Year Infectious Disease Report for Columbiana County, a report he said shows that a majority of the diseases are easily preventable conditions just by people being more conscious about their health. Chlamydia and Hepatitis C infections accounted for 50 percent of the 212 valid disease reports received by the Columbiana County Health Department in 2008, coming in at number one and number two on the list.” [truncated]

### **Test may have exposed Vets to deadly diseases**

<http://cbs4.com/local/va.disease.colonoscopy.2.965833.html>

“Miami VA Healthcare System urges testing because of improperly sterilized tubes used in endoscopic procedures between 2004 and 2009. The Miami Veterans Affairs Healthcare System (MVAHS) has a warning for 3,260 veterans who were patients in endoscopic procedures during a 5-year period: Come in for free tests because there's a chance you were exposed to hepatitis B, hepatitis C or HIV.

MVAHS says those affected are veterans who had endoscopic procedures between May 2004 and March 12, 2009. Doctors say some of the tubing used was not disinfected according to the manufacturer's recommendations. A special Care Call center has been set up that is available 7 days a week, 24 hours a day.” [truncated]

### **Drugs team give out cocaine straws**

[http://www.kentonline.co.uk/kol08/article/default.asp?article\\_id=59340](http://www.kentonline.co.uk/kol08/article/default.asp?article_id=59340)

“Pieces of paper designed for snorting cocaine are being handed out to drug users across Kent, to stop them using rolled-up bank notes and spreading disease. The Maidstone-based Kent Drug and Alcohol Action Team, (KDAAT), responsible for the county’s drug treatment services, commissioned drugs charity KCA to make the notes.

The message on them reads: “Evidence suggests that the sharing of cocaine straws is a factor in the transmission of Hepatitis C. Reduce your chances of catching Hep C by using one of these single use notes instead of a bank note.”” [truncated]

### **Nurse gets injury payout after 36 years**

<http://www.thelocal.se/18284/20090318/>

“A Swedish nurse who contracted Hepatitis C after coming into contact with an infected needle has had the cause of her sickness recognized by the authorities as a workplace injury after a 36 year wait. Agneta Bjurman had just qualified as a nurse when she inadvertently pricked herself with a syringe after carrying out tests on a man who was seriously ill. Shortly afterwards she began to feel unwell, but it took some time before she made the connection between the deterioration of her health and the incident with the needle.

Many years after the initial accident, in 1994, she was eventually diagnosed with Hepatitis C. But only now has the Swedish Social Insurance Agency (Försäkringskassan) agreed to accept that her illness was work-related, entitling her to some financial compensation.” [truncated]

### **Vertex Hep C Drug Improves Cure Rate in Study**

<http://www.thestreet.com/print/story/10474626.html>

“Vertex Pharmaceuticals' experimental hepatitis C drug telaprevir is capable of significantly improving cure rates in the most difficult-to-treat patients, according to final results from a phase II study released Wednesday afternoon. The new data come from Vertex's PROVE 3 study, which enrolled 453 patients who had failed prior treatment with the current standard drug regimen for hepatitis C -- a 48-week course of long-acting interferon plus ribavirin. In the phase II study, these patients were randomized to receive either treatment with a combination of telaprevir plus the standard therapy or retreatment with the standard therapy alone.

In all, 51% of patients treated with a 24-week regimen that included 12 weeks of telaprevir reported undetectable levels of the hepatitis C virus six months after treatment. In hepatitis C parlance, that's known as a sustained virologic response, or SVR. Simply stated, these patients are considered cured of hepatitis C. By comparison, only 14% of the patients retreated with 48 weeks of standard therapy alone achieved an SVR, or cure, six months after treatment.” [truncated]

### **Progress Reported Against Gene Involved in Hepatitis C**

Finding could lead to new treatments for the disease, researchers say

<http://health.usnews.com/articles/health/healthday/2009/03/18/progress-reported-against-gene-involved-in.html>

“ Nearly 100 genes that support replication of the hepatitis C virus (HCV) in the human body have been identified by Massachusetts General Hospital researchers. They also found that blocking several of the genes suppressed replication of the virus.

"We may be a few years away from developing therapies based on these findings, but this study is a proof of principle that targeting host factors is a viable therapeutic strategy," Dr. Andrew Tai, of the hospital's gastrointestinal unit and lead researcher on the study, said in a hospital news release.” [truncated]

### **Digestive and liver diseases: no joking matter**

[http://www.southtownstar.com/lifestyles/1479355\\_031709toyourhealth.article](http://www.southtownstar.com/lifestyles/1479355_031709toyourhealth.article)

Maintaining a healthy digestive system is vital to your health and comfort.

But many people ignore the signs of digestive illness and fail to seek relief from their discomfort because they are embarrassed to discuss the symptoms or their own health histories... Another digestive disease, hepatitis C, requires discussions about potentially embarrassing aspects of a patient's personal history, including drug use and sexual activity.” [truncated]

### **Tattoo secrets revealed: What Pamela Anderson wishes she had known**

<http://www.examiner.com/x-322-Health-Care-Examiner~y2009m3d15-Tattoo-secrets-revealed-What-Barbie-doesnt-want-you-to-know>

“Last time I mentioned Tattoo Barbie, the 50 year old toy that teaches girls how cool it will be when they can get a real tattoo of their own For now they can just practice. Well, tattoos are not child's play. And complications from tattoos are the dirty little secret no one wants to talk about. Sure most people want to think that they're sexy and a sign of creativity or a quirky personality. But like the Sneeches, when everyone has one, isn't it just, well, average?

The evidence has been mounting for the past decade that tattoos are not as safe as most believe—even when done in commercial tattoo establishments. Tattoo inks are classified as cosmetics, so they aren't regulated or approved by the Food and Drug Administration (FDA). The pigments and

dyes used in tattoo inks aren't approved for injection under the skin. Long-term effects of these are unknown. They are also not regulated in most states. So, the risk those who wish to release their inner creativity is greater than most believe.”[truncated]

### **It's time to consider needle exchange program**

<http://www.reporternews.com/news/2009/mar/15/its-time-to-consider-needle-exchange-program/?printer=1/>

“Few images of drug use are more potent than that of the needle -- the needle in the shaky hand of a junkie searching the tracks on his arm or leg for a vein still able to receive one more injection; the needle hanging from the arm of an addict unconscious or dead from an overdose; the contaminated needle passing its deadly load of HIV or hepatitis to the next user and, through him, to his wife or lover and their unborn child.

A contaminated needle is an extremely efficient transmitter of a blood-borne disease. According to the Centers for Disease Control and Prevention, more than a third of AIDS cases in the United States have occurred among injecting drug users (IDUs), their sexual partners and their offspring. Hepatitis C, the most dangerous variant of that disease, is found in the blood of 70 to 90 percent of all adult IDUs.” [truncated]

### **Vertex pays \$100M for hep C-focused ViroChem**

<http://www.masshightech.com/stories/2009/03/09/daily49-Vertex-pays-100M-for-hep-C-focused-ViroChem.html>

“Biotech Vertex Pharmaceuticals Inc. has wrapped its \$100 million acquisition of ViroChem Pharma Inc., giving Vertex access to ViroChem’s hepatitis C virus drug research. ViroChem is a privately held company based in Laval, Quebec. Cambridge-based Vertex said that under the deal’s terms, Vertex will pay \$100 million in cash and 10.7 million shares of its common stock. The shares issued for the merger will be available for resale when the registration statement is filed. Under terms of the deal, Vertex also owns worldwide rights to the ViroChem HCV drug development portfolio.

More specifically, ViroChem offers HCV Polymerase Inhibitors to Vertex. This will enable Vertex to create new combinations of specifically targeted antiviral therapies for hepatitis C in the treatment of HCV infection. Two of them are VCH-222 and VCH-759, which have demonstrated reductions in plasma HCV RNA when dosed as single agents and were well tolerated in early clinical studies. In the second half of the year, Vertex expects to begin clinical evaluation of new combination regimens of its HCV protease inhibitor telaprevir. The HCV protease inhibitor telaprevir is currently in Phase 3 clinical development.” [truncated]

### **Army Believed to Have Infected 16 With Hepatitis**

<http://www.newsinferno.com/archives/5049>

“Media outlets are breaking with news that Army officials are confirming that 16 patients have tested positive for hepatitis b and c. The Associated Press (AP) reported that the Army said the patients were likely exposed to the dangerous blood borne illnesses because of improper injection practices.

The 16 patients at the William Beaumont Army Medical Center were just some of the over 2,000 diabetics who might have been exposed to hepatitis b (HBV) and hepatitis c (HBC) and other blood borne illnesses, said the AP. It sees that multiple patients were administered injections from the same insulin pen, it noted. Smart Brief said that, according to the El Paso Times, each insulin pen is meant to be used by one individual, but the insulin pens were injected into multiples patients from August 2007 until the end of January. Journal Now said the program “systematically” injected multiple patients from the same pen; Lieutenant Colonel Sandy LaFon said that it remains unclear if the HBV and HBC infections originated from the shoddy injections or if there were previously undiagnosed infections.” [truncated]

### **Schering say FDA expands hepatitis drug labels**

<http://www.forbes.com/feeds/ap/2009/03/11/ap6155863.html>

“The Food and Drug Administration expanded the label for Schering-Plough Corp.'s hepatitis C drugs Pegintron and Rebetol, allowing the company to market the drugs for patients who have not recovered from the disease after previous treatment.

Schering-Plough said Wednesday that the FDA approved the drugs for the treatment chronic hepatitis C in patients with compensated liver disease. They were already approved for use in "treatment-naïve" patients, or those who had never taken any drugs for the liver disease.” [truncated]

### **Allmans shine their light on the Beacon**

[http://www.nj.com/entertainment/music/index.ssf/2009/03/allmans\\_shine\\_their\\_light\\_on\\_t.html](http://www.nj.com/entertainment/music/index.ssf/2009/03/allmans_shine_their_light_on_t.html)

“ The Allman Brothers Band's 15 shows at the Beacon Theatre this month are billed as a 40th anniversary celebration. But their meaning goes deeper than that. The shows are dedicated to guitarist Duane Allman, the band's original leader and guiding force, who died in a 1971 motorcycle accident. And they mark the resumption of the band's annual Beacon stands after singer-keyboardist Gregg Allman's bout with hepatitis C forced the cancellation of last year's shows.

Gregg Allman has recovered. The band, a septet featuring two other original members (drummers Butch Trucks and Jaimoe), is back together. And even the Beacon is in great shape, following a seven-month, \$16 million renovation. To help mark the anniversary and honor Duane Allman, a series of guest stars -- none officially confirmed ahead of time -- has been lined up to appear at various shows.” [truncated]

### **UPDATE 3-Human Genome hepatitis C drug disappoints, shares crash**

<http://in.reuters.com/article/marketsNewsUS/idINBNG43626320090309>

“ Human Genome Sciences' drug to treat chronic hepatitis C met the main goal in a late-stage trial, but failed to show numerically better efficacy compared to standard-of-care, raising questions about the drug's adoption and sending shares crashing to an all-time low. Analysts had expected the trial to meet its main goal of non-inferiority compared to Pegasys, but they had also said that the trial must show numerically better sustained virologic response (SVR) rates to convince the market of the drug's commercial viability.” [truncated]

### **Hepatitis outbreaks caused by carelessness**

<http://www.clinicaladvisor.com/Hepatitis-outbreaks-caused-by-carelessness/PrintArticle/128401/>

“Sloppy clinical practices have caused 33 outbreaks of hepatitis B or hepatitis C infection in the past decade, the CDC reports after its first full-scale review of its own investigations (Ann Intern Med. 2009;150:33-39). As a result, more than 60,000 patients were told they needed diagnostic testing, 448 actually acquired the disease, and several lawsuits for malpractice have been filed.” [truncated]

### **Proteomics prove accurate in identifying liver cancer**

<http://www.thebostonchannel.com/bethisrael/18851367/detail.html>

“As the incidence of liver cancer continues to grow-- fueled in large part, by rising rates of hepatitis C infections – so too does the need for tests to help diagnose the disease at an earlier stage. A study appearing in the January 15, 2008, issue of Clinical Cancer Research demonstrates that a novel mass-spectrometry based form of proteomic profiling is more accurate than traditional biomarkers in distinguishing liver cancer patients from patients with hepatitis C liver cirrhosis, particularly with regard to identifying patients with small, curable tumors. Led by researchers at Beth Israel Deaconess Medical Center (BIDMC), the study could help lead to earlier diagnostic methods – and subsequent treatments -- for liver cancer.” [truncated]

### **Firefighter first to die in line of duty in Martin County fire-rescue's history**

<http://www.msnbc.msn.com/id/29466908/>

“ Hundreds gathered Monday to attend a funeral for a Martin County firefighter who died from an illness he contracted on the job. Fred Pierno Jr. died Wednesday at his Port St. Lucie home following a more than two-year battle with Hepatitis C virus, which he contracted while performing his duties with the Martin County Fire-Rescue Division.”

### **FTC clears ZymoGenetics-Bristol-Myers deal for hepatitis C drug development – Update**

<http://www.rttnews.com/ArticleView.aspx?Id=869188&SMap=1>

“ ZymoGenetics Inc. announced that its collaboration with Bristol-Myers Squibb Co. (BMY: News ) for hepatitis C compound PEG-Interferon lambda has been cleared by the United States Federal Trade Commission and Department of Justice clearance under provisions of the Hart-Scott-Rodino Antitrust Improvements Act.

PEG-Interferon lambda, (IL-29) is a novel type 3 interferon currently in Phase 1b development for Hepatitis C and is expected to be a more targeted therapy. Now that the collaboration agreement has become effective, following clearance, ZymoGenetics will receive payment of an \$85.0 million licensing fee.’ [truncated]

### **Hep C in HIVers may cause rapid liver disease**

<http://www.ebar.com/news/article.php?sec=news&article=3819>

“Dr. Daniel Fierer spoke about HIV-hepatitis C coinfection at a forum in San Francisco last week. While HIV continues to garner the lion's share of attention regarding gay men's health, a second forum in as many months focused on the growing epidemic of hepatitis C among HIV-positive men who have sex with men – and presenters noted that rapid liver disease could be a result.” [truncated]

### **Kerry urges probe of unsanitary conditions at VA**

[http://www.boston.com/news/politics/politicalintelligence/2009/03/kerry\\_urges\\_pro.html](http://www.boston.com/news/politics/politicalintelligence/2009/03/kerry_urges_pro.html)

“Senator John F. Kerry this afternoon urged the inspector general at the Department of Veterans Affairs to investigate sanitation standards at VA hospitals, following reports this week that facilities in Florida and Tennessee rinsed, but did not disinfect equipment used in colonoscopies. As many as 9,000 patients may have had invasive procedures with contaminated equipment, potentially exposing them to infectious diseases including hepatitis.” [truncated]

### **Hepatitis screening drive launched**

[http://www.dailytimes.com.pk/default.asp?page=2009\03\22\story\\_22-3-2009\\_pg11\\_6](http://www.dailytimes.com.pk/default.asp?page=2009\03\22\story_22-3-2009_pg11_6)

“ISLAMABAD: The Directorate of Health Services of the Capital Development Authority (CDA) launched a screening campaign to detect Hepatitis B & C patients in staff of various hotels in the city. A press statement, issued on Saturday, said CDA health directorate would test staff of hotel, motels, restaurants, barber shops and salons for the disease. In this connection, 1,028 people had so far been screened, out of which 24 tested positive for Hepatitis B and 55 for Hepatitis C. This is an alarming situation, which needs to be tackled on war footing to stop the disease from becoming an epidemic. Dr Saeed Ahmed of CDA said Hepatitis B and C cases were increasing in the city rapidly. He appealed to general public to take precautionary measures against the disease.”

### **Global Challenges | Increase in heroin availability in Australia posing risk of HIV**

[http://www.kaisernetwork.org/daily\\_reports/rep\\_index.cfm?DR\\_ID=57539](http://www.kaisernetwork.org/daily_reports/rep_index.cfm?DR_ID=57539)

“The Australian National Council on Drugs on Monday said that increased amounts of heroin entering the country from the Middle East and Asia could contribute to the spread of HIV among injection drug users, the Sydney Morning Herald reports. The council's Asia-Pacific Committee reported that heroin trafficking has increased and that border detections of the drug were the highest on record in 2006 and 2007.

According to committee chair Robert Ali, heroin use and overdose deaths in Australia have decreased since 2001, but overall global production has increased, creating new risks. He said that an increase in the availability of heroin could result in "recruitment of new drug users," adding, "It's recruiting a new group of users into injecting who think there is no HIV and don't know much about hepatitis C and just feeling that it's not risky. There's a perception that all of this has gone away, that it's no longer a problem." He added that there is "a real risk" of HIV and hepatitis C among IDUs.”[truncated]

### **Using HIV as model, Anadys develops drug cocktail ingredient for hepatitis C**

<http://www.xconomy.com/san-diego/2009/03/17/using-hiv-as-model-anadys-develops-drug-cocktail-ingredient-for-hepatitis-c/2/>

“HIV was transformed from a terminal illness into a chronic disease in wealthy countries in the late 1990s, once scientists learned to mix anti-viral drugs into a potent cocktail. That was supposed to hold the virus in check by attacking it from many different angles, keeping it from developing resistance to any one drug.

The same philosophy is now at work in hepatitis C, a chronic viral infection that causes liver damage.” [truncated]

### **Doctor fears needle disease outbreak**

[http://mns1.com/northern-news-services/stories/papers/mar13\\_09drg1.html](http://mns1.com/northern-news-services/stories/papers/mar13_09drg1.html)

SOMBA K'E/YELLOWKNIFE – “Intravenous crack cocaine, a huge factor in the HIV and hepatitis C outbreaks in Vancouver over the last few decades, is becoming a growing problem in Yellowknife, according to one emergency room doctor. Dr. David Pontin, a physician at Stanton Territorial Hospital, said he is beginning to see IV crack-related cases of hepatitis C in the ER.

In a letter addressed to the territorial government, Pontin wrote: "We have a situation here that is akin to kindling waiting for a flame. Our homeless population is highly addicted already and the introduction of IV crack use is the flame that will cause an explosion of HIV and hepatitis C." Crack cocaine in smoking form has given rise to hepatitis C and HIV problems in the past due to unsafe sex practised while on the drug. But melted down and injected, crack cocaine really kicks the spread of these diseases into high gear, he said." [truncated]

### **Sick, seeking answers**

<http://news.therecord.com/News/Local/article/497647>

“Troy Anderson was already carrying the virus that was silently attacking his liver when he walked into a navy recruiting office on Duke Street in 1986. Twenty-three years later, he has only to look a few blocks from his Queen Street apartment to be reminded of his eagerness and ignorance that day.

But Anderson, now 43, doesn't have to look nearly as far for a reminder of the virus that was with him then and is with him now. With his hepatitis C in its advanced stages, he lives with wild swings in his weight, fatigue, near-constant pain and an expert opinion that he only has a few years left to live.

For 15 years, Anderson was sick with the disease without knowing it. Eight of those years were spent in the navy, where he received regular blood tests -- but he alleges incompetence or irresponsibility kept military doctors from diagnosing his illness. It wasn't until 2000 that his hepatitis C was diagnosed by a civilian doctor. The physician suggested he had 10 years left to live.” [truncated]

### **Hepatitis C group creates alert card (Japan)**

<http://www.yomiuri.co.jp/dy/national/20090323TDY03101.htm>

“About 700 people with hepatitis C have created a card that contains information regarding their condition to alert medical staff in case of an emergency.

The card is aimed at notifying ambulance crews, doctors and other medical professionals that the owner of the card carries the hepatitis virus. It is hoped this will help medical staff avoid infection when the card owner is bleeding but cannot speak due to unforeseeable circumstances, such as being involved in a road accident.” [truncated]

### **Have a heart, give a liver**

<http://www.yourottagasouth.com/article/11118>

“Susan Kingston, a Kemptville woman suffering from liver cirrhosis, sits in her home with loyal friend Tanner. Susan needs a new liver in order to live beyond the next couple of years and is seeking a donor. Susan Kingston is going to die. That is, unless she finds a new liver.

Without it, she could have anywhere from two to four years left. Kingston has put out a plea for help after her last visit to doctors at Toronto's General Hospital made it clear that the chances of receiving a new liver in time to survive just isn't likely to happen.

"They said, 'You're O-positive – there's no chance we will be calling you,'" said Kingston in her home near Kemptville. "As the list is long, I would have to be bedridden in the hospital and airlifted to Toronto before I would be put higher on the list.'" [truncated]

### **Music and coffee spread awareness**

<http://www.dailytitan.com/features/music-and-coffee-spread-awareness-1.1617060>

"When a friend asked her to spread awareness about Hepatitis C, Kelly Zirbes willingly accepted the task and got to work. Unknown to herself when she started, her devotion to the cause led her to become a successful advocate with an effective and contemporary style, speaking through music.

As the founder of the non-profit organization Hepatitis C Awareness Inc., Zirbes incorporates musical performances at her company's events to entice others to learn about the virus."

[truncated]

### **Liver cancer from hepatitis looms large in RI**

<http://www.thejakartapost.com/news/2009/03/16/ahmadiyah-refugees.html>

"Indonesians are becoming increasingly more vulnerable to cancer of the liver, with more than 40,000 new cases detected each year, health experts warn. "Around 42,600 new cases of liver cancer occur every year in the country," health expert Terawan Agus Putranto said Saturday during a seminar on cancer diagnosis and therapy in Jakarta.

"Most of the cases stem from hepatitis, which is a prevalent disease among Indonesians," added the radiology specialist from Gading Pluit Hospital in North Jakarta.

He said careless use of needles and unmonitored blood transfusions had contributed significantly to the spread of hepatitis, which is transferable through blood, feces and sexual contact."

[truncated]

### **Campaign addresses unsafe injection practices**

<http://include.nurse.com/apps/pbcs.dll/article?AID=/20090309/NATIONAL01/103090149/-1/frontpage&template=printart>

"Nurses should know better. Syringes, IVs, and vials are never used more than once. It's basic nursing practice taught in every nursing school program. But something has gone wrong. A spate of hepatitis B and C infections traced to unsafe injection practices at ambulatory care centers across the country has prompted the U.S. Centers for Disease Control and Prevention to join a new national education campaign emphasizing safe injection practices to nurses and other healthcare workers." [truncated]

### **Poor infection control caused kidney unit hep C infections**

<http://www.modernmedicine.com/modernmedicine/Pathology/Poor-Infection-Control-Caused-Kidney-Unit-Hep-C-In/ArticleNewsFeed/Article/detail/585870?contextCategoryId=40144>

"A failure to adequately test patients for hepatitis C and poor infection control led to the infection with the virus of nine hemodialysis patients in New York City, according to a report published in the Mar. 6 issue of the U.S. Centers for Disease Control and Prevention's Morbidity and Mortality Weekly Report. Renee Hallack, of New York State Department of Health, and

colleagues report on an investigation into a private outpatient facility that treated between 70 and 100 patients at 30 dialysis stations each day. In May and July 2008, three cases of seroconversion from anti-hepatitis C virus negative to anti-hepatitis C virus positive were reported to the state health department and a subsequent investigation revealed that from 2001 to 2008 there were an additional six cases.’ [truncated]

### **9m suffering from hepatitis C, Senate told (Pakistan)**

<http://www.thenews.com.pk/print1.asp?id=166167>

“The Senate was informed on Friday that around 8.8 million people in Pakistan are suffering from deadly hepatitis C while another 5.6 million are affected by hepatitis B.

In written reply to a question, minister for health Aijaz Hussain Jhokrani said the figures have been compiled by a recent sero-prevalence study conducted by Pakistan Medical Research Council. “The quantum of hepatitis C and B are 4.9 percent and 2.5 percent respectively,” the minister added. He said the availability of diagnostic facilities and awareness campaigns have un-earthed the hidden burden of the disease.” [truncated]

### **AcroMetrix announces the release of OptiQuant-S hepatitis C virus (HCV) panel**

<http://news.prnewswire.com/DisplayReleaseContent.aspx?ACCT=104&STORY=/www/story/03-03-2009/0004981739&EDATE=>

“ AcroMetrix, a leading manufacturer of molecular quality control standards and controls for clinical diagnostic and blood testing laboratories, announced today the release of the OptiQuant-S HCV RNA Quantification Panel. This new panel utilizes AcroMetrix's proprietary SynTura(TM) Technology and provides laboratories with a critical component to fully optimize the Hepatitis C molecular assays available in today's market.

Viral Hepatitis B and C now account for greater than 75% of all cases of liver disease around the world(1). HCV patients are routinely monitored for changes in the amount of virus (i.e. viral load) present in the patient when undergoing therapy for the disease. Physicians rely on the accuracy of the viral load test result provided by the laboratory to adjust and manage the drug regiment for the patient.” [truncated]

### **Synthetic blood could be in circulation within 10 years**

[http://www.timesonline.co.uk/tol/life\\_and\\_style/health/article5992387.ece](http://www.timesonline.co.uk/tol/life_and_style/health/article5992387.ece)

“For Bruce Norval, it is a breakthrough but one he is nevertheless wary of. He is one of more than 4,000 haemophilia sufferers who contracted Hepatitis C through contaminated blood transfusions in the 1970s and 1980s, so is cautiously optimistic about the research project conducted by Scottish scientists into the manufacture of synthetic blood from embryonic stem cells. “It will address a lot of problems,” he says, “but we need to be able to monitor its safety and learn from the mistakes of the past.”

The three-year clinical trial, which is being led by Professor Marc Turner, the director of the Scottish National Blood Transfusion Service, — the universal blood group which can be transfused into 98% of the population without being rejected — from the stem cells. If successful, scientists believe the blood will be disease-free and provide limitless supplies for transfusions, operations and emergency procedures, reducing the reliance on donors. By the end

of the trial, they hope to be in a position to inject small amounts of the synthetic blood into volunteers to test its safety and viability, and within 10 years the process could be established on an industrial scale.”[truncated]

### **Free hepatitis C screenings set (Illinois)**

[http://www.nwherald.com/articles/2009/03/27/r\\_ftxfgcixqyq02km947i6q/index.xml](http://www.nwherald.com/articles/2009/03/27/r_ftxfgcixqyq02km947i6q/index.xml)

WOODSTOCK – In honor of Public Health Week, which will be April 6-12, the McHenry County Department of Health is offering free hepatitis C screenings to residents 18 and older. Screenings are available April 8, 9, 15, 16, 22 and 23 at the Annex B facility, 2200 N. Seminary Ave., Woodstock. Appointments are required...For information about the free hepatitis C screenings or to schedule an appointment, call the health department at 815-334-4500.”

[truncated]

### **Tattooing blamed for sharp rise in Hep C rates**

<http://www.northernstar.com.au/story/2009/04/01/tattooing-blamed-for-sharp-rise-in-hep-c-rates/>

“HEALTH WARNING: Health educators from the Hepatitis C Council of NSW Leon Fernandes (left), and Harpreet Kalsi. Young people who tattoo themselves with home kits purchased on the Internet risk contracting the potentially debilitating hepatitis C. Two hep C experts visiting the North Coast this week yesterday told The Northern Star the latest surge in the number of people with the disease were young people tattooing themselves and their friends. The kits can cost as little as \$80, but a lack of hygiene meant potential infections; those infected would pay a higher price - possibly for the rest of their lives.” [truncated]

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## **CLINICAL TRIALS, COHORT STUDIES, PILOT STUDIES**

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### **Early Changes in Hepatitis C Virus (HCV) Levels in Response to Peginterferon and Ribavirin Treatment in Patients with Chronic HCV Genotype 1 Infection.**

Hoofnagle JH, Wahed AS, Brown Jr RS, et al. J Infect Dis. 2009 Apr 15;199(8):1112-1120

[http://www.ncbi.nlm.nih.gov/pubmed/19284286?ordinalpos=38&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19284286?ordinalpos=38&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

Early changes in hepatitis C virus (HCV) RNA levels were assessed in a large cohort of African American and white patients with chronic hepatitis C due to HCV genotype 1 who underwent therapy with peginterferon alfa-2a and ribavirin in the Study of Viral Resistance to Antiviral Therapy of Hepatitis C (Virahep-C). Analyses were restricted to 341 patients who completed the first 28 days of therapy without dose modification. HCV RNA levels decreased in virtually all patients, but the amount of the change varied markedly. The overall 28-day decrease in HCV RNA levels was at least as predictive of a sustained virological response as the first- or second-phase viral kinetics responses. Factors associated with a smaller decrease in the HCV RNA level between baseline and day 28 included African American race, higher initial HCV RNA level, more severe hepatic fibrosis, and higher body weight. African American patients with similar 28-day decreases in viral levels as white patients were still less likely to achieve a sustained virological response. These **RESULTS** suggest that racial differences in the response to antiviral therapy are due to greater unresponsiveness to intracellular actions of interferon in African American individuals and that standard doses of peginterferon and ribavirin may be suboptimal for patients with higher body weights.

### **Granulocyte colony stimulating factor in HCV genotype-1 patients who develop Peg-IFN-alpha2b related severe neutropenia: A preliminary report on treatment, safety and efficacy.**

Koskinas J, Zacharakis G, Sidiropoulos J, et al. J Med Virol. 2009 Mar 24;81(5):848-852. [Epub ahead of print]

[http://www.ncbi.nlm.nih.gov/pubmed/19319942?ordinalpos=3&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19319942?ordinalpos=3&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

Dose reductions of Peg-IFN $\alpha$  because of severe neutropenia may affect the virologic response in patients with hepatitis C infection (HCV). Granulocyte colony-stimulating factor (G-CSF) has been used occasionally but studies addressing its safety and efficacy in the current treatment of HCV infection are missing. The database of 232 naïve patients with HCV genotype-1 who received PEG-IFN $\alpha$ 2b 1.5 mcg/kg/week plus Ribavirin 800-1,400 mg/day and completed the treatment was examined. Nineteen patients who exhibited significant neutropenia and received 150-300 microg G-CSF (Group A) with 19 matched control patients who had dose reductions of Peg-IFN $\alpha$  according to the standard recommendations (Group B) were examined. None of the patients had treatment modifications due to thrombocytopenia or anemia. The mean decline of the neutrophils was similar in groups A and B (1,760 +/- 1,030/mm<sup>3</sup>) at 11 +/- 8.6 weeks and 1,630 +/- 890 at 12.3 +/- 6.1, respectively). Nadir neutrophil values were also not statistically different. Patients who received G-CSF two before IFN $\alpha$ , maintained neutrophils between 1,400/mm<sup>3</sup> and 2,700/mm<sup>3</sup> and remained on G-CSF for 29 weeks (2-40). Virologic response at the end of treatment was observed in 12/19 (63%) patients and at 6 months follow-up in 6/19 (32%) in group A as compared to 9/19 (47%) and 4/19 (21%) in group B, respectively. No side effects related to G-CSF were encountered. Administration of G-CSF 2 days before Peg-IFN $\alpha$  is safe, maintains sustained neutrophil count, improves adherence to treatment and seems to increase the virologic response in patients infected with HCV genotype 1 who develop Peg-IFN- $\alpha$ 2b related severe neutropenia.

### **Re-treatment with peginterferon alfa-2a and ribavirin in patients with chronic hepatitis C who have relapsed or not responded to a first course of pegylated interferon-based therapy.**

Yoshida EM, Sherman M, Bain VG, et al. Can J Gastroenterol. 2009 Mar;23(3):180-184. [http://www.ncbi.nlm.nih.gov/pubmed/19319382?ordinalpos=4&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19319382?ordinalpos=4&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**BACKGROUND:** Pegylated interferon (pegIFN) and ribavirin combination therapy remains the first-line treatment for chronic hepatitis C virus (HCV) infection. In contrast to the wealth of studies in treatment-naïve patients, the effectiveness of retreatment in patients who have previously failed pegIFN-based therapy is largely unreported. **AIM:** To assess the effectiveness of the retreatment of patients who have previously failed an initial course of pegIFN-based therapy with pegIFN $\alpha$ -2a and ribavirin. **METHODS:** A post-hoc analysis of a multicentre open-label study was performed. Patients received pegIFN $\alpha$ -2a and ribavirin at a dose of 800 mg/day and later 1000 mg/day to 1200 mg/day for 24 to 48 weeks at the discretion of the investigator. Outcomes at week 12 (early virological response [EVR]) and week 24 (sustained virological response [SVR]) were analyzed.

**RESULTS:** Eighty-seven patients who had relapsed after previous pegIFN-based therapy (n=28; 78% genotype 1) or were nonresponders (n=59; 71% genotype 1) were analyzed. Of the relapsers, 86% achieved an EVR and 68% achieved an SVR. In relapsers to pegIFN monotherapy (n=15) or pegIFN plus ribavirin (n=13), 60% and 77% achieved an SVR, respectively. Fibrosis and genotype did not affect the likelihood of SVR in relapsers although this may be the result of the relatively small number of patients. In previous nonresponders, an EVR was achieved in 53% but an SVR occurred in only 17%. In nonresponders to pegIFN monotherapy (n=9) and pegIFN plus ribavirin (n=50), 33% and 14% achieved an SVR, respectively. Genotype did not affect SVR in nonresponders. Only 10% with a METAVIR score of F3 or F4 on liver biopsy achieved an SVR.

**CONCLUSIONS:** Relapse after previous pegIFN-based therapy is associated with a strong probability of treatment success whereas retreatment of those with previous nonresponse does not.

**Is smoking a prognostic factor in patients with chronic hepatitis C?** De Luca L, De Angelis C, Fagoonee S, et al. *Minerva Gastroenterol Dietol.* 2009 Jun;55(2):139-43.

[http://www.ncbi.nlm.nih.gov/pubmed/19305373?ordinalpos=12&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19305373?ordinalpos=12&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

The progression of chronic liver diseases is characterized by a common histopathological pathway comprising fibrosis formation and distortion of hepatic architecture which are the hallmark of evolution to cirrhosis. Several factors are responsible for the severity and progression of chronic hepatitis C. Here, we describe the most important data regarding the association between regular smoking and histological hepatic lesions. Some reports have shown that the proportion of patients with moderate or significant histological activity gradually increases with the daily consumption of tobacco. Moreover, fibrosis is associated with regular smoking in some studies. However, controversies result from other studies. Nicotine is mainly metabolised by the liver, and its administration in experimental animals showed development of steatosis and focal or confluent hepatic necrosis, probably linked to the oxidative stress associated with lipid peroxidation. In chronic hepatitis C patients, preliminary studies have suggested that hypoxia caused by smoking may induce expression of the cytokines vascular endothelial growth factor (VEGF) and VEGF-D and their corresponding soluble tyrosine kinase receptors fms-like tyrosine kinase receptor and kinase insert domain receptor. Since this issue is controversial and smoking is in any case unsafe, stopping is recommended for patients with liver diseases.

**Major hepatic resection for hepatocellular carcinoma with or without portal vein embolization: Perioperative outcome and survival.** Palavecino M, Chun YS, Madoff DC, et al. *Surgery.* 2009 Apr;145(4):399-

405. [http://www.ncbi.nlm.nih.gov/pubmed/19303988?ordinalpos=14&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19303988?ordinalpos=14&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**BACKGROUND:** Preoperative portal vein embolization (PVE) is performed to minimize perioperative risks of major hepatic resection for hepatocellular carcinoma (HCC), but its effects on tumor growth are ill defined. Perioperative outcome and survival after major hepatic resection for HCC, with and without PVE, were investigated. **METHODS:** Patients that underwent major hepatic resection (> or =3 segments) for HCC between January 1998 and May 2007 were analyzed retrospectively. Preoperative PVE was performed when the remnant liver volume was predicted to be insufficient. **RESULTS:** A total of 54 patients underwent major hepatic resection for HCC: 21 patients with PVE before resection (PVE group) and 33 patients without PVE (non-PVE group). PVE and non-PVE groups had similar rates of fibrosis or cirrhosis, hepatitis C virus, hepatitis B virus, American Joint Committee on Cancer stage, preoperative transarterial chemoembolization, overall postoperative complications, and positive margin (P = nonsignificant for all rates). There were no perioperative deaths in the PVE group and 6 (18%) deaths in the non-PVE group (P = .038). Median follow-up was 21 months. Excluding perioperative deaths, overall survival rates at 1, 3, and 5 years were 94%, 82%, and 72%, respectively, in the PVE group and 93%, 63%, and 54%, respectively, in the non-PVE group (P = .35). Similarly, disease-free survival (DFS) rates were not significantly different between the groups, with 1-, 3-, and 5-year DFS rates of 84%, 56%, and 56%, respectively, in the PVE group and 66%, 49%, and 49%, respectively, in the non-PVE group (P = .38). **CONCLUSION:** PVE before major hepatic resection for HCC is associated with

improved perioperative outcome. Excluding perioperative mortality, overall survival and DFS rates were similar between patients with and without preoperative PVE.

**Autoantibodies in chronic hepatitis C virus infection and their association with disease profile.** Williams MJ, Lawson A, Neal KR, et al. *J Viral Hepat.* 2009 Mar 3. [Epub ahead of print] [http://www.ncbi.nlm.nih.gov/pubmed/19302340?ordinalpos=18&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19302340?ordinalpos=18&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**Summary.** Autoantibodies are commonly detected in chronic hepatitis C (HCV) but their significance remains uncertain. We assessed the prevalence of anti-nuclear (ANA) and anti-smooth muscle (ASM) antibodies within a cohort of 963 treatment-naïve HCV patients. We also assessed for differences between autoantibody-positive and autoantibody-negative patients in demographics, markers of disease activity and response to anti-viral treatment. One hundred and seventy-two patients (17.9%) had at least one autoantibody, of which were 104 (10.8%) ASM, 54 (5.6%) ANA and 14 (1.5%) positive for both. Autoantibody-positive patients were older (43 vs 39 years,  $P = 0.001$ ) caused by an age-related increase in ANA (but not ASM). There were no differences in gender, alcohol intake, ethnicity or viral genotype. The presence of autoantibodies, and specifically ASM, was associated with an increase in interface hepatitis score amongst men (1.1 vs 0.8,  $P = 0.005$ ) but no difference in other necroinflammatory measures, liver function tests or immunoglobulins (Ig). There was no difference in initial fibrosis stage or rate of fibrosis progression. Autoantibodies did not affect response to anti-viral treatment. **We conclude** that autoantibodies are frequent in HCV infection. Anti-nuclear antibodies increase with age, whereas ASM antibodies are associated with interface hepatitis in men. Neither autoantibody carries increased risk of fibrosis progression or failure of therapy.

**Patients achieving clearance of HCV with interferon therapy recover from decreased retinol-binding protein 4 levels.** Iwasa M, Hara N, Miyachi H, et al. *J Viral Hepat.* 2009 Mar 3. [Epub ahead of print] [http://www.ncbi.nlm.nih.gov/pubmed/19302338?ordinalpos=20&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19302338?ordinalpos=20&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**Summary.** Retinol-binding protein 4 (RBP4) is a recently identified adipokine that is elevated in the blood in several insulin-resistant states. We investigated the association between plasma RBP4 and histological and biochemical characteristics of chronic hepatitis C (CHC), as well as changes in RBP4 levels following interferon therapy. Eighty-one patients with CHC infected with genotype 1 received treatment with peginterferon plus ribavirin. Histological data were available for 41 out of 81 patients before treatment, and the degree of fibrosis, inflammation and steatosis was assessed. Plasma levels of RBP4 were determined in serial samples (before, at the end of treatment, and at 6 months post-treatment). RBP4 levels were lower in CHC patients than in control subjects (34.6 +/- 12.3 mug/mL vs 46.2 +/- 10.5 mug/mL;  $P \leq 0.001$ ). Higher RBP4 levels were linked to lower alanine aminotransferase (ALT) ( $P < 0.01$ ), higher cholinesterase ( $P < 0.01$ ), hyperlipidaemia ( $P < 0.01$ ), hyperglycaemia ( $P < 0.05$ ), and higher platelet ( $P < 0.01$ ) count in CHC patients. Plasma RBP4 levels tended to decrease concomitantly with the grade of histological fibrosis, activity, and steatosis. RBP4 levels at baseline were not a predictor of the response to antiviral therapy in CHC patients. After peginterferon plus ribavirin therapy, only patients who had achieved clearance of hepatitis C virus had higher post-treatment RBP4 levels. This study suggests that an association between RBP4 levels and abnormal metabolic features, and that liver function may determine RBP4 levels in CHC patients. This is further supported by the observation that RBP4 levels increased significantly after treatment only in sustained virological response (SVR) patients and reached levels comparable to those of healthy subjects.

**Smoking is associated with steatosis and severe fibrosis in chronic hepatitis C but not B.**

Tsochatzis E, Papatheodoridis GV, Manolakopoulos S, et al. *Scand J Gastroenterol.* 2009 Mar 18:1-8. [Epub ahead of print]

[http://www.ncbi.nlm.nih.gov/pubmed/19296398?ordinalpos=25&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19296398?ordinalpos=25&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**OBJECTIVE.** The **RESULTS** of retrospective studies suggest an association between smoking, insulin resistance, steatosis and fibrosis in patients with chronic hepatitis C (CHC); no data are available for chronic hepatitis B (CHB). The purpose of this study was to evaluate the relationship, if any, of such factors on liver fibrosis in a cohort of patients with CHB and CHC. **Material and METHODS.** The study prospectively included 271 consecutive patients with CHB (n=95) or CHC (n=176) who had undergone liver biopsies. Each patient completed a questionnaire on smoking habits; anthropometric measurements and laboratory examinations were carried out and histological lesions were recorded. **RESULTS.** In CHC patients, severe fibrosis was independently associated with a higher body mass index (BMI) (OR: 1.180, 95% CI: 1.028-1.354; p=0.019), heavy smoking (OR: 3.923, 95% CI:1.356-11.348; p=0.012), higher alanine aminotransferase (ALAT) levels (OR: 1.010, 95% CI: 1.003-1.017; p=0.005) and alkaline phosphatase (ALP) levels (OR: 1.016, 95% CI: 1.001-1.030; p=0.03) and presence of necroinflammation (OR: 11.165, 95% CI: 1.286-96.970; p=0.029). Moreover, steatosis was independently associated with high gamma-glutamyl transpeptidase (GGT) values, heavy smoking and presence of necroinflammation. In CHB patients, no association between smoking habits and fibrosis or steatosis was noted. **CONCLUSIONS.** Heavy smoking is associated with severe fibrosis in CHC but not CHB. Heavy smoking is also significantly associated with steatosis in CHC and this could be the link between smoking and fibrosis progression.

**Treatment Outcomes With Pegylated Interferon and Ribavirin for Male Prisoners With Chronic Hepatitis C.**

Chew KW, Allen SA, Taylor LE, et al. *J Clin Gastroenterol.* 2009 Mar 17.

[Epub ahead of print]

[http://www.ncbi.nlm.nih.gov/pubmed/19295448?ordinalpos=26&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19295448?ordinalpos=26&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**GOALS:** To report our experience with pegylated interferon and ribavirin treatment of hepatitis C virus (HCV) RNA-positive inmates at the Rhode Island Department of Corrections.

**BACKGROUND:** An estimated 1 out of 3 HCV-infected individuals will spend time in a jail or prison within a 1-year period, making prisons a unique setting for management of chronic HCV.

**STUDY:** Chart review of all inmates identified as having initiated HCV treatment between October 2000 and April 2004. HCV-infected individuals were identified by HCV antibody screening at intake for known risk factors, elevated aminotransferase levels, or per individual request. Treatment followed standard guidelines with weight-based dosing of pegylated interferon-alpha2b and ribavirin. End points were completion of therapy plus 6 months for sustained virologic response (SVR), therapy discontinuation, and loss to follow-up. **RESULTS:** The cohort included 71 male patients, was mostly white (80%), and genotype 1 (65%). All 9 African Americans (AA) had genotype 1. Of 59 patients having liver biopsy, 41 had early stage disease. Overall SVR was 28%. Response rate was lower for genotype 1 compared with genotypes 2 and 3 (SVR 18% vs. 60% and 50%). Of inmates with genotype 1, no difference existed in treatment response by race (SVR 22% AA vs. 18% white). Thirty-three patients completed treatment, 26 stopped for side effects, and 5 for initial nonresponse. Eleven were lost to follow-up. **CONCLUSIONS:** Acceptable HCV treatment outcomes can be

achieved in prisons. Our small study indicates no difference in treatment response by AA versus white race for genotype 1.

**Clinical Implications of Alpha-fetoprotein in Chronic Hepatitis C.** Tai WC, Hu TH, Wang JH, et al. J Formos Med Assoc. 2009 Mar;108(3):210-8

[http://www.ncbi.nlm.nih.gov/pubmed/19293036?ordinalpos=28&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19293036?ordinalpos=28&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**BACKGROUND/Purpose:** Chronic hepatitis C (CHC) shows a significant association with cirrhosis and hepatocellular carcinoma (HCC). Alpha-fetoprotein (AFP) is important in the diagnosis of HCC, but elevated AFP levels have also been observed in CHC without HCC. We evaluated the clinical correlation between elevated AFP levels and CHC. **METHODS:** From April 1999 to November 2004, 654 CHC patients with no evidence of HCC from imaging studies were collected by chart review. **RESULTS:** The prevalence of elevated AFP levels ( $\geq 15$  ng/mL) was 23.9%. Univariate analysis revealed that age, histological activity index (HAI) fibrosis score of 3/4, HAI inflammation score  $\geq 7$ , aspartate aminotransferase (AST) and alanine transaminase (ALT) levels, AST/ALT ratio, and total bilirubin level were associated with elevated AFP levels. Multivariate analysis revealed that age ( $\geq 55$  vs.  $< 55$  years), HAI inflammation score ( $\geq 7$  vs.  $< 7$ ), ALT ( $> 150$  vs.  $\leq 150$  U/L), and platelet count ( $\leq 150 \times 10^9$  vs.  $> 150 \times 10^9$  cells/L) were associated with elevated AFP levels. Multivariate analysis also revealed that hepatitis C virus (HCV) genotype 1b, platelet count  $\leq 150 \times 10^9$  cells/L, AST  $> 80$  U/L and AFP  $\geq 6$  ng/mL were associated with advanced fibrosis. Using a cut-off AFP level of  $\geq 6.0$  ng/mL, the sensitivity and specificity of diagnosing fibrosis score 3/4 was 74.3% and 68.4%, respectively. Using a cut-off AFP level of  $\geq 15.0$  ng/mL, the sensitivity and specificity of diagnosing fibrosis score 3/4 was 35.7% and 91.1%, respectively. **CONCLUSION:** Elevated AFP levels were observed in 23.9% of patients with CHC. Elevated AFP levels correlated positively with age, HAI inflammation score, ALT elevation, and thrombocytopenia. In addition, HCV genotype 1b, thrombocytopenia, AST elevation, and AFP level  $\geq 6$  ng/mL were associated with advanced fibrosis.

**Early prediction of sustained virological response at day 3 of treatment with albinterferon-alpha-2b in patients with genotype 2/3 chronic hepatitis C.** Neumann AU, Bain VG, Yoshida EM, et al. Liver Int. 2009 Mar 11. [Epub ahead of print]

[http://www.ncbi.nlm.nih.gov/pubmed/19291180?ordinalpos=30&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19291180?ordinalpos=30&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**ABSTRACT BACKGROUND:** Albinterferon-alpha-2b (albIFN) is a long-acting fusion polypeptide composed of albumin and IFN-alpha-2b. In a phase 2 study of albIFN 1500 mug q2wk or q4wk in patients with genotype 2/3 chronic hepatitis C, albIFN demonstrated sustained virological response (SVR) rates of 62-77% (intent-to-treat population). **AIMs:** To assess the association of initial viral kinetics during albIFN therapy with baseline factors and SVR prediction. **METHODS:** In all, 43 patients were treated with albIFN 1500 mug (q2wk/q4wk) plus ribavirin (RBV) 800 mg/day for 24 weeks. Hepatitis C virus (HCV)-RNA levels were measured by real-time polymerase chain reaction, insulin resistance by homeostasis model assessment of insulin resistance (HOMA-IR) and serum albIFN levels by enzyme-linked immunosorbent assay. Prediction analysis was performed in a per protocol 28-patient subset who were  $\geq 80\%$  adherent to albIFN/RBV and had HCV-RNA levels measured at treatment day 3. **RESULTS:** Day-3 HCV-RNA level and first-phase viral decline as well as second-phase slope of viral decline were significantly associated with SVR. In adherent patients, 82.1% had a day-3 viral load  $< 4.2 \log_{10}$  IU/ml or first-phase decline  $> 1.25 \log_{10}$  IU/ml, which was predictive of SVR, both positively (95.7%; sensitivity:

100%) and negatively (100%; specificity: 83.3%). As low first-phase decline was associated with a high pretreatment HOMA-IR index (P=0.004) and a low day-3 serum albIFN level (P=0.01).

**CONCLUSIONS:** First-phase viral decline with albIFN/RBV was predictive of SVR in this study and may be modulated in part by IR.

**Retention rate and side effects in a prospective trial on hepatitis C treatment with pegylated interferon alpha-2a and ribavirin in opioid-dependent patients.** Ebner N, Wanner C, Winklbaaur B, et al. *Addict Biol.* 2009 Apr;14(2):227-37.  
[http://www.ncbi.nlm.nih.gov/pubmed/19291011?ordinalpos=31&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19291011?ordinalpos=31&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

Hepatitis C viral (HCV) infection is present in 30 to 98% of intravenous drug users. Intravenous substance abuse represents the main route of HCV transmission in industrialized countries. A multi-centre, randomized, controlled, prospective study assessed sustained virological response (SVR), adverse events such as depressive episodes and retention rate of HCV treatment in opioid-dependent patients. Stabilized, opioid-dependent patients with chronic HCV infection (genotype 2 or 3) received pegylated interferon alpha-2a in combination with ribavirin 800 mg/day (Group A) or 400 mg/day (Group B). Participants were randomized, blocked and stratified by genotype and viral load. A standardized psychiatric assessment, Beck Depression Inventory (BDI) and Van Zerssen's list of complaints were administered at each study visit. In 31 months, 300 opioid-dependent patients were screened; 190 (63.3%) were hepatitis C antibody positive. According to study protocol, out of 75 'potential-to-treat' patients with genotype 2 or 3, 17 stable patients (22.6%) were included in the study. All participants completed the study. Significant haemoglobin decreases occurred in both Groups A (P = 0.001) and B (P = 0.011). All the patients had an end-of-treatment (week 24) HCV RNA negativity. Fifteen (88.2%) achieved SVR at week 48. Overall, 52.9% developed depressive symptoms during treatment. Because of the prompt initiation of antidepressant medication at first appearance of depressive symptoms, no severe depressive episodes occurred. Our data show a high retention rate and reliability, and good viral response for both treatments. Hepatitis C treatment in stable opioid-dependent patients was efficacious, suggesting that addiction clinics can offer antiviral therapy in combination with agonistic treatment as part of multi-disciplinary treatment.

**Severe autoimmune cytopenias in treatment-naive hepatitis C virus infection: clinical description of 16 cases.** Dufour JF, Pradat P, Ruivard M, et al. *Eur J Gastroenterol Hepatol.* 2009 Mar;21(3):245-53.

[http://www.ncbi.nlm.nih.gov/pubmed/19279468?ordinalpos=43&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19279468?ordinalpos=43&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**OBJECTIVE:** To describe the prevalence, main characteristics, and treatment of severe autoimmune cytopenias [autoimmune hemolytic anemia (AIHA), autoimmune thrombocytopenic purpura (AITP)] in patients with chronic hepatitis C virus (HCV) infection. **METHODS:** Retrospective chart review of patients with chronic HCV infection seen at our institution. Two additional departments contributed eight more patients to assess therapy of HCV-related autoimmune cytopenias. **RESULTS:** Eight patients (seven AITP, one AIHA) fulfilled the inclusion criteria in our population of 4345 HCV-infected patients. The number of patients with AITP was much greater than would be expected by chance (P<0.0001). Patients with HCV-related AITP were older and demonstrated more immunological markers than a group of 40 controls. Eight additional patients (six AITP, two Evans syndrome) were included. We only assessed the response for AITP patients because of the single case of AIHA. Patients with AITP had a poor response to initial

corticosteroids [one complete response (CR), three partial response (PR), and four failures]. Intravenous immunoglobulins led to transient efficacy in three of four patients. In second-line therapy, five of seven patients responded to splenectomy. Rituximab proved effective in increasing platelets in two patients. Of eight patients treated with antiviral therapy (IFN-alpha+/-ribavirin), five responded (three CR, two PR). **CONCLUSION:** AITP occurs more commonly in patients with chronic HCV infection than would be expected by chance. HCV-positive AITP requires a treatment strategy different from that used in HCV-negative AITP. On the basis of the results from our study and a literature analysis, we propose an algorithm for treatment of severe HCV-related autoimmune cytopenias.

### **Treatment of hepatitis C in hemodialysis patients using pegylated interferon**

**alpha-2a in Turkey.** Kose S, Gurkan A, Akman F, Kelesoglu M, Uner U. J Gastroenterol. 2009 Mar 11. [Epub ahead of print]

[http://www.ncbi.nlm.nih.gov/pubmed/19277451?ordinalpos=45&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19277451?ordinalpos=45&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**PURPOSE:** Hepatitis C virus (HCV) is prevalent in renal insufficient patients. The **AIM** of the present study was to evaluate the efficacy and tolerability of pegylated interferon alpha-2a (peg-IFN-alpha-2a) among these patients. **METHODS:** Among 437 patients within total hemodialysis population in hemodialysis units, in total 83 patients (19.0%) were anti-HCV positive and of these 83 patients, 33 (39.7%) were HCV-RNA positive. Treatment was initiated in 33 patients who had chronic HCV infection. All patients were found to be HCV-RNA positive. During treatment, peg-IFN-alpha-2a (40 kDa), 135 mug/week was used on these 33 patients. **RESULTS:** Twenty-six (78.8%) of the 33 patients enrolled in the study completed the treatment. Two patients (6.0%) did not complete treatment because they had serious adverse events such as anemia and thrombocytopenia. At the onset of treatment, while all of 26 patients were HCV RNA positive, HCV RNA turned to negative in all 26 patients 3 months after treatment. **CONCLUSIONS:** At the end of the study, peg-IFN-alpha-2a treatment of patients with chronic hepatitis C on maintenance hemodialysis may improve prognosis and their quality of life.

### **Effective prediction of outcome of combination therapy with pegylated interferon alpha 2b plus ribavirin in Japanese patients with genotype-1 chronic hepatitis C using early viral kinetics and new indices.**

Nomura H, Miyagi Y, Tanimoto H, et al. J Gastroenterol. 2009 Mar 10. [Epub ahead of print]

[http://www.ncbi.nlm.nih.gov/pubmed/19277449?ordinalpos=46&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19277449?ordinalpos=46&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**BACKGROUND:** The rates of sustained virologic response (SVR) and relapse with pegylated interferon alpha 2b (peginterferon) plus ribavirin in patients with genotype-1 chronic hepatitis C (CHC) are approximately 50 and 30%, respectively. We investigated whether SVR and transient response (TR) can be differentiated during treatment using new indices calculated from early viral kinetics and the timing of when hepatitis C virus (HCV)-RNA becomes undetectable. **METHODS:** Peginterferon alpha 2b (1.5 mug/kg per week) plus weight-based ribavirin (600-1,000 mg/day) were administered to 141 patients with genotype-1 CHC for 48 weeks. The HCV-RNA loads were measured at baseline, 24 h, week 1, and week 2. The rebound index (RI, viral load at week 1 divided by viral load at 24 h) and the second rebound index (RI-2nd, viral load at week 2 divided by viral load at 24 h) were calculated. **RESULTS:** With SVR, the viral load was reduced at 24 h, did not rise during week 1 (RI  $\leq$  1.0), and was significantly reduced at week 2 (P < 0.05). Viral loads with TR and non-response increased at week 1. The SVR rate was 90% with RI  $\leq$  1.0, 96% with rapid viral responders, and 93% with RI-2nd < 0.7 and week 8 early viral responders. The SVR rate with

these 3 groups was 90% and administration for 48 weeks was recommended. With other groups, the SVR rate was 23% and the TR rate was 77%. Administration for 72 weeks was therefore recommended. **CONCLUSIONS:** We distinguished SVR from TR during treatment using two indices (RI and RI-2nd) and the timing of HCV-RNA negativity.

**Rituximab in cryoglobulinemic peripheral neuropathy.** Cavallo R, Roccatello D, Menegatti E, et al. J Neurol. 2009 Mar 5. [Epub ahead of print]  
[http://www.ncbi.nlm.nih.gov/pubmed/19263187?ordinalpos=64&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19263187?ordinalpos=64&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

Type II mixed cryoglobulinemia is sustained by an oligoclonal production of IgM sharing rheumatoid activity and can be associated with renal, cutaneous, rheumatologic or neurological manifestations. Peripheral neuropathy is a major cause of morbidity in hepatitis C virus-associated mixed cryoglobulinemia and is often refractory to any treatment. Rituximab induces a selective depletion of IgM-producing B cells, and both case reports on monoclonal IgM-related polyneuropathy as well as studies on small series of patients with interferon alpha-resistant mixed cryoglobulinemia have suggested that it may be beneficial. Thirteen patients affected by type II mixed cryoglobulinemia with polyneuropathy were treated. Rituximab was administered intravenously at a dose of 375 mg/m<sup>2</sup> on days 1, 8, 15 and 22. Two more doses were given 1 and 2 months later. No other immunosuppressive drugs were added. Response was evaluated by assessing the changes in the clinical neurological condition, in electromyographic indices and in laboratory parameters (including cryocrit, viral load, complement levels and rheumatoid factor) over at least 12 months. Sensory symptoms disappeared or improved following treatment. A significant improvement in the clinical neuropathy disability score was observed. Electromyography examination revealed that the amplitude of compound motor action potential had increased. Viral load did not significantly change. Side effects were negligible. In this open prospective study, rituximab appeared to be effective and safe in the treatment of patients with type II cryoglobulinemia-associated neuropathy.

**Combination therapy of peginterferon and ribavirin for chronic hepatitis C patients with genotype 1b and low-virus load.** Arase Y, Suzuki F, Akuta N, et al. Intern Med. 2009;48(5):253-8. Epub 2009 Mar 2.  
[http://www.ncbi.nlm.nih.gov/pubmed/19252344?ordinalpos=71&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19252344?ordinalpos=71&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**OBJECTIVE:** The **AIM** of this study was to evaluate the efficacy of combination therapy of peginterferon and ribavirin in patients infected with hepatitis C virus (HCV) genotype 1b and low virus load. **METHODS:** Inclusion criteria were HCV-genotype 1b, serum HCV RNA level of < 100 KIU/mL at the initiation time of treatment. A total of 60 were enrolled in this retrospective cohort study. The treatment period of combination therapy was 39.8+/-16.1 weeks. **RESULTS:** Of the 60 study patients, 47 had sustained virological response (SVR) by the intention to treat analysis. SVR occurred when serum HCV RNA was negative 8 weeks after the initiation of the treatment (p=0.004) and continuance of negative HCV RNA during treatment was > or = 30 week (p=0.016). In rapid virological response, all of seven patients with continuance of negative HCV RNA 20 to 29 weeks during treatment had SVR. In early virological response nine of 10 patients with continuance of negative HCV RNA of 30 to 39 week during treatment had SVR. **CONCLUSION:** The duration of combination therapy for chronic hepatitis C should be determined based on the time of attainment of negative HCV RNA in patients with genotype 1b and low-virus load.

**Incidence of prolonged length of stay after orthotopic liver transplantation and its influence on outcomes.** Smith JO, Shiffman ML, Behnke M, et al. *Liver Transpl.* 2009 Mar;15(3):273-9. [http://www.ncbi.nlm.nih.gov/pubmed/19243008?ordinalpos=73&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19243008?ordinalpos=73&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

Orthotopic liver transplantation (OLT) is the only effective treatment for end-stage liver disease. Although most patients do well and are discharged promptly, some require prolonged length of stay (PLOS). The prevalence of PLOS, associated factors, and their impact on survival are not well defined. We reviewed our adult OLT database for patients who survived > 30 days. PLOS was defined as hospitalization > 30 days following OLT. Of 521 OLT recipients, 68 (13%) had PLOS with a median duration of 50 days versus only 10 days for patients discharged within 30 days. Significant differences in pre-OLT variables between patients with and without PLOS included the mean wait list time ( $P = 0.001$ ), hospitalization at the time of OLT ( $P = 0.001$ ), and prior OLT ( $P = 0.041$ ). Factors independently associated with PLOS included intensive care unit status at the time of OLT [odds ratio (OR), 4; 95% confidence interval (CI), 1.6-10.4], OLT prior to Model for End-Stage Liver Disease implementation (OR, 2.27; 95% CI, 1.04-5.26), in-hospital post-OLT bacterial infection (OR, 9.34; 95% CI, 4.65-18.86), gastrointestinal bleeding (OR, 4.34; 95% CI, 1.4-14.08), renal failure (OR, 10.86; 95% CI, 5.07-23.25), and allograft rejection (OR, 3.7; 95% CI, 1.23-11.11). One-year graft survival and patient survival were significantly less in those with PLOS (for both,  $P < 0.0001$ ). Among PLOS patients, factors independently associated with increased 1-year mortality were donor age (OR, 1.07; 95% CI, 1.009-1.13), primary diagnosis of hepatitis C virus (OR, 6.89; 95% CI, 1.40-34.48), in-hospital post-OLT bacterial infection (OR, 13.3; 95% CI, 2.11-83.33), and cardiac complications (OR, 20.4; 95% CI, 1.51-250; c-statistic for the model, 0.85). In **CONCLUSION**, PLOS following OLT is associated with a significant decrease in survival despite a marked increase in cost and resource utilization. Efforts to modify those factors that contribute to PLOS may reduce this event, improve survival, and reduce OLT-associated costs.

**Impact of hepatitis C virus infection on children and their caregivers: quality of life, cognitive, and emotional outcomes.** Rodrigue JR, Balistreri W, Haber B, et al. *J Pediatr Gastroenterol Nutr.* 2009 Mar;48(3):341-7. [http://www.ncbi.nlm.nih.gov/pubmed/19242286?ordinalpos=74&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19242286?ordinalpos=74&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**OBJECTIVE:** Hepatitis C virus (HCV) infection is associated with decreased quality of life (QOL) and neurocognitive dysfunction in adults, but little is known about its impact on children and their caregivers. **PATIENTS AND METHODS:** We studied the QOL, behavioral, emotional, and cognitive functioning of 114 treatment-naïve children with HCV enrolled in a placebo-controlled, randomized, multisite clinical trial evaluating peginterferon alpha-2a alone or with ribavirin. Baseline assessment included measures of children's QOL, cognitive functioning, behavioral adaptation, and depression. Caregivers' QOL also was assessed. **RESULTS:** Relative to published normative data, caregivers were more likely to believe that their children's health was poor and would likely worsen ( $t = 3.93$ ;  $P < 0.0001$ ), and reported higher concern about their children's health status ( $t = 6.63$ ;  $P < 0.0001$ ) and that this concern limited family activities ( $t = 2.45$ ;  $P < 0.01$ ); they also viewed their children as having more internalizing behavioral problems ( $t = 1.98$ ;  $P < 0.05$ ). Only 2 (2%) children had a score in the clinically depressed range. Children with HCV had worse cognitive functioning than the normative sample but significantly better functioning than children with attention-deficit/hyperactivity disorder. Caregivers' QOL scores did not differ significantly from the normative sample, but infected mothers had lower QOL than noninfected caregivers. Caregivers were highly distressed about their children's medical circumstances. **CONCLUSIONS:** Although HCV infection, in its early stages, does not lead to global impairment

in QOL, cognitive, behavioral, or emotional functioning in children, it is associated with higher caregiver stress and strain on the family system, and it may be associated with some cognitive changes in children.

**Randomized trial of high-dose interferon-alpha-2b combined with ribavirin in patients with chronic hepatitis C: Correlation between amino acid substitutions in the core/NS5A region and virological response to interferon therapy.** Mori N, Imamura M, Kawakami Y, et al. *J Med Virol.* 2009 Apr;81(4):640-9.

[http://www.ncbi.nlm.nih.gov/pubmed/19235866?ordinalpos=76&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19235866?ordinalpos=76&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

The **AIM** of this study was to compare the efficacy of high-dose interferon (IFN)-alpha-2b with standard dose of IFN-alpha-2b in combination with ribavirin (RBV) for patients with chronic hepatitis C virus (HCV) infection, and to investigate the predictive factors associated with virological response. Two hundred Japanese patients with high HCV viral load (>100 KIU/ml) were randomized to 6 or 10 mega units (MU) of 24-week IFN-alpha-2b with RBV. Predictive factors were investigated; including pretreatment amino acid (aa) sequences of the core region and the IFN-sensitive determining region (ISDR). The sustained virological response rate was not different in the two groups (24% vs. 30%) but the incidence of depression was significantly higher in the 10 MU group than 6 MU group (7% vs. 0%,  $P = 0.02$ ). Younger age (<60) and HCV genotype (2a/b) were significant predictors of sustained virological response. In patients infected with genotype 1b, substitutions of core aa 70 and/or 91 were predictive for non-virological response ( $P < 0.001$ ), and substitutions in the ISDR was observed frequently in virological responders. Early viral kinetics study showed that serum HCV core antigen decreased more slowly in both patients with aa 70 and/or 91 substitutions in the core and with absence of substitutions in the ISDR. In **CONCLUSION**, the use of a higher dose of IFN-alpha-2b in combination with RBV did not improve virological response but resulted in higher incidence of depression. Amino acid substitutions in the core and ISDR are predictive of virological response to the therapy in patients with genotype 1b and high viral load.

**Mutations in the interferon sensitivity-determining region of hepatitis C virus genotype 2a correlate with response to pegylated-interferon-alpha 2a monotherapy.**

Hayashi K, Katano Y, Honda T, et al. *J Med Virol.* 2009 Mar;81(3):459-66.

[http://www.ncbi.nlm.nih.gov/pubmed/19152412?ordinalpos=93&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19152412?ordinalpos=93&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

The interferon sensitivity-determining region (ISDR) is thought to be inhibited by the double-stranded RNA-dependent protein kinase (PKR). Several studies have reported a relationship between the ISDR and interferon (IFN) responsiveness. However, this relationship is controversial. The **AIM** of this study was to investigate whether genomic heterogeneity of the ISDR among patients with hepatitis C virus (HCV) genotype 2a affects the response to pegylated-IFN-alpha 2a monotherapy. Eighty patients (47 men, 33 women; mean age: 54.2 +/- 12.9 years) infected with HCV genotype 2a were evaluated. HCV viral loads were determined by real-time PCR. The ISDR (amino acids 2193-2228) was examined by direct sequencing. Thirty-one patients received subcutaneous injections of pegylated-IFN-alpha 2a (180 microg) once weekly for 24 weeks, and 35 patients received injections for 48 weeks. Fourteen patients withdrew from treatment. Of the remaining 66 patients, 51 (77.3%) showed a sustained virologic response. Factors related to sustained virologic response on multivariate analysis were rapid virologic response (negative HCV at 4 weeks; odds ratio: 0.033; 95% confidence interval (95% CI) 0.003-0.363;  $P = 0.0052$ ) and the number of mutations in the ISDR (odds ratio: 0.025; 95% CI 0.001-0.476;  $P = 0.0141$ ). There were

no significant differences in other factors, including sex, age, aspartate aminotransferase, alanine aminotransferase, platelet count, duration of treatment, and HCV viral load. Rapid virologic response and the ISDR sequence variations are significantly associated with response to pegylated-IFN-alpha 2a monotherapy in Japanese patients with HCV genotype 2a.

**A matched case-controlled study of 48 and 72 weeks of peginterferon plus ribavirin combination therapy in patients infected with HCV genotype 1b in Japan: amino acid substitutions in HCV core region as predictor of sustained virological response.** Akuta N, Suzuki F, Hirakawa M, et al. *J Med Virol.* 2009 Mar;81(3):452-8.

[http://www.ncbi.nlm.nih.gov/pubmed/19152407?ordinalpos=94&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19152407?ordinalpos=94&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

Substitution of amino acid (aa) 70 and 91 in the core region of HCV genotype 1b is a useful pretreatment predictor of efficacy of 48-week peginterferon (PEG-IFN) plus ribavirin (RBV) therapy. Here, we determined the efficacy of 72-week PEG-IFN/RBV and the predictive factors to such therapy in a case-control study matched for sex, age, and periods from the start of treatment to initial point of HCV RNA-negative. We compared the treatment efficacy of 72-week regimen in 65 patients with that of 48-week in 130 patients, who were infected with HCV genotype 1b and treated with PEG-IFN/RBV. They consisted mainly of late virological responders (LVR) (HCV RNA-positive at 12 weeks and negative at 24 weeks after start of treatment). Sustained virological response (SVR) was achieved by 61.5% and 32.3% of patients of the 72- and 48-week groups, respectively, while non-virological response was noted in 9.2% and 29.2% of the respective groups. Multivariate analysis identified substitution of aa 70 and 91 (Arg70 and/or Leu91) and duration of treatment (72-week) as independent parameters that significantly influenced SVR. For Arg70 and/or Leu91 of core region, SVR rate was significantly higher in 72- (68.0%) than 48-week group (37.8%). For wild-type of ISDR, SVR rate was significantly higher in 72- (61.2%) than in 48-week group (29.3%). We conclude that 72-week PEG-IFN/RBV improves SVR rate for LVR, especially those with Arg70 and/or Leu91 of core region or wild-type of ISDR. Substitution of aa 70 and 91 is also a useful pretreatment predictor of response to 72-week PEG-IFN/RBV. Copyright 2009 Wiley-Liss, Inc.

**Long-term follow-up of patients with hepatitis C with a normal alanine aminotransferase.**

Kumada T, Toyoda H, Kiriya S, et al. *J Med Virol.* 2009 Mar;81(3):446-51.

[http://www.ncbi.nlm.nih.gov/pubmed/19152400?ordinalpos=96&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19152400?ordinalpos=96&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

An attempt was made to identify factors influencing the cumulative probability of an increased alanine aminotransferase (ALT) level and hepatocarcinogenesis in hepatitis C patients with a normal ALT level initially. A total of 398 consecutive patients with a normal ALT level initially for 6 months or more and follow-up period longer than 3 years during the period January 1995 to December 2004 were included. Patients were classified by ALT level into three groups: Group A (3-20 IU/L), Group B (21-30 IU/L), and Group C (31-35 IU/L). Factors associated with the cumulative probability of increased ALT level and hepatocarcinogenesis were evaluated. Women in groups B and C and men in Group C showed high cumulative probabilities of increased ALT levels. Factors associated with increased ALT were a high ALT level (Group B, relative risk; 1.758 [95% confidence interval: 1.290-2.392],  $P < 0.001$ , Group C, 3.328 [2.256-4.909],  $P < 0.001$ ), high lactate dehydrogenase level (2.352 [1.445-3.829],  $P = 0.001$ ), or low total cholesterol level (1.957 [1.330-2.882],  $P = 0.001$ ). Factors associated with incidence of hepatocellular carcinoma were increased age (3.088 [1.025-9.308],  $P = 0.045$ ), high ALT level (Group C, 5.803 [1.530-22.066],  $P = 0.010$ ), and high total bilirubin level (8.309 [2.235-30.888],  $P = 0.002$ ). In patients with hepatitis C with a normal

ALT level initially, an ALT level of 21-35 IU/L is a risk factor for an increased ALT level and hepatocarcinogenesis. Copyright 2009 Wiley-Liss, Inc.

**Sustained virological response reduces incidence of onset of type 2 diabetes in chronic hepatitis C.** Arase Y, Suzuki F, Suzuki Y, et al. *Hepatology*. 2009 Mar;49(3):739-44.

[http://www.ncbi.nlm.nih.gov/pubmed/19127513?ordinalpos=98&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19127513?ordinalpos=98&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

Diabetes is present in patients with chronic hepatitis C virus infection. The **AIM** of this retrospective cohort study was to assess the cumulative development incidence and predictive factors for type 2 diabetes after the termination of interferon therapy in Japanese patients positive for hepatitis C virus (HCV). A total of 2,842 HCV-positive patients treated with interferon (IFN) monotherapy or combination therapy with IFN and ribavirin were enrolled. The mean observation period was 6.4 years. An overnight (12-hour) fasting blood sample or a casual blood sample was taken for routine analyses during follow-up. The primary goal was the onset of type 2 diabetes. Evaluation was performed by using the Kaplan-Meier method and Cox proportional hazard analysis. Of 2,842 HCV patients, 143 patients developed type 2 diabetes. The cumulative development rate of type 2 diabetes was 3.6% at 5 years, 8.0% at 10 years, and 17.0% at 15 years. Multivariate Cox proportional hazard analysis revealed that type 2 diabetes development after the termination of IFN therapy occurred when histological staging was advanced (hazard ratio 3.30; 95% confidence interval [CI] 2.06-5.28;  $P < 0.001$ ), sustained virological response was not achieved (hazard ratio 2.73; 95% CI 1.77-4.20;  $P < 0.001$ ), the patient had pre-diabetes (hazard ratio 2.19; 95% CI 1.43-3.37;  $P < 0.001$ ), and age was  $\geq 50$  years (hazard ratio 2.10; 95% CI 1.38-3.18;  $P < 0.001$ ).

**CONCLUSION:** Our results indicate sustained virological response causes a two-thirds reduction in the risk of type 2 diabetes development in HCV-positive patients treated with IFN.

**Severe hepatocellular injury with apoptosis induced by a hepatitis C polymerase inhibitor.**

Feldstein A, Kleiner D, Kravetz D, Buck M. *J Clin Gastroenterol*. 2009 Apr;43(4):374-81.

[http://www.ncbi.nlm.nih.gov/pubmed/19098685?ordinalpos=100&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19098685?ordinalpos=100&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**GOALS:** To describe the mechanisms of severe hepatocellular injury with apoptosis in 2 patients receiving hepatitis C virus (HCV)-796. **BACKGROUND:** HCV-796 is a hepatitis C polymerase inhibitor approved by the US Food and Drug Administration for a phase 2 study of the treatment of hepatitis C in combination with PEG-Interferon and ribavirin. **RESULTS:** The injury occurred after more than 12 weeks of treatment, with a  $>20$ -fold increase in serum alanine aminotransferase and aspartate aminotransferase, and a marked increase in total (and direct) bilirubin in the absence of cholestasis. There was no evidence of autoimmune or viral hepatitis. Involvement of the mitochondrial apoptotic pathway was demonstrated by (1) release of cytochrome C into the cytosol; (2) association of cytochrome C with apoptotic protease activating factor-1 in the cytosol; (3) activation of initiator caspase 9; (4) activation of effector caspase 3; (5) increased serum caspase-3 cleaved cytokeratin-18 peptide; (6) nuclear fragmentation; (7) mitochondrial structural abnormalities; (8) expression of light chain 3 B, an indicator of autophagy; (9) probable autophagy of mitochondria by autophagosomes; and (10) probable phagocytosis of apoptotic hepatocytes by activated macrophages. Immunoglobulin G immune complexes were identified in the hepatocytes and localized to the endoplasmic reticulum and Golgi of these patients after the drug-induced liver disease, reflecting a primary or secondary target. Hepatitis C treatment was discontinued at weeks 15 and 19 in patients 1 and 2, respectively. After more than 6 months off the medication, both patients normalized the serum alanine aminotransferase, aspartate aminotransferase, and total bilirubin with

undetectable HCV RNA. **CONCLUSIONS:** HCV-796 may cause severe hepatocellular injury and apoptosis, with a marked immune reaction in susceptible patients.

**Is the rapid virologic response a positive predictive factor of sustained virologic response in all pretreatment status genotype 1 hepatitis c patients treated with peginterferon-alpha2b and ribavirin?**

de Segadas-Soares JA, Villela-Nogueira CA, Perez RM, et al. *J Clin Gastroenterol.* 2009 Apr;43(4):362-6.

[http://www.ncbi.nlm.nih.gov/pubmed/19077732?ordinalpos=103&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19077732?ordinalpos=103&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**INTRODUCTION:** Currently it is not yet defined if the rapid virologic response (RVR) can predict a sustained virologic response (SVR) in relapsers and nonresponders. **OBJECTIVE:** To evaluate treatment-RVR as a predictive factor of SVR in genotype 1 hepatitis C treatment naive, relapsers, and nonresponder patients treated with pegylated interferon-alpha (PEG-IFN-alpha2b) and ribavirin. **METHODS:** One hundred sixty-seven genotype 1 hepatitis C patients who were treated with PEG-IFN-alpha2b and ribavirin and had SVR assessed were included. Hepatitis C virus RNA analysis at the fourth week of treatment was performed in all patients. The exclusion criteria were hepatitis B virus and/or HIV co-infection. A comparative analysis was performed between the groups with and without RVR and a logistic regression model was applied. **RESULTS:** One hundred sixty-seven patients were analyzed, 103 (62%) were naives, 22 (13%) relapsers, and 42 (25%) nonresponders. The SVR rates were 44% in naives, 68% in relapsers, and 12% in nonresponders. RVR was attained in 51/167 (31%) patients and in this group the SVR was higher than in those without RVR (75% vs. 23%;  $P < 0.001$ ). This difference was also observed in all subgroups: naives (71% vs. 29%;  $P = 0.001$ ), relapsers (92% vs. 40%;  $P = 0.02$ ), and nonresponders (50% vs. 8%;  $P = 0.06$ ). A stepwise logistic regression model identified RVR and absence of cirrhosis as the factors independently associated to SVR. **CONCLUSIONS:** RVR and absence of cirrhosis are the strongest predictive factors of SVR in HCV genotype 1 patients. Assessment of RVR is very useful in all pretreatment status patients in predicting SVR and provides information for individualizing therapy.

**Clinical, virologic, histologic, and biochemical outcomes after successful HCV therapy: a 5-year follow-up of 150 patients.**

George SL, Bacon BR, Brunt EM, et al. *Hepatology.* 2009

Mar;49(3):729-38.

[http://www.ncbi.nlm.nih.gov/pubmed/19072828?ordinalpos=104&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19072828?ordinalpos=104&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

One hundred fifty patients with sustained virologic response (SVR) after treatment of chronic hepatitis C were enrolled in a long-term clinical follow-up study; patients were followed for 5 years for liver-related outcomes and evidence of biochemical or virologic relapse. Patients with stage 2 or greater fibrosis on pretreatment biopsy were invited to undergo a long-term follow-up biopsy after their fourth year of follow-up. One hundred twenty-eight patients (85%) were followed through their fourth year, and long-term follow-up biopsies were obtained from 60 patients (40%). Forty-nine patients had paired pretreatment and long-term follow-up biopsies blindly rescored. Forty of these patients (82%) had a decrease in fibrosis score, and 45 (92%) had a decrease in combined inflammation score. Ten patients (20%) had normal or nearly normal livers on long-term follow-up biopsy. Two patients with pretreatment cirrhosis developed hepatocellular carcinoma (HCC), and one died. All the other patients with pretreatment cirrhosis or advanced fibrosis had improved fibrosis scores on long-term follow-up biopsy. No patient had conclusive evidence of virologic

relapse. Three patients had persistently elevated alanine aminotransferase levels; two of these had new liver disease. **CONCLUSION:** In a cohort of 150 patients with SVR followed for 5 years, the majority of patients had good outcomes. Serum virologic relapse was not seen, but two patients with pretreatment cirrhosis developed HCC, and one died. In a blind rescoring of 49 paired pretreatment and long-term follow-up biopsies, 82% improved fibrosis scores and 92% improved at least one component of inflammation. A minority of patients had normal or nearly normal liver tissue on long-term follow-up biopsy. Patients with cirrhosis pretreatment are at a low but real risk of HCC after SVR.

**Narcotic analgesics and progression of fibrosis in patients with chronic hepatitis C.** Vallejos C, Bordin-Wosk T, Pockros L, Feng A, Pockros P. *J Clin Gastroenterol.* 2009 Apr;43(4):357-61. [http://www.ncbi.nlm.nih.gov/pubmed/19034042?ordinalpos=107&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19034042?ordinalpos=107&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

Narcotic analgesics are commonly prescribed drugs in patients with chronic hepatitis C (CHC) infection. In vitro data have shown that morphine enhances hepatitis C virus replication in human hepatic cells, however the effect of narcotics on hepatitis C virus disease progression remains uncertain. The **AIM** of this study was to evaluate the potential effects of narcotic analgesic use on the progression of hepatic fibrosis in patients with CHC infection. We identified CHC patients who had been seen at our institution and had undergone a liver biopsy between 1990 and 2005. Their charts were reviewed for the presence of narcotic analgesic and known risk factors for progression of hepatic fibrosis including male sex, age  $>$  or  $=40$ , obesity, diabetes, and alcohol abuse. All biopsy were reviewed and fibrosis scores were standardized using the Batts and Ludwig scoring system (stage 0 to 4). A total of 1147 evaluable patients were identified and 171 of these had narcotic analgesic use. In univariate analysis, narcotic analgesic use was associated with the presence of alcohol abuse ( $P<0.001$ ), obesity ( $P=0.02$ ), and advanced fibrosis defined as stage 3 to 4 fibrosis ( $P=0.02$ ), but not with male sex or diabetes. In multivariate logistic regression analysis, obesity [odds ratio (OR) 1.68 (confidence interval (CI), 1.21-2.33)], alcohol abuse [OR 1.45 (CI, 1.04-2.02)], age  $>$  or  $=40$  [OR 1.85 (CI, 1.22-2.89)], and diabetes [OR 2.43 (CI, 1.41-4.14)] all independently predicted advanced liver fibrosis but narcotic analgesic use did not [OR 1.71 (CI, 0.99-2.89)]. As the amount of narcotic analgesic use increased from no use, to  $<3$  months use, to  $>$  or  $=3$  months use, the frequency of obesity, alcohol abuse, and advanced fibrosis increased accordingly ( $P=0.005$ ), suggesting that it is difficult to separate these known risk factors from narcotic use as the cause for advanced fibrosis in this population.

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## BASIC AND APPLIED SCIENCE, PRE-CLINICAL STUDIES

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**Early gene expression profiles of patients with chronic hepatitis C treated with pegylated interferon-alfa and ribavirin.** Younossi ZM, Baranova A, Afendy A, et al. *Hepatology.* 2009 Mar;49(3):763-74.

[http://www.ncbi.nlm.nih.gov/pubmed/19140155?ordinalpos=97&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19140155?ordinalpos=97&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

Responsiveness to hepatitis C virus (HCV) therapy depends on viral and host factors. Our **AIM** was to assess sustained virologic response (SVR)-associated early gene expression in patients with HCV receiving pegylated interferon-alpha2a (PEG-IFN-alpha2a) or PEG-IFN-alpha2b and ribavirin with the duration based on genotypes. Blood samples were collected into PAXgene tubes prior to treatment as well as 1, 7, 28, and 56 days after treatment. From the peripheral blood cells, total RNA was extracted, quantified, and used for one-step reverse transcription polymerase chain reaction to

profile 154 messenger RNAs. Expression levels of messenger RNAs were normalized with six "housekeeping" genes and a reference RNA. Multiple regression and stepwise selection were performed to assess differences in gene expression at different time points, and predictive performance was evaluated for each model. A total of 68 patients were enrolled in the study and treated with combination therapy. The **RESULTS** of gene expression showed that SVR could be predicted by the gene expression of signal transducer and activator of transcription-6 (STAT-6) and suppressor of cytokine signaling-1 in the pretreatment samples. After 24 hours, SVR was predicted by the expression of interferon-dependent genes, and this dependence continued to be prominent throughout the treatment. **CONCLUSION:** Early gene expression during anti-HCV therapy may elucidate important molecular pathways that may be influencing the probability of achieving virologic response.

#### **Identification of a lipid kinase as a host factor involved in hepatitis C virus RNA replication.**

Vaillancourt FH, Pilote L, Cartier M, et al. *Virology*. 2009 Mar 20. [Epub ahead of print] [http://www.ncbi.nlm.nih.gov/pubmed/19304308?ordinalpos=13&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19304308?ordinalpos=13&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

A functional screen of an adenovirus-delivered shRNA library that targets approximately 4500 host genes was performed to identify cellular factors that regulate hepatitis C virus (HCV) sub-genomic RNA replication. Seventy-three hits were further examined by siRNA oligonucleotide-directed knockdown, and silencing of the PI4KA gene was demonstrated to have a significant effect on the replication of a HCV genotype 1b replicon. Using transient siRNA oligonucleotide transfections and stable shRNA knockdown clones in HuH-7 cells, the PI4KA gene was shown to be essential for the replication of all HCV genotypes tested (1a, 1b and 2a) but not required for bovine viral diarrhea virus (BVDV) RNA replication.

#### **Preclinical Characterization of PF-00868554, a Potent Nonnucleoside Inhibitor of the Hepatitis C Virus RNA-dependent RNA Polymerase.**

Shi ST, Herlihy KJ, Graham JP, et al. *Antimicrob Agents Chemother*. 2009 Mar 23. [Epub ahead of print] [http://www.ncbi.nlm.nih.gov/pubmed/19307358?ordinalpos=9&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19307358?ordinalpos=9&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

PF-00868554 is a non-nucleoside inhibitor of the hepatitis C virus (HCV) RNA polymerase, which exerts its inhibitory effect by binding to the thumb-base domain of the protein. It is a potent and selective inhibitor, with a mean IC<sub>50</sub> of 0.019 microM against genotype 1 polymerases and a mean EC<sub>50</sub> of 0.075 microM against the genotype 1b-Con1 replicon. To determine the in vitro antiviral activity of PF-00868554 against various HCV strains, a panel of chimeric replicons was generated in which polymerase sequences derived from genotype 1a and 1b clinical isolates were cloned into the 1b-Con1 subgenomic reporter replicon. Our **RESULTS** indicate that PF-00868554 has potent in vitro antiviral activity against a majority (95.8%) of genotype 1a and 1b replicons, with an overall mean EC<sub>50</sub> of 0.059 microM. PF-00868554 showed no cytotoxic effect in several human cell lines up to the highest concentration evaluated (320 microM). Furthermore, the antiviral activity of PF-00868554 was retained in the presence of human serum proteins. An in vitro resistance study of PF-00868554 identified M423T as the predominant resistance mutation, resulting in a 761-fold reduction in susceptibility to PF-00868554 but no change in susceptibility to IFN- $\alpha$  and a polymerase inhibitor that binds to a different region. PF-00868554 also showed good pharmacokinetic (PK) properties in preclinical animal species. Our **RESULTS** demonstrate that PF-00868554 has potent and broad-spectrum antiviral activity against genotype 1 HCV strains, supporting its use as an oral antiviral agent in HCV-infected patients.

**Chronic hepatitis C in the advanced adult and elderly subjects.** Gattoni A, Parlato A, Vangieri B, Bresciani M, Petracaro M. *Minerva Gastroenterol Dietol.* 2009 Jun;55(2):145-57.

[http://www.ncbi.nlm.nih.gov/pubmed/19305374?ordinalpos=11&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19305374?ordinalpos=11&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

Aging is associated with a complex remodeling of the immune system. While adaptive immune responses show impairment with aging, innate immune responses tend to improve it. Low numbers of CD3+, CD4+ and CD8 T cells have been observed in aged individuals. B lymphocytes tend to diminish as well. However, an increase in NK cells and effector T lymphocytes (CD28- CD8) can be shown. Effector T lymphocytes are characterized by: 1) expression of markers of cytotoxicity; 2) high levels of NK activity; 3) expression of the same inhibitory receptors as NK cells; 4) no cytokine production. For effector T lymphocyte-mediated cytotoxicity of virus-infected cells to occur, viral epitopes need to be exposed on the cell surface in the absence of MHC class I molecule expression, just as it has been shown with NK cells. Indeed, chronic infection with intracellular parasites is known to hinder MHC class I expression on cell surface. In elderly patients with chronic hepatitis C, infected hepatocytes can be shown to express a wide variety of HCV antigens, reflecting latency or active replication, as opposed to low or absent MHC class I expression. This favors elimination of infected hepatocytes by NK cells and effector T lymphocytes. A negative correlation has been observed between outcome of hepatitis and patients' age. Liver biopsies from elderly patients generally show chronic active hepatitis or cirrhosis, which are far less commonly observed in young patients or young adults. Overproduction of proinflammatory cytokines, namely TNF- $\alpha$ , IL-1 and IL-6, is responsible for enhanced immunopathogenesis and underlies a more extensive damage to liver parenchyma. Since interferon- $\alpha$  has been shown to upregulate MHC class I molecule expression on infected hepatocytes, it may turn useful as a tool to inhibit NK cell- and effector T lymphocyte-mediated cytotoxicity. Thus, a rationale exists to recommend interferon- $\alpha$  administration in hepatitis C patients, especially in elderly patients. If the data presented here can contribute to foster research into interferon- $\alpha$  treatment of elderly patients with hepatitis C, our goal will be reached.

**Early viraemia clearance during antiviral therapy of chronic hepatitis C improves dendritic cell functions.** Pachiadakis I, Chokshi S, Cooksley H, et al. *Clin Immunol.* 2009 Mar 19. [Epub ahead of print]

[http://www.ncbi.nlm.nih.gov/pubmed/19303818?ordinalpos=15&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19303818?ordinalpos=15&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

Plasma and cellular HCV RNA and core antigen were tested in monocyte-derived DC (MDDC) from chronic hepatitis C patients undergoing treatment with peg-interferon alpha2b/ribavirin. DC allostimulatory capacity, HCV-specific T-cell reactivity and IL-12 production were measured at baseline and treatment week (TW)12. Using DC and autologous CD4(+)T-cells, obtained at baseline and TW12, we performed cross-over experiments to determine the relative role of DC and/or T-cells for impaired immune reactivity to HCV. HCV RNA and HCV core plasma levels had an impact on DC phenotype and allostimulatory capacity. In contrast, HCV genome/core protein, although detectable in DC from some patients had no effect on DC function. Antiviral immunity at TW12 was not improved in patients who remained HCV RNA positive, while early viraemia clearance (TW12) improved antiviral responses. The cross-over experiment revealed that changes in DC, rather than CD4(+)T cells have a major role for enhanced anti-HCV responses.

**Selection Pressure from Neutralizing Antibodies Drives Sequence Evolution during Acute Infection with Hepatitis C Virus.** Dowd KA, Netski DM, Wang XH, Cox AL, Ray SC.

*Gastroenterology.* 2009 Mar 17. [Epub ahead of print]

[http://www.ncbi.nlm.nih.gov/pubmed/19303013?ordinalpos=17&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19303013?ordinalpos=17&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**BACKGROUND AND AIMS:** Despite recent characterization of hepatitis C virus-specific neutralizing antibodies, it is not clear to what extent immune pressure from neutralizing antibodies drives viral sequence evolution in vivo. This lack of understanding is particularly evident in acute infection, the phase when elimination or persistence of viral replication is determined and during which the importance of the humoral immune response has been largely discounted. **METHODS:** We analyzed envelope glycoprotein sequence evolution, and neutralization of sequential autologous hepatitis C virus pseudoparticles in eight individuals throughout acute infection. **RESULTS:** Amino acid substitutions occurred throughout the envelope genes, primarily within the hypervariable region 1 of E2. When individualized pseudoparticles expressing sequential envelope sequences were used to measure neutralization by autologous sera, antibodies neutralizing earlier sequence variants were detected at earlier time points than antibodies neutralizing later variants, indicating clearance and evolution of viral variants in response to pressure from neutralizing antibodies. To demonstrate the effects of amino acid substitution on neutralization, site-directed mutagenesis of a pseudoparticle envelope sequence revealed amino acid substitutions in hypervariable region 1 that were responsible for a dramatic decrease in neutralization sensitivity over time. In addition, high-titer neutralizing antibodies peaked at the time of viral clearance in all spontaneous resolvers, while chronically evolving subjects displayed low-titer or absent neutralizing antibodies throughout early acute infection. **CONCLUSIONS:** These findings indicate that during acute hepatitis C virus infection in vivo, virus-specific neutralizing antibodies drive sequence evolution and, in some individuals, play a role in determining the outcome of infection.

**Inhibition of intracellular hepatitis C virus replication by nelfinavir and synergistic effect with interferon-alpha.** Toma S, Yamashiro T, Arakaki S, et al. J Viral Hepat. 2009 Mar 3. [Epub ahead of print]

[http://www.ncbi.nlm.nih.gov/pubmed/19302339?ordinalpos=19&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19302339?ordinalpos=19&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**Summary.** Liver diseases associated with hepatitis C virus (HCV) infection have become the major cause of mortality in patients with human immunodeficiency virus (HIV) infection since the introduction of highly active anti-retroviral therapy. HCV-related liver disease is more severe in HIV-infected patients than in non-HIV-infected patients, but the standard therapies used to treat chronic hepatitis C in HCV/HIV coinfecting patients are the same as those for patients infected with HCV alone. HIV protease inhibitors might have potential to down-regulate HCV load of HCV/HIV coinfecting patients. In this study, we evaluated the effects of nelfinavir on intracellular HCV replication using the HCV replicon system. We constructed an HCV replicon expressing a neomycin-selectable chimeric firefly luciferase reporter protein. Cytotoxicity and apoptosis induced by nelfinavir were assessed and synergism between nelfinavir and interferon (IFN) was calculated using CalcuSyn analysis. Nelfinavir dose-dependently repressed HCV replication at low concentrations (IC<sub>50</sub>, 9.88 μmol/L). Nelfinavir failed to induce cytotoxicity or apoptosis at concentrations that inhibited HCV replication. Clinical concentrations of nelfinavir (5 μmol/L) combined with IFN showed synergistic inhibition of HCV replication in our replicon model. Our **RESULTS** suggest that the direct effects of nelfinavir on the HCV subgenome and its synergism with IFN could improve clinical responses to IFN therapy in HCV/HIV coinfecting patients.

**Low interleukin-10 production by monocytes of patients with a self-limiting hepatitis C virus infection.** Martin-Blondel G, Gales A, Bernad J, et al. J Viral Hepat. 2009 Mar 11. [Epub ahead of print]

[http://www.ncbi.nlm.nih.gov/pubmed/19302337?ordinalpos=21&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19302337?ordinalpos=21&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**Summary.** Host factors seem to be crucial for the spontaneous clearance of hepatitis C virus (HCV). Monocytes play a pivotal role in innate immunity and help regulate adaptive responses. This study assesses the characteristics of monocytes from patients with self-limiting HCV infections. We studied 35 consecutive patients [11 with a self-limiting HCV infection, 16 chronically infected with HCV and sustained virological responders (SVR) following antiviral therapy, and eight chronically infected HCV but untreated] and eight healthy donors (HD). The production of interleukin (IL)-10, tumour necrosis factor-alpha (TNF-alpha) and IL-12p40 by monocytes stimulated with lipopolysaccharides(LPS) or HCV Core protein was measured by enzyme-linked immunoassay. Monocyte surface markers were analysed by flow cytometry. LPS and Core protein triggered IL-10 and TNF-alpha production, but monocytes from self-limiting infection patients produced significantly less IL-10 and TNF-alpha than those of SVR, chronically infected or HD ( $P < 0.05$ ), while IL-12p40 production was unchanged. This cytokine production profile did not appear to be due to expansion of the CD14(+) CD16(+) monocyte subset or to a classical or alternative activation monocyte profile. Monocytes from self-limiting infection patients had more CCR7 than those from SVR or chronically infected patients ( $P < 0.05$ ). Monocytes of self-limiting infection patients appear to produce little IL-10 and TNF-alpha in response to viral or unspecific stimulation and to have a higher CCR7 expression. This profile seems to be independent to a particular monocyte subset or activation state. Low IL-10 production may help establish an effective immune response and spontaneous HCV clearance.

**Residues in a Highly Conserved Claudin-1 Motif Are Required for Hepatitis C Virus Entry and Mediate the Formation of Cell-Cell Contacts.** Cukierman L, Meertens L, Bertaux C, Kajumo F, Dragic T. *J Virol.* 2009 Mar 18. [Epub ahead of print]

[http://www.ncbi.nlm.nih.gov/pubmed/19297469?ordinalpos=23&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19297469?ordinalpos=23&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

Claudin-1, a component of tight junctions between liver hepatocytes, is a hepatitis C virus (HCV) late-stage entry cofactor. To investigate the structural and functional role of various Claudin-1 domains in HCV entry, we applied a mutagenesis strategy. Putative functional intracellular Claudin-1 domains were not important. However, we identified seven novel residues in the first extracellular loop that are critical for entry of HCV isolates drawn from six different subtypes. Most of the critical residues belong to the highly conserved claudin motif W30-GLW51-C54-C64. Alanine substitutions of these residues did not impair Claudin-1 cell surface expression or lateral protein interactions within the plasma membrane, including Claudin-1-Claudin-1 and Claudin-1-CD81 interactions. However, these mutants no longer localized to cell-cell contacts. Based on our observations, we propose that cell-cell contacts formed by Claudin-1 may generate specialized membrane domains that are amenable to HCV entry.

**Hepatitis C virus and ethanol alter antigen presentation in liver cells.** Osna NA. *World J Gastroenterol.* 2009 Mar 14;15(10):1201-8.

[http://www.ncbi.nlm.nih.gov/pubmed/19291820?ordinalpos=29&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19291820?ordinalpos=29&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

Alcoholic patients have a high incidence of hepatitis C virus (HCV) infection. Alcohol consumption enhances the severity of the HCV disease course and worsens the outcome of chronic hepatitis C. The accumulation of virally infected cells in the liver is related to the HCV-induced inability of the immune system to recognize infected cells and to develop the immune responses. This review covers the effects of HCV proteins and ethanol on major histocompatibility complex (MHC)

class I- and class II-restricted antigen presentation. Here, we discuss the liver which functions as an immune privilege organ; factors, which affect cleavage and loading of antigenic peptides onto MHC class I and class II in hepatocytes and dendritic cells, and the modulating effects of ethanol and HCV on antigen presentation by liver cells. Altered antigen presentation in the liver limits the ability of the immune system to clear HCV and infected cells and contributes to disease progression. HCV by itself affects dendritic cell function, switching their cytokine profile to the suppressive phenotype of interleukin-10 (IL-10) and transforming growth factor beta (TGFbeta) predominance, preventing cell maturation and allostimulation capacity. The synergistic action of ethanol with HCV results in the suppression of MHC class II-restricted antigen presentation. In addition, ethanol metabolism and HCV proteins reduce proteasome function and interferon signaling, thereby suppressing the generation of peptides for MHC class I-restricted antigen presentation. Collectively, ethanol exposure further impairs antigen presentation in HCV-infected liver cells, which may provide a partial explanation for exacerbations and the poor outcome of HCV infection in alcoholics.

**The effect of obesity on intrahepatic cytokine and chemokine expression in chronic hepatitis C infection.** Palmer C, Corpuz T, Guirguis M, et al. Gut. 2009 Mar 15. [Epub ahead of print]

[http://www.ncbi.nlm.nih.gov/pubmed/19289381?ordinalpos=32&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19289381?ordinalpos=32&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**BACKGROUND:** Obese subjects with chronic hepatitis C virus (HCV) infection have more rapidly progressive liver disease. **OBJECTIVE:** We **AIMed** to compare the intrahepatic cytokine and chemokine profiles in obese and lean subjects with chronic HCV infection using qRT-PCR and immunohistochemistry. **METHODS:** Liver biopsies from 55 subjects were studied, including 20 with chronic hepatitis C (CHC), 25 with non-alcoholic fatty liver disease (NAFLD) and 10 non-diseased liver. **RESULTS:** Compared to the control groups, the liver injury in CHC was characterized by increased expression of interferon (IFN)-gamma and tumour necrosis factor (TNF)-alpha, and chemokines such as RANTES, IP-10 and MCP-1. In comparison with lean -HCV infected subjects, obese-HCV infected subjects had increased hepatic expression of IFN-gamma ( $p=0.004$ ) and TNF-alpha ( $p<0.001$ ) as well as increased expression of IP-10 ( $p=0.009$ ) and MCP-1 ( $p<0.001$ ). Localization of these inflammatory chemokines revealed that in comparison to lean-HCV subjects, HCV infected liver from obese subjects exhibited increased expression of IP-10 ( $p<0.001$ ) and MCP-1 ( $p=0.02$ ) in the inflammatory infiltrate of the portal tracts. In parallel, there was increased CD3+ T cell infiltration in the liver of obese-HCV subjects. **CONCLUSIONS:** The data provide important mechanistic information on the cause of hepatic injury in obese-HCV subjects including: 1) enhanced TH-1 cytokine response-to promote hepatocellular injury; 2) increased expression of the chemokines IP-10 and MCP-1 at both the mRNA and protein levels-to enhance inflammatory cell recruitment; 3) differing localization of these chemokines within the liver of obese-HCV versus lean-HCV subjects and; 4) increased CD3+ cells expression in the liver of obese-HCV subject.

**The pathway of hepatitis C virus mRNA recruitment to the human ribosome.** Fraser CS, Hershey JW, Doudna JA. Nat Struct Mol Biol. 2009 Mar 15. [Epub ahead of print]

[http://www.ncbi.nlm.nih.gov/pubmed/19287397?ordinalpos=35&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19287397?ordinalpos=35&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

Eukaryotic protein synthesis begins with mRNA positioning in the ribosomal decoding channel in a process typically controlled by translation-initiation factors. Some viruses use an internal ribosome entry site (IRES) in their mRNA to harness ribosomes independently of initiation factors. We show

here that a ribosome conformational change that is induced upon hepatitis C viral IRES binding is necessary but not sufficient for correct mRNA positioning. Using directed hydroxyl radical probing to monitor the assembly of IRES-containing translation-initiation complexes, we have defined a crucial step in which mRNA is stabilized upon initiator tRNA binding. Unexpectedly, however, this stabilization occurs independently of the AUG codon, underscoring the importance of initiation factor-mediated interactions that influence the configuration of the decoding channel. These **RESULTS** reveal how an IRES RNA supplants some, but not all, of the functions normally carried out by protein factors during initiation of protein synthesis.

**Infection of B cells with hepatitis C virus for the development of lymphoproliferative disorders in patients with chronic hepatitis C.** Inokuchi M, Ito T, Uchikoshi M, Shimozuma Y, et al. *J Med Virol.* 2009 Apr;81(4):619-27.

[http://www.ncbi.nlm.nih.gov/pubmed/19235854?ordinalpos=78&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19235854?ordinalpos=78&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

Infection with hepatitis C virus (HCV) is associated with lymphoproliferative disorders, represented by essential mixed cryoglobulinemia and B-cell non-Hodgkin's lymphoma, but the pathogenic mechanism remains obscure. HCV may infect B cells or interact with their cell surface receptors, and induce lymphoproliferation. The influence of HCV infection of B cells on the development of lymphoproliferative disorders was evaluated in 75 patients with persistent HCV infection. HCV infection was more prevalent (63% vs. 16%, 14%, or 17%  $P < 0.05$  for each), and HCV RNA levels were higher ( $3.35 \pm 3.85$  vs.  $1.75 \pm 2.52$ ,  $2.15 \pm 2.94$  or  $2.10 \pm 2.90$  log copies/100 ng,  $P < 0.01$  for each) in B cells than CD4(+), CD8(+) T cells or other cells. Negative-strand HCV RNA, as a marker of viral replication, was detected in B cells from four of the 75 (5%) patients. Markers for lymphoproliferative disorders were more frequent in the 50 patients with chronic hepatitis C than the 32 with chronic hepatitis B, including cryoglobulinemia (26% vs. 0%,  $P < 0.001$ ), low CH(50) levels (48% vs. 3%,  $P = 0.012$ ), and the clonality of B cells (12% vs. 0%,  $P < 0.01$ ). By multivariate analysis, HCV RNA in B cells was an independent factor associated with the presence of at least one marker for lymphoproliferation (odds ratio: 1.98 [95% confidence interval: 1.36-7.24],  $P = 0.027$ ). Based on the **RESULTS** obtained, the infection of B cells with HCV would play an important role in the development of lymphoproliferative disorders.

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## HIV/HCV COINFECTION

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**Risk factors for HCV infection. Focus on ethnic and cultural characteristics.**

Pellicano R, De Angelis C, De Luca L, et al. *Minerva Gastroenterol Dietol.* 2009 Jun;55(2):159-62. [http://www.ncbi.nlm.nih.gov/pubmed/19305375?ordinalpos=10&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19305375?ordinalpos=10&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

A precise understanding of the source of infection and modes of transmission of hepatitis C virus (HCV) is a worldwide priority in terms of public health. This is more evident where multi-ethnic customs cohabit. Despite the knowledge on risk factors for HCV transmission, nearly 50% of infected patients do not have a history suggesting a parenteral route of acquisition. In the present paper, the authors, focusing on ethnic and cultural aspects of HCV transmission, emphasize the need for health education in order to avoid the acquisition and the diffusion of the infection. With the current globalization and large-scale migrations, only by following a preventive strategy based on disseminate information risk behaviours may be modified.

**Ten-year incidence and risk factors of bone fractures in a cohort of treated HIV1-infected adults.** Collin F, Duval X, Le Moing V, et al. AIDS. 2009 Mar 18. [Epub ahead of print][http://www.ncbi.nlm.nih.gov/pubmed/19300202?ordinalpos=22&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19300202?ordinalpos=22&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

In the ANRS CO8 APROCO-COPILOTE cohort of patients treated with combination antiretroviral therapy since 1997-1999, the incidence density of bone fractures was 3.3 for 1000 patient-years [95% confidence interval (CI) = 2.0-4.6]. The rate was 2.9-fold (95% CI = 1.3-6.5) higher among patients with excessive alcohol consumption and 3.6-fold (95% CI = 1.6-8.1) higher in those with hepatitis C virus (HCV) coinfection. Specific monitoring of HCV/HIV-coinfected patients and active promotion of alcohol cessation should be recommended for the prevention of bone fractures.

**Saquinavir exposure in HIV-infected patients with chronic viral hepatitis.** Moltó J, Llibre JM, Ribera E, et al. J Antimicrob Chemother. 2009 Mar 11. [Epub ahead of print]  
[http://www.ncbi.nlm.nih.gov/pubmed/19279052?ordinalpos=44&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19279052?ordinalpos=44&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**OBJECTIVES** The **AIM** of this study was to assess the influence of hepatitis B virus or hepatitis C virus co-infection and the extent of liver fibrosis on saquinavir and ritonavir pharmacokinetics in HIV-infected subjects without liver function impairment. **METHODS** A cross-sectional, comparative study enrolling HIV-infected adults receiving saquinavir/ritonavir 1000/100 mg twice daily or 1500/100 mg once daily was conducted. Patients with chronic viral hepatitis (HEP+) were grouped as having advanced liver fibrosis (HEP+/FIB+) or not (HEP+/FIB-) based on the FIB-4 index. Saquinavir and ritonavir trough concentrations (C(trough)) in plasma were determined by HPLC. The geometric mean ratio (GMR) was used to compare saquinavir and ritonavir C(trough) between HEP- and HEP+ patients, and the influence of the extent of liver fibrosis on saquinavir and ritonavir pharmacokinetics was explored using analysis of variance. **RESULTS** One hundred and thirty-eight patients on twice-daily saquinavir/ritonavir (67 HEP-, 71 HEP+) and 36 patients on once-daily saquinavir/ritonavir (12 HEP-, 24 HEP+) were included. Saquinavir C(trough) was comparable between HEP- and HEP+ patients receiving either saquinavir/ritonavir 1000/100 mg twice daily [GMR 0.91, 95% confidence interval (CI) 0.60-1.37; P = 0.655] or 1500/100 mg once daily (GMR 0.88, 95% CI 0.39-1.97; P = 0.752). Similarly, ritonavir C(trough) was also comparable between HEP- and HEP+ patients. The extent of liver fibrosis was not significantly related to saquinavir or ritonavir C(trough) in patients receiving either of the two studied doses.

**CONCLUSIONS** Saquinavir C(trough) was not increased in HIV-infected patients with chronic viral hepatitis in the absence of liver function impairment. These results confirm that no specific dose modification of saquinavir/ritonavir should be recommended in this setting.

**Response-guided therapy for chronic hepatitis C virus infection in patients coinfecting with HIV: a pilot trial.** Van den Eynde E, Crespo M, Esteban JI, et al. Clin Infect Dis. 2009 Apr 15;48(8):1152-9.  
[http://www.ncbi.nlm.nih.gov/pubmed/19275492?ordinalpos=49&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19275492?ordinalpos=49&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**BACKGROUND:** To study the feasibility of a response-guided therapy for chronic hepatitis C virus (HCV) infection in patients coinfecting with human immunodeficiency virus (HIV) in a tertiary care hospital. **METHODS:** Treatment duration was individualized on the basis of week 4 and week 12 virologic response. Sixty patients were enrolled and received pegylated interferon alfa-2b (1.5 microg/kg per week) plus weight-based ribavirin (800-1400 mg/day). Patients who achieved a rapid virologic response, defined as viral load <50 IU/mL at treatment week 4, completed 24 weeks

of therapy. Patients who did not achieve a rapid virologic response were reassessed at treatment week 12. Patients with a complete early virologic response, defined as an HCV RNA level <600 IU/mL, were treated for 48 weeks. Patients with a partial response, defined as a decrease in the viral load  $>$  or  $= 2 \log_{10}$  and an HCV RNA level  $>$  or  $= 600$  IU/mL, who attained an undetectable viral load at week 24 were treated for 60 weeks. The primary efficacy end point was sustained virologic response, defined as HCV RNA <50 IU/mL, 24 weeks after the end of treatment. **RESULTS:** Overall, 33 (55%) of 60 patients achieved a sustained virologic response: 11 (44%) of 25 patients with HCV genotype 1, 3 (27%) of 11 patients with genotype 4, and 19 (79%) of 24 patients with genotype 3. One-third of patients showed a rapid virologic response. Of patients with genotype 1, there was a rapid virologic response in 4 (16%) of 25; with genotype 4, in 1 (9%) of 11; and with genotype 3, in 14 (58%) of 24. Of the 19 patients with a rapid virologic response, 17 (89.5%) eradicated the virus after 24 weeks of therapy. The rate of sustained virologic response was significantly higher among patients with genotype 3 and low pretreatment HCV RNA levels. A high relapse rate (46%) after 48 weeks of therapy occurred among patients infected with genotypes 1 or 4 who first achieved undetectable viral load at treatment week 12. **CONCLUSION:** A response-guided therapy is feasible and may be useful to optimize the individual outcome of HCV treatment in patients coinfecting with HIV.

**Nevirapine pharmacokinetics in HIV-infected and HIV/HCV-coinfecting individuals.** Vogel M, Bertram N, Wasmuth JC, et al. *J Antimicrob Chemother.* 2009 Mar 6. [Epub ahead of print] [http://www.ncbi.nlm.nih.gov/pubmed/19270314?ordinalpos=53&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19270314?ordinalpos=53&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**OBJECTIVE** An increased risk of drug-related liver injury has been repeatedly reported in individuals infected with hepatitis C virus (HCV) receiving the antiretroviral drug nevirapine. This study was undertaken to assess the differences in the pharmacokinetics of nevirapine between patients with HIV/HCV coinfection and HIV infection that could explain higher rates of hepatotoxicity. **METHODS** A 12 h pharmacokinetic analysis was performed in 18 patients: 7 HIV/HCV-coinfecting and 11 HIV-monoinfecting. Advanced liver disease was an exclusion criterion in order to assess the impact of chronic HCV infection alone. **RESULTS** Comparing the two groups, no difference was observed between minimum and maximum drug levels or total drug exposure in terms of area under the curve. **CONCLUSIONS** Hepatitis C coinfection does not alter the pharmacokinetics of nevirapine in patients with preserved liver function.

**Longitudinal Trends in Hazardous Alcohol Consumption Among Women With Human Immunodeficiency Virus Infection, 1995-2006.** Cook RL, Zhu F, Belnap BH, et al. *Am J Epidemiol.* 2009 Mar 6. [Epub ahead of print] [http://www.ncbi.nlm.nih.gov/pubmed/19270052?ordinalpos=54&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19270052?ordinalpos=54&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

Hazardous alcohol consumption among women with human immunodeficiency virus (HIV) infection is associated with several adverse health and behavioral outcomes, but the proportion of HIV-positive women who engage in hazardous drinking over time is unclear. The authors sought to determine rates of hazardous alcohol consumption among these women over time and to identify factors associated with this behavior. Subjects were 2,770 HIV-positive women recruited from 6 US cities who participated in semiannual follow-up visits in the Women's Interagency HIV Study from 1995 to 2006. Hazardous alcohol consumption was defined as exceeding daily ( $\geq 4$  drinks) or weekly ( $> 7$  drinks) consumption recommendations. Over the 11-year follow-up period, 14%-24% of the women reported past-year hazardous drinking, with a slight decrease in hazardous drinking over time. Women were significantly more likely to report hazardous drinking if they were unemployed,

were not high school graduates, had been enrolled in the original cohort (1994-1995), had a CD4 cell count of 200-500 cells/mL, were hepatitis C-seropositive, or had symptoms of depression. Approximately 1 in 5 of the women met criteria for hazardous drinking. Interventions to identify and address hazardous drinking among HIV-positive women are urgently needed.

**Assessment of liver fibrosis by transient elastography in persons with hepatitis C virus infection or HIV-hepatitis C virus coinfection.** Kirk GD, Astemborski J, Mehta SH, et al. Clin Infect Dis. 2009 Apr 1;48(7):963-72.

[http://www.ncbi.nlm.nih.gov/pubmed/19236273?ordinalpos=75&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19236273?ordinalpos=75&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**BACKGROUND:** Transient elastography is a novel, noninvasive method for staging liver fibrosis. We compared elastography with histologic methods among hepatitis C virus (HCV)-infected and human immunodeficiency virus (HIV)-HCV-coinfected participants in an urban, predominantly black study population. **METHODS:** Participants recruited from the AIDS Linked to the Intravenous Experience and the Johns Hopkins HIV Clinical Cohort studies underwent elastography to determine liver stiffness measurements. Liver biopsy specimens were staged F0-F4 in accordance with the Metavir score. Diagnostic accuracy and determination of liver stiffness cutoff values, compared with histologic methods, were determined by receiver operating characteristic analysis. Logistic regression methods identified parameters associated with discordant classification status. **RESULTS:** Of 192 participants, 139 (72%) were coinfecting with HIV and HCV, 121 (63%) had insignificant fibrosis, and 48 (25%) had cirrhosis. Overall, the area-under-the-curve receiver operating characteristic was 0.87 for detection of both significant fibrosis (95% confidence interval, 0.82-0.92) and cirrhosis (95% confidence interval, 0.81-0.93). With use of cutoff values of 9.3 kPa for fibrosis and 12.3 kPa for cirrhosis, 79%-83% of participants were correctly classified by liver stiffness measurement (compared with histologic methods); accuracy appeared to be higher among HIV-uninfected participants than among HIV-infected participants. Most discordance occurred when liver stiffness measurements indicated liver disease and histologic examination did not (in 16% of participants); the patients with these discordant results were more likely to have attributes that increased the odds of significant fibrosis, such as elevated serum fibrosis markers or HIV-related immunosuppression, compared with persons in whom low fibrosis was predicted by both examination of a biopsy specimen and elastography. **CONCLUSIONS:** For most HCV-infected persons, fibrosis stage predicted by elastography is similar to that predicted by examination of a biopsy specimen. Elastography-based measurement of liver stiffness holds promise to expand liver disease screening and monitoring, particularly among injection drug users.

**Hepatitis C, human immunodeficiency virus and metabolic syndrome: interactions.**

Kotler DP. Liver Int. 2009 Mar;29 Suppl 2:38-46.

[http://www.ncbi.nlm.nih.gov/pubmed/19187071?ordinalpos=81&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19187071?ordinalpos=81&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

Significant concerns have been raised about the metabolic effects of antiretroviral medication, including the classic triad of dyslipidaemia, insulin resistance (IR) and characteristic alterations in fat distribution (lipoatrophy and lipohypertrophy). Co-infection with hepatitis C appears to exacerbate IR, reduce serum lipids and induce prothrombotic changes in the treated human immunodeficiency virus patient. The effects of co-infection are complex. While combination antiretroviral therapy has been shown to be associated with an increased risk of cardiovascular events through promotion of dyslipidaemia, IR and fat redistribution, co-infection exacerbates IR while reducing serum lipids. Co-infection also promotes a prothrombotic state characterized by endothelial dysfunction and platelet activation, which may enhance risk for cardiovascular disease. Consideration must be given

to selection of appropriate treatment regimens and timing of therapy in co-infected patients to minimize metabolic derangements and, ultimately, reduce cardiovascular risk.

**Nonalcoholic Fatty Liver Disease Among HIV-Infected Persons.** Crum-Cianflone N, Dilay A, Collins G, et al. *J Acquir Immune Defic Syndr.* 2009 Apr;50(5):464-473. [http://www.ncbi.nlm.nih.gov/pubmed/19225402?ordinalpos=86&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19225402?ordinalpos=86&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**OBJECTIVE::** To describe the prevalence and factors associated with nonalcoholic fatty liver disease (NAFLD) among HIV-infected persons not infected with hepatitis C virus (HCV).  
**DESIGN::** A cross-sectional study among HIV-infected patients in a large HIV clinic.  
**METHODS::** NAFLD was defined as steatosis among patients without viral hepatitis (B or C) coinfection or excessive alcohol use. The prevalence of NAFLD was identified by ultrasound examination evaluated by 2 radiologists blinded to the clinic information; liver biopsies were performed on a subset of the study population. Factors associated with NAFLD were evaluated by proportional odds logistic regression models. **RESULTS::** Sixty-seven of 216 patients (31%) had NAFLD based on ultrasound evaluation. Among those with NAFLD, steatosis was graded as mild in 60%, moderate in 28%, and severe/marked in 12%. Factors associated with the degree of steatosis on ultrasound examination in the multivariate model included increased waist circumference [odds ratio (OR) 2.1 per 10 cm,  $P < 0.001$ ], elevated triglyceride levels (OR 1.2 per 100 mg/dL,  $P = 0.03$ ), and lower high-density lipoprotein levels (OR 0.7, per 10 mg/dL,  $P = 0.03$ ). African Americans were less likely to have NAFLD compared with whites (14% vs. 35%), although this did not reach statistical significance (OR 0.4,  $P = 0.08$ ). Similar associations were noted for the subset of patients diagnosed by liver biopsy. CD4 cell count, HIV viral load, duration of HIV infection, and antiretroviral medications were not independent risk factors associated with NAFLD after adjustment for dyslipidemia or waist circumference. **CONCLUSIONS::** NAFLD was common among this cohort of HIV-infected HCV-seronegative patients. NAFLD was associated with a greater waist circumference, low high-density lipoprotein, and high triglyceride levels. Antiretroviral medications were not associated with NAFLD; prospective studies are needed to confirm this finding.

**Characteristics and treatment outcomes among HIV-infected individuals in the Australian Trial in Acute Hepatitis C.** Matthews GV, Hellard M, Haber P, et al. *Clin Infect Dis.* 2009 Mar 1;48(5):650-8. [http://www.ncbi.nlm.nih.gov/pubmed/19191653?ordinalpos=90&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19191653?ordinalpos=90&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**BACKGROUND:** The Australian Trial in Acute Hepatitis C (ATAHC) is a National Institutes of Health-funded prospective cohort study of the natural history and efficacy of treatment in individuals with recently acquired hepatitis C. Enrollment is open to both human immunodeficiency virus (HIV)-infected and -uninfected individuals. The **AIM** of this article was to evaluate characteristics and virological outcomes among HIV-infected individuals enrolled in ATAHC.  
**METHODS:** Eligibility criteria included the first positive result of testing for anti-hepatitis C virus (HCV) antibody within 6 months and either clinical hepatitis diagnosed within the past 12 months or documented anti-HCV seroconversion within the past 24 months. **RESULTS:** Of the initial 103 patients enrolled, 27 (26%) were HIV infected. HIV-infected patients were more likely to be older, to have HCV genotype 1 infection and high levels of HCV RNA at baseline than were HCV-monoinfected patients. Sexual acquisition accounted for the majority (56%) of HCV infections among HIV-infected patients, compared with only 8% of HCV-monoinfected patients. The median duration from estimated HCV infection to treatment was 30 weeks. Treatment with 24 weeks of

pegylated interferon and ribavirin resulted in rates of undetectability of HCV RNA of 95%, 90%, and 80% at weeks 12, 24, and 48, respectively. Undetectability at week 4 was achieved in 44% of patients and yielded positive and negative predictive values for sustained virological response of 100% and 33%, respectively. **CONCLUSIONS:** Significant differences were demonstrated between HIV-infected and HIV-uninfected individuals enrolled in ATAHC. Treatment responses among HIV-infected individuals with both acute and early chronic infection are encouraging and support regular HCV screening of high-risk individuals and early treatment for recently acquired HCV infection.

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## COMPLEMENTARY & ALTERNATIVE THERAPY

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**Isoflavone consumption and subsequent risk of hepatocellular carcinoma in a population-based prospective cohort of Japanese men and women.** Kurahashi N, Inoue M, Iwasaki M, et al. *Int J Cancer*. 2009 Apr 1;124(7):1644-9.

[http://www.ncbi.nlm.nih.gov/pubmed/19089922?ordinalpos=101&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19089922?ordinalpos=101&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

The incidence of hepatocellular carcinoma (HCC) is much higher in men than in women. Several experiment and epidemiological studies have suggested that estrogen might play an inhibitory role in the development of HCC. Because isoflavones have a similar structure as 17beta-estradiol and appear to have an anti-estrogenic effect in women and estrogenic effect in men, we hypothesized that the effect of isoflavones on HCC differs by sex. We investigated the association between isoflavones (genistein and daidzein) and soy products and HCC in Japan in a population-based prospective study in 19,998 Japanese (7,215 men and 12,783 women) aged 40-69 years. During 11.8 years of follow-up, 101 subjects (69 men and 32 women) were newly diagnosed with HCC. Case patients were grouped according to consumption of isoflavones and soy products and stratified by hepatitis virus infection. Hazard ratios (HRs) and 95% confidence intervals (CIs) for HCC were calculated by Cox proportional-hazards modeling. In women, genistein and daidzein were dose-dependently associated with an increased risk of HCC, with multivariable HRs for the highest versus lowest tertile of 3.19 (95%CI = 1.13-9.00, p(trend) = 0.03) and 3.90 (95% CI = 1.30-11.69, p(trend) = 0.01), respectively. No association between isoflavones and HCC was observed in men. These results persisted when analysis was restricted to subjects positive for either or both hepatitis C and B virus. In **CONCLUSION**, isoflavone consumption may be associated with an increased risk of HCC in women. Women with hepatitis virus infection may be advised to abstain from isoflavone consumption. Further studies are warranted to confirm these findings.

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## EPIDEMIOLOGY, DIAGNOSTICS, AND MISCELLANEOUS WORKS

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**Perinatal transmission of hepatitis C virus infection.** Indolfi G, Resti M. *J Med Virol*. 2009 Mar 24;81(5):836-843. [Epub ahead of print]

[http://www.ncbi.nlm.nih.gov/pubmed/19319981?ordinalpos=1&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19319981?ordinalpos=1&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

In industrialized countries, hepatitis C virus (HCV) is the most common cause of chronic liver disease in children. Perinatal transmission is the leading cause of infection. Perinatal transmission is confined almost always to women with detectable HCV ribonucleic acid (RNA) in the peripheral blood by the polymerase chain reaction but all children born to women with anti-HCV antibodies should be tested for HCV. Some but not all studies found that a high concentration of serum HCV RNA is associated with a higher risk of transmission. Maternal peripheral blood mononuclear cell

infection by HCV, membrane rupture of longer than 6 hr before delivery, and procedures exposing the infant to maternal blood infected with HCV during vaginal delivery are associated with an increased risk of transmission. Maternal coinfection with HCV and human immunodeficiency virus, maternal history of intravenous drug use and of HCV infection of the sexual partner of the mother predict the risk of perinatal transmission and are dependent on the peripheral blood mononuclear cell infection by HCV. Delivery by Cesarean section is not recommended in pregnant women infected with HCV. Infected mothers can breast feed safely their infants if the nipples are not damaged. A previous delivery of a child infected perinatally with HCV does not increase the risk of transmission in subsequent pregnancies. Immunogenetic factors and HCV genotypes are not related to HCV perinatal transmission. Despite an increased understanding of the risk factors involved in perinatal transmission of HCV, to date little is known about the transmission mechanisms and timing.

**Lack of association between genotypes and subtypes of HCV and occurrence of hepatocellular carcinoma in Egypt.** Ryu SH, Fan X, Xu Y, Elbaz T, et al. J Med Virol. 2009 Mar 24;81(5):844-847. [Epub ahead of print]

[http://www.ncbi.nlm.nih.gov/pubmed/19319951?ordinalpos=2&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19319951?ordinalpos=2&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

The distribution of hepatitis C virus (HCV) genotypes was evaluated in individuals with hepatocellular carcinoma (HCC) and cirrhosis in Egypt. A total of 206 patients sero-positive for HCV-RNA among 400 surveyed individuals (186 with HCC, 100 with cirrhosis, and 114 healthy volunteers) were analyzed for HCV genotype. Of 206 patients, 129 had HCC, 65 had cirrhosis without HCC, and 12 were healthy volunteers. Phylogenetic analysis of sequence showed that of 206 samples, 186 contained HCV genotype 4 (90.3%), while 20 had HCV genotype 1 (9.7%). Among subjects with genotype 4, subtype 4a was predominant (79%), other subtypes included 4d, 4m, 4n, and 4o. Among those with HCV genotype 1, 15 had subtype 1g and five subtype 1a. Although subtype 4a was noted slightly more frequently in HCC (76%) compared to cirrhosis (66%) and controls (50%), there was no statistically significant difference between these three groups ( $P = 0.08$ ). In **CONCLUSION**, HCV genotype 4 predominates in Egypt. There was no association between subtypes of genotype 4 and the development of HCC.

**Evaluation of immigration status, race and language barriers on chronic hepatitis C virus infection management and treatment outcomes.** Giordano C, Druyts EF, Garber G, Cooper C. Eur J Gastroenterol Hepatol. 2009 Mar 21. [Epub ahead of print]

[http://www.ncbi.nlm.nih.gov/pubmed/19318966?ordinalpos=5&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19318966?ordinalpos=5&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**OBJECTIVE:** Hepatitis C virus (HCV) prevalence in certain Canadian immigrant populations is higher than that of the overall population. Disparities in care related to immigration status as well as to race and language are well recognized. Identifying and understanding these disparities is vital to the provision of optimal and inclusive HCV care. **METHODS AND MATERIALS:** HCV RNA-positive patients assessed at The Ottawa Hospital Viral Hepatitis Clinic between June 2000 and June 2007 were identified using a clinical database. As measures of access to care, liver biopsy rates, treatment initiation rates, supportive care provision (i.e. erythropoietin for treatment-related anemia) and sustained virological response (SVR) rates were assessed as a function of immigration status, race and spoken language. **RESULTS:** Nine hundred and ten patients were evaluated, of which 20% were immigrants. Biopsy rates (54 vs. 51%), HCV treatment initiation (37 vs. 38%), erythropoietin prescription (13 vs. 18%) and SVR rates (52 vs. 51%) did not differ between immigrants and Canadian-born individuals. Spoken language and race did not influence access to treatment. SVR was predicted by genotype, HIV status and race. **CONCLUSION:** In the context

of a multidisciplinary, multilingual universal health care system, by studying the influence of barriers to HCV investigation and successful therapy can be abrogated.

**Recurrence of hepatitis C virus genotype-4 infection following orthotopic liver transplantation: natural history and predictors of outcome.** Mudawi H, Helmy A, Kamel Y, et al. *Ann Saudi Med.* 2009 Mar-Apr;29(2):91-7.

[http://www.ncbi.nlm.nih.gov/pubmed/19318754?ordinalpos=6&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19318754?ordinalpos=6&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**BACKGROUND AND OBJECTIVES:** There are few reports on hepatitis C virus genotype 4 (HCV-4) recurrences after orthotopic liver transplantation (OLT). Therefore, we undertook a study to determine the epidemiological, clinical and virological characteristics of patients with biopsy-proven recurrent HCV infection and analyzed the factors that influence recurrent disease severity. We also compared disease recurrence and outcomes between HCV-4 and other genotypes.

**PATIENTS AND METHODS:** All patients who underwent OLT (locally or abroad) for HCV related hepatic cirrhosis from 1991 to 2006 and had recurrent HCV infection were identified. Clinical, laboratory and pathological data before and after OLT were collected and analyzed.

**RESULTS:** Of 116 patients who underwent OLT for hepatitis C, 46 (39.7%) patients satisfied the criteria of recurrent hepatitis C. Twenty-nine (63%) patients were infected with HCV genotype 4. Mean (SD) for age was 54.9 (10.9) years. Nineteen of the HCV genotype 4 patients (65.5%) were males, 21 (72.4%) received deceased donor grafts, and 7 (24.1%) developed  $\geq 1$  acute rejection episodes. Pathologically, 7 (24.1%) and 4 (13.8%) patients had inflammation grade 3-4 and fibrosis stage 3-4, respectively. Follow-up biopsy in 9 (31%) HCV genotype 4 patients showed stable, worse and improved fibrosis stage in 5, 2 and 2 patients, respectively. Of the 7 patients in the recurrent HCV group who died, 6 were infected with genotype 4 and 4 of them died of HCV-related disease.

**CONCLUSION:** This analysis suggests that HCV recurrence following OLT in HCV-4 patients is not significantly different from its recurrence for other genotypes.

**FibroScan and ultrasonography in the prediction of hepatic fibrosis in patients with chronic viral hepatitis.** Wang JH, Changchien CS, Hung CH, et al. *J Gastroenterol.* 2009 Mar 25. [Epub ahead of print]

[http://www.ncbi.nlm.nih.gov/pubmed/19308312?ordinalpos=7&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19308312?ordinalpos=7&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**BACKGROUND:** The **AIM** of this study was to assess the diagnostic performances of liver stiffness measurement (LSM), ultrasonography (US) and their combined use in predicting the extent of hepatic fibrosis. **METHODS:** Consecutive patients with chronic hepatitis B (HBV) or hepatitis C virus (HCV) infections, with indications for liver biopsy, were prospectively enrolled. LSM was performed on the same day as biopsy. US scores, including assessment of liver surface, liver parenchyma, intrahepatic vessels and spleen index, were used to assess the degree of hepatic fibrosis. The pathological findings were used as a reference standard and diagnostic accuracy was assessed and compared. **RESULTS:** Three-hundred and twenty patients, including 199 men and 121 women, with a mean age of 50.8 years, were analyzed. There were 214 (66.9%) HCV patients, 88 (27.5%) HBV patients and 18 (5.6%) patients with both HCV and HBV. LSM correlated significantly with the hepatic fibrosis (F) scores, necro-inflammatory activity and US scores in multivariate analysis. The diagnostic accuracy of LSM is significantly superior to US, and equal to combined LSM with US, in the prediction of all HCV-related fibrosis scores. The cut-off value of LSM is 6 kPa for diagnosing  $F \geq 1$ , with a positive predictive value of 91%. Also, the cut-off value is 12 kPa for the prediction of cirrhosis, with a negative predictive value of 94%. **CONCLUSIONS:**

LSM is useful for predicting hepatic fibrosis and excluding cirrhosis. A combination of LSM and US does not improve the accuracy in assessing hepatic fibrosis.

### **Improvement in Dissolution of Liver Fibrosis in an Animal Model by Tetrathiomolybdate.**

Hou G, Dick R, Brewer GJ. *Exp Biol Med* (Maywood). 2009 Mar 23. [Epub ahead of print] [http://www.ncbi.nlm.nih.gov/pubmed/19307461?ordinalpos=8&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19307461?ordinalpos=8&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

The **BACKGROUND** for this study is that we have observed some improvement in cirrhosis in Wilson's disease patients treated with the anticopper medicine, zinc, and another anticopper drug, tetrathiomolybdate, has completely prevented hepatic fibrosis in the carbon tetrachloride mouse model. We hypothesize that in existing cirrhosis, there may be a fine balance between fibrosis formation and fibrosis dissolution, which may be pushed in the direct of dissolution by anticopper drugs. Thus, in this study, we produced hepatic fibrosis in mice by treatment with carbon tetrachloride, than gave half the fibrotic mice tetrathiomolybdate for 3 months, while the other half of the fibrotic mice received nothing for 3 months and served as controls. Tetrathiomolybdate caused a dramatic and significant reduction in fibrosis as measured by hydroxyproline (the major amino acid constituent level of collagen) levels, almost back to baseline levels, compared to controls, who had only a slight and nonsignificant reduction. It is clear from this animal study that dissolution of preexisting fibrosis can be strongly catalyzed by lowering copper levels with tetrathiomolybdate. It now becomes important to evaluate whether this approach will work in the human epidemic of cirrhotic disease resulting from diseases such as alcoholism, nonalcoholic steatohepatitis, and hepatitis C.

### **Liver cancer mortality among male prison inmates in Texas, 1992-2003.**

Harzke AJ, Baillargeon JG, Goodman KJ, Pruitt SL. *Prev Med*. 2009 Mar 13. [Epub ahead of print] [http://www.ncbi.nlm.nih.gov/pubmed/19289141?ordinalpos=34&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19289141?ordinalpos=34&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**OBJECTIVES:** Prevalence estimates for several liver cancer risk factors-hepatitis C, hepatitis B, and history of alcohol abuse-are substantially higher in U.S. prison populations than in the general population. However, liver cancer mortality data from these populations are lacking. The primary **AIMS** of this study were to examine trends in liver cancer mortality rates from 1992-2003 among male prisoners in the Texas Department of Criminal Justice (TDCJ) and to compare these rates to general population rates. **METHODS:** TDCJ data on male decedents (N=4,026) were linked with Texas Vital Statistics multiple-cause-of-death data. Crude average annual liver cancer death rates, average annual percent changes, and standardized mortality ratios were estimated. **RESULTS:** Crude liver cancer death rates increased by an average annual 6.1% among male prisoners, which was considerably higher than the average annual percent change among similarly aged males in Texas (2.0%) and the U.S. (2.9%). The number of liver cancer deaths among male prisoners was 4.7 (4.0-5.6) and 6.3 (5.3-7.5) times higher than the expected number of deaths estimated using age-specific rates from these reference populations. **CONCLUSIONS:** From 1992-2003, liver cancer death rates and rate increases were elevated among Texas male prisoners. Findings support previous recommendations for targeted prevention, screening, and treatment of liver cancer risk factors in prison populations.

### **Treatment strategies for a patient with rheumatoid arthritis and hepatitis C.**

Giannitti C, Bellisai F, Ferri C, Galeazzi M. *Expert Opin Pharmacother*. 2009 Mar;10(4):579-87. [http://www.ncbi.nlm.nih.gov/pubmed/19286138?ordinalpos=36&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19286138?ordinalpos=36&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**BACKGROUND:** The poor prognosis of rheumatoid arthritis (RA) can be aggravated by the concomitant presence of chronic hepatitis C virus (HCV) infection and there are no guidelines for the treatment of patients affected by both conditions. **OBJECTIVE:** To propose new therapeutic strategies for patient affected by RA and concomitant HCV chronic infection. **METHODS:** Review of the literature on the usage of cyclosporine-A (CsA) and anti-tumour-necrosis-factor (TNF)-alpha agents for the treatment of patients affected by RA and HCV. **RESULTS/CONCLUSION:** CsA exerts an inhibitory effect on HCV replication and it is safe in patients affected by RA and HCV. Anti-TNF-alpha agents are safe and efficacious in patient with RA and HCV. Anti-TNF-alpha and CsA can be safely given in combination in RA patients with HCV infection.

**Estimating hepatitis C infection acquired in England, 1986-2000.** Balogun MA, Vyse AJ, Hesketh LM, et al. *Epidemiol Infect.* 2009 Mar 10;1-6. [Epub ahead of print]  
[http://www.ncbi.nlm.nih.gov/pubmed/19272197?ordinalpos=51&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19272197?ordinalpos=51&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**SUMMARY** Hepatitis C is a global health problem and in the UK seroprevalence studies have mainly concentrated on specific high-risk groups. The **AIM** of this study was to determine changes in the prevalence of antibody to hepatitis C virus in England using residual specimens collected between 1986 and 2000 reflecting the general population. A cross-sectional study design using a convenience collection of serum specimens from adult patients submitted to laboratories in the years 1986, 1991, 1996 and 2000 from a total of 19 laboratories around England were investigated. The main outcome was to determine anti-HCV prevalence and the average incidence occurring between 1986 and 2000 and factors associated with infection. Multivariable analysis of **RESULTS** from all years showed there was a significant difference in prevalence between males and females ( $P < 0.001$ ), birth cohort ( $P < 0.001$ ) and by health region ( $P < 0.001$ ). An average of 0.72% (95% CI 0-1.65%) of those susceptible to HCV born between 1950 and 1970 were estimated to have acquired the infection between 1986 and 2000. Analysis of this convenience serum collection suggests that HCV prevalence is low in the general population, and is associated with period of birth, gender and health region. There was evidence to support a low incidence of HCV infection in those born between 1950 and 1970 over the period 1986-2000 which, at the population level, equated to a substantial burden of infection (106 000 persons). Continued surveillance and prevention targeted at injecting drug users are essential for the control of hepatitis C in the UK.

**Antibody to hepatitis B core antigen as a screening test for occult hepatitis B virus infection in Egyptian chronic hepatitis C patients.** El-Sherif A, Abou-Shady M, Abou-Zeid H, et al. *J Gastroenterol.* 2009 Mar 7. [Epub ahead of print]  
[http://www.ncbi.nlm.nih.gov/pubmed/19271112?ordinalpos=52&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19271112?ordinalpos=52&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**PURPOSE:** The presence of hepatitis B virus (HBV) DNA in liver tissue and/or in serum in the absence of detectable hepatitis B surface antigen (HBsAg) is called occult HBV infection. This pattern was identified in patients with chronic hepatitis C virus (HCV) infection. The **AIM** of this study was to determine the role of antibodies to hepatitis B core antigen (anti-HBc) as a screening test for occult HBV infection in Egyptian chronic HCV patients. **METHODS:** One hundred chronic HCV patients negative for HBsAg were included and subdivided into two groups according to anti-HBc-IgG seroreactivity. Group A included 71 patients positive for anti-HBc (53 men and 18 women, mean age +/- SD 48.8 +/- 9.6 years), and group B included 29 patients negative for anti-HBc (18 men and 11 women, mean age +/- SD 46.6 +/- 11.7 years). All patients were subjected to full clinical assessment, routine laboratory investigations, abdominal ultrasonography and

quantification of HBV-DNA by real-time PCR. **RESULTS:** Chronic HCV patients positive for anti-HBc have more severe liver disease compared with anti-HBc negative patients. Although HBV-DNA in the serum was detected in 22.5% of anti-HBc-positive chronic HCV patients, it was not detected in any of anti-HBc-negative chronic HCV patients. There was no significant difference in any of the clinical and laboratory data tested between anti-HBc-positive patients with and without HBV-DNA in the serum. **CONCLUSION:** A significant number of patients with anti-HBc had detectable levels of HBV-DNA in the serum. Egyptian chronic HCV patients have a high prevalence of occult HBV infection.

**Does cirrhosis affect quality of life in hepatitis C virus-infected patients?** Hsu PC, Krajden M, Yoshida EM, et al. *Liver Int.* 2009 Mar;29(3):449-58.

[http://www.ncbi.nlm.nih.gov/pubmed/19267865?ordinalpos=57&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19267865?ordinalpos=57&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**BACKGROUND:** Hepatitis C virus (HCV) infection is a major cause of chronic liver disease and is associated with impairments in health-related quality of life. **AIMS:** To evaluate quality of life (QOL) in cirrhotic (compensated and decompensated) and non-cirrhotic patients with chronic HCV infection, using preference-based (utilities) and non-preference-based **METHODS** of evaluating QOL. **METHODS:** In a tertiary care setting, 271 patients completed a self-administered time trade-off utility instrument, the Health Utility Index Mark 2 and Mark 3, and the Hepatitis Quality of Life Questionnaire Version 2. Mean QOL scores were compared across HCV disease stages and sociodemographical categories. We examined the association between QOL and disease stage using linear regression adjusting for age, education, marital status, log income and Charlson comorbidity scores. Mean utility scores were compared across disease stages using a propensity score method. **RESULTS:** Mean utilities were lower than general population norms (0.81-0.92) and ranged from 0.62 to 0.82 in non-cirrhotic patients (n=197), 0.56-0.84 in compensated cirrhotic patients (n=17) and 0.55-0.76 for decompensated cirrhotic patients (n=57). No significant association found was between disease stage and utility for current health status. Higher income, fewer comorbidities and living in a married or common-law relationship were significantly associated with higher utilities and better QOL. No significant difference in utilities was found between disease stages using propensity score matching. **CONCLUSIONS:** Our study confirms that changes in HCV disease stage explain only small changes in QOL and suggests that factors such as underlying comorbidities, income and marital status have a greater effect on QOL than disease stage.

**Hepatitis C virus transmission at an outpatient hemodialysis unit--New York, 2001-2008.** Centers for Disease Control and Prevention (CDC). *MMWR Morb Mortal Wkly Rep.* 2009 Mar 6;58(8):189-94.

[http://www.ncbi.nlm.nih.gov/pubmed/19265779?ordinalpos=58&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19265779?ordinalpos=58&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

In July 2008, the New York State Department of Health (NYSDOH) received reports of three hemodialysis patients seroconverting from anti-hepatitis C virus (HCV) negative to anti-HCV positive in a New York City hemodialysis unit during the preceding 6 months. NYSDOH conducted patient interviews and made multiple visits to the hemodialysis unit to observe hemodialysis treatments, assess infection control practices, evaluate HCV surveillance activities, review medical records, and conduct interviews with staff members. This report summarizes the **RESULTS** of that investigation, which found that six additional patients had HCV seroconversion during 2001--2008 and that the hemodialysis unit had numerous deficiencies in infection control policies, procedures, and training. Of the total of nine seroconversions, the sources for four HCV infections were identified phylogenetically and epidemiologically as four other patients in the unit. The unit's

policy for routine patient testing for HCV infection was not in accordance with CDC recommendations, and the few recommendations followed were not implemented consistently. Hemodialysis units should routinely assess compliance to ensure complete and timely adherence with CDC recommendations to reduce the risk for HCV transmission in this setting.

**Patterns of viraemia in haemodialysis patients with hepatitis C.** Dzekova-Vidimliski P, Asani A, Selim G, et al. Prilozi. 2009 Dec;29(2):201-12.

[http://www.ncbi.nlm.nih.gov/pubmed/19259047?ordinalpos=66&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19259047?ordinalpos=66&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

Clinical features, aminotransferases levels, and antibody to HCV have only limited correlation with the activity of liver disease and cannot accurately predict persistence versus eradication of the virus in haemodialysis patients. Although permanent loss of serum HCV RNA appears to correlate with resolution of the disease, little is known about the predictive value of a single HCV RNA value. The **AIM** of the study was to evaluate the viraemia in the serum of HCV antibody positive haemodialysis patients during a period of 3 years. The study group consisted of 65 HCV antibody positive patients from our dialysis unit. HCV antibodies were measured every 6 months by ELISA third-generation assay. The presence of serum HCV RNA was assessed by reverse-transcriptase polymerase chain reaction (RT-PCR) once a year during the period of 3 years. Serum levels of aminotransferases were measured monthly with standard automated analyzers. There were three different patterns of viraemia after the third assessment of the serum HCV RNA in HCV antibody positive patients: 47% (30/65) were persistently HCV RNA positive, 38% (25/65) were intermittently HCV RNA positive, and 15% (10/65) were persistently HCV RNA negative. The dominant genotype was 1a, detected in 97% of the patients positive for HCV RNA. The HCV RNA persistently positive patients had significantly higher levels of ALT compared to HCV RNA persistently negative patients (50.07 +/- 30.0 vs. 28.5 +/- 10.0 U/L,  $p < 0.027$ ). There was no significant difference between the three groups of patients according to age, haemodialysis duration, and serum levels of AST. This pattern of intermittent viraemia clearly showed that a single negative result of the presence of serum HCV RNA in an HCV antibody positive patient should not be taken as a proof of a persistent resolution of HCV. Thus, repeated testing for HCV RNA is necessary to assess viraemia accurately in HCV antibody positive patients. HCV antibody positive patients who were persistently serum HCV RNA negative could be potentially infectious because of the possibility of the persistence of occult hepatitis C.

**Severity of liver disease predicts the development of glucose abnormalities in patients with chronic hepatitis B or C following achievement of sustained virological response to antiviral therapy.** Chehadeh W, Al-Nakib W. J Med Virol. 2009 Apr;81(4):610-8.

[http://www.ncbi.nlm.nih.gov/pubmed/19235842?ordinalpos=79&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19235842?ordinalpos=79&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

A higher prevalence of glucose abnormalities has been reported in patients with hepatitis C virus (HCV) infection compared to patients with hepatitis B virus (HBV) infection. However, previous studies considered some confounding factors and ignored others, which might influence the comparative risk assessment between HBV and HCV infections. Fasting plasma glucose concentration, severity of liver disease and viral load were determined in 220 patients with HCV genotype 4 infection, and 200 patients with HBV infection. Patients completing antiviral therapy were followed-up, and the fasting plasma glucose levels were determined in patients with and without sustained virological response. The prevalence of glucose abnormalities in HCV infection (41%) was significantly higher than that in HBV infection (16%). However, when controlling the severity of liver disease and other risk factors, the prevalence of glucose abnormalities in patients

with HCV infection was comparable to that in patients with HBV infection. After attaining of sustained virological response, a decrease of the median fasting plasma glucose value was observed only in chronic hepatitis C. In the group of patients with normal fasting plasma glucose levels, an association of nonsustained virological response with the development of impaired fasting glucose was only observed in chronic hepatitis C. The severity of liver disease was a common predictor of impaired fasting glucose in hepatitis B and C infections. These results indicate that high prevalence of glucose abnormalities can be associated with HBV- and HCV-related liver disease, and that clearance of HCV, but not HBV, may improve glucose metabolism.

**Hepatitis C virus, steatosis and lipid abnormalities: clinical and pathogenic data.** Negro F, Sanyal AJ. *Liver Int.* 2009 Mar;29 Suppl 2:26-37.

[http://www.ncbi.nlm.nih.gov/pubmed/19187070?ordinalpos=82&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19187070?ordinalpos=82&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

Abnormal accumulation of fat in the liver (steatosis) is commonly observed in hepatitis C virus (HCV) infection, and the severity of steatosis has been well correlated with the degree of hepatic fibrosis. In patients with chronic HCV infection, steatosis may occur in conjunction with other metabolic risk factors such as insulin resistance and the metabolic syndrome. This was observed primarily in patients infected with non-genotype 3 virus. Otherwise, in HCV-infected patients, especially those infected with genotype 3a, reductions in total cholesterol as well as high-density lipoprotein and low-density lipoprotein cholesterol are observed compared with matched controls, and the normalization of these parameters appears to be an important correlate of the response to antiviral therapy. In that setting, the pathogenic mechanisms involved in HCV-induced steatosis are mediated in large part by the HCV core protein, whose expression is associated with lipid droplet accumulation, changes in lipogenic gene expression and/or the activity of lipogenic proteins, and effects on mitochondrial oxidative function. The importance of genes such as peroxisome proliferator-activated receptor- $\alpha$  and the proteasome activator PA28- $\gamma$  in HCV-mediated steatosis has been elucidated from studies in genetically altered mice, and the manipulation of these and other pathways may provide an avenue for therapeutic intervention.

**Hepatitis C, insulin resistance and diabetes: clinical and pathogenic data.** Serfaty L, Capeau J. *Liver Int.* 2009 Mar;29 Suppl 2:13-25.

[http://www.ncbi.nlm.nih.gov/pubmed/19187069?ordinalpos=83&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19187069?ordinalpos=83&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

Epidemiological data indicate a strong risk for development of insulin resistance (IR), and, ultimately, overt diabetes mellitus (DM) in patients with chronic hepatitis C virus (HCV) infection. Steatosis, or fatty liver, is closely linked with IR in persons without HCV, such as those with metabolic syndrome, primarily due to increased visceral fat leading to altered adipokine production and increased free fatty acid (FFA) release. Moreover, there is evidence that liver fat can have an impact on the development of hepatic IR independently of changes in adipose tissue. Multiple mechanisms can account for the development of IR in patients with chronic HCV. In particular, there is evidence for a triangular interaction between steatosis, inflammatory processes and IR. In patients infected by the genotype 1 virus, steatosis is strongly related to IR, leading to a metabolic steatosis, while, in genotype 3 patients, steatosis is related to viral load in the context of a viral steatosis. Chronic inflammatory processes in the liver may be mediated by persistently activated macrophages and other immune cells, with concomitant overproduction of pro-inflammatory cytokines such as tumour necrosis factor- $\alpha$ . Activation of inflammatory pathways, together with increased levels of FFAs, can disrupt hepatocyte intracellular pathways and inhibit insulin signalling, leading to IR. Molecular studies have also shown that the HCV core protein can directly inhibit the

insulin signalling pathway and increase reactive oxygen species production, both of which can further exacerbate IR. The available data provide an understanding of chronic HCV whereby chronic inflammatory processes, steatosis and IR contribute to each other, leading to an increased risk of DM, and its associated poor outcomes, in persons with chronic HCV.

### **Metabolic syndrome, non-alcoholic fatty liver disease and hepatitis C virus:**

**impact on disease progression and treatment response.** Younossi ZM, McCullough AJ. Liver Int. 2009 Mar;29 Suppl 2:3-12.

[http://www.ncbi.nlm.nih.gov/pubmed/19187068?ordinalpos=84&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19187068?ordinalpos=84&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

Non-alcoholic fatty liver disease (NAFLD), a spectrum of liver disease ranging from simple steatosis to non-alcoholic steatohepatitis, is increasingly recognized as the hepatic manifestation of metabolic syndrome and is an important cause of liver-related morbidity and mortality. It is among the most common forms of liver disease. NAFLD reflects abnormal partitioning of fat, such that fat deposition is increased in the liver, and provides a link between NAFLD and the metabolic syndrome, a constellation of metabolic disorders that can also be associated with visceral fat or central adiposity. Together, the features of the metabolic syndrome presage overt diabetes and increase cardiovascular risk. Hepatitis C virus (HCV) appears to exacerbate the metabolic syndrome by eliciting increased insulin resistance (IR) and promoting truncal obesity. Moreover, the concomitant presence of HCV and NAFLD is associated with an increased likelihood of diabetes, hypertension and/or hypertriglyceridaemia. Metabolic abnormalities have been shown to influence response to treatment such that the presence of IR or obesity reduces the likelihood of a sustained virological response (SVR); conversely, SVR has been demonstrated to ameliorate IR and improve beta-cell function. Clinically, these data suggest that attention must be paid not only to optimizing antiviral response but also to screening for and treatment of the various components of the metabolic syndrome.

### **Lay management of chronic disease: a qualitative study of living with hepatitis C**

**infection.** Stoller EP, Webster NJ, Blixen CE, et al. Am J Health Behav. 2009 Jul-Aug;33(4):376-90.

[http://www.ncbi.nlm.nih.gov/pubmed/19182983?ordinalpos=91&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19182983?ordinalpos=91&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**OBJECTIVES:** To examine management strategies and goals reported by people diagnosed with chronic hepatitis C. **METHODS:** We analyzed data from semistructured interviews (N = 42) and from electronic sources [illness narratives (N = 79) and Internet threaded discussions (N = 264)]. Line-by-line coding, comparisons, and team discussions generated catalogs of lay management strategies and goals. We analyzed code-based files to identify informants' selection of specific strategies for each goal. **RESULTS:** We classified lay management strategies into 3 categories: medical self-care, behavior change, and coping. These strategies were used selectively in addressing multiple goals, categorized as fighting the virus, strengthening the body, and managing consequences. **CONCLUSIONS:** results underscore the diversity of strategies for living with a disease characterized by uncertain prognosis and variable expression of symptoms.

### **A new HCV genotype 6 subtype designated 6v was confirmed with three complete genome sequences.**

Wang Y, Xia X, Li C, et al.. J Clin Virol. 2009 Mar;44(3):195-9.

[http://www.ncbi.nlm.nih.gov/pubmed/19179105?ordinalpos=92&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19179105?ordinalpos=92&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

**BACKGROUND:** Although hepatitis C virus (HCV) genotype 6 is classified into 21 subtypes, 6a-6u, new variants continue to be identified. **OBJECTIVE:** To characterize the full-length genomes

of three novel HCV genotype 6 variants: KMN02, KM046 and KM181. **STUDY DESIGN:** From sera of patients with HCV infection, the entire HCV genome was amplified by RT-PCR followed by direct DNA sequencing and phylogenetic analysis. **RESULTS:** The sera contained HCV genomes of 9461, 9429, and 9461nt in length, and each harboured a single ORF of 9051nt. The genomes showed 95.3-98.1% nucleotide similarity to each other and 72.2-75.4% similarity to 23 genotype 6 reference sequences, which represent subtypes 6a-6u and unassigned variants km41 and gz52557. Phylogenetic analyses demonstrated that they were genotype 6, but were subotypically distinct. Based on the current criteria of HCV classification, they were designed to represent a new subtype, 6v. Analysis of E1 and NS5B region partial sequences revealed two additional related variants, CMBD-14 and CMBD-86 that had been previously reported in northern Thailand and sequences dropped into Genbank. **CONCLUSION:** Three novel HCV genotype 6 variants were entirely sequenced and designated subtype 6v.

**Analysis of gene transcription in sera during chronic hepatitis C infection.** Carpentier A, Conti F, Carrière M, et al. *J Med Virol.* 2009 Mar;81(3):473-80.

[http://www.ncbi.nlm.nih.gov/pubmed/19152403?ordinalpos=95&itool=Email.EmailReport.Pubmed\\_ReportSelector.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19152403?ordinalpos=95&itool=Email.EmailReport.Pubmed_ReportSelector.Pubmed_RVDocSum)

Alternative, non-invasive techniques are necessary to monitor the progression of liver disease during chronic hepatitis C. Firstly, because serum is the most accessible material for studies using qPCR in microplates, gene transcription was compared in 219 selected genes involved in the pathogenesis of hepatitis C virus (HCV) infection between sera, PBMCs and liver samples collected simultaneously from five patients infected chronically. Secondly, using sera, gene profiles were compared between HCV-infected patients (n = 10) and healthy controls (n = 10). In addition, the influence of alcohol intake was examined in patients infected with HCV genotype-1. Firstly, amplifiable mRNAs were obtained in all samples. After amplification, significant correlations were observed between: liver versus serum; liver versus PBMCs; and serum versus PBMCs ( $r(2) = 0.37$ ,  $r(2) = 0.54$ ,  $r(2) = 0.49$ , respectively). A comparison of gene transcription by gene involved in T- and B-cell markers, adhesion molecules, apoptosis, liver matrix turnover and inflammation, revealed comparable, significant correlations between serum and liver, ( $r(2) = 0.30$ ,  $r(2) = 0.60$ ,  $r(2) = 0.51$ ,  $r(2) = 0.51$ ,  $r(2) = 0.26$ , and  $r(2) = 0.61$  respectively). Secondly, a quantitative analysis of gene expression in sera between genotype-1b-infected patients and healthy controls revealed that 41 genes involved closely in T-cell activation and apoptosis were over-expressed significantly in patients infected with HCV. In these patients, alcohol consumption was associated with an increased expression of six genes involved in the inflammatory response, together with a decrease of genes associated with dendritic cell function. It is concluded that in patients infected with HCV, serum can be used to evaluate expression of liver genes. Further prospective studies are clearly needed to validate the initial results and to define the relevant genes. Copyright 2009 Wiley-Liss, Inc.