

HEPATITIS C CARING AMBASSADORS PROGRAM NEWSLETTER
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IN THE NEWS

Hepatitis C Patients Taxing Medical System

<http://www.forbes.com/lifestyle/health/feeds/hscout/2005/12/30/hscout529386.html>

The use of health-care resources by hepatitis C patients in the United States has been increasing by 25 percent to 30 percent a year, says a Duke University study in the December issue of *Hepatology*.

About 3 million people in the United States have chronic hepatitis C virus (HCV), and many of them contracted it in the 1970s, before testing and safe needle-sharing practices became widespread. Health experts have been predicting an increasing impact on the health system as these people grow older.

The Duke researchers analyzed HCV patient hospitalization trends from 1994 to 2001, HCV-related doctors' visits from 1996 to 2002, and prescription drug data for HCV patients from 1998 to 2000.

The study found that HCV-related hospitalizations, hospital days, total charges and deaths increased by more than 20 percent per year. That's three times higher than all-cause hospitalizations. The largest increases were seen in patients in their 40s and 50s, who spent more time in a hospital, incurred greater costs, and died more often than HCV patients in other age groups.

The study also found that doctor office visits by HCV patients increased by 36 percent a year, and spending on HCV drug therapy rose from \$78 per \$100,000 of new prescriptions in 1998 to \$259 per \$100,000 in 2000.

"The study documents accelerating use of health-care resources by patients with HCV, indicating that the future burden of HCV infection will match and may exceed analysts' forecasts," the study authors wrote.

French Researchers Say HIV Infection Significantly Modifies the Natural History of HCV Infection

http://www.hivandhepatitis.com/hiv_hcv_co_inf/2005/ads/010405_a.html

Recent research suggests that up to 30% of HIV positive individuals are coinfecting with hepatitis C virus (HCV). In studies conducted in the pre-HAART era, the late consequences of HCV-related chronic liver disease were overshadowed by extra-hepatic causes of deaths, related to severe immune deficiency, and the impact of HCV infection on mortality of HIV-infected patients was low.

Although the development of HAART has resulted in a significant decrease in morbidity and mortality among HIV patients, this clear benefit allowed the expression of liver-related complications associated with HCV chronic infection. The degree of impact of HCV on HIV remains controversial, but HIV infection significantly modifies the natural history of HCV infection.

HIV infection increases levels of HCV viremia by 2- to 8-fold, say French researchers, which results in a significant decrease in spontaneous recovery of acute hepatitis. HIV co-infection also worsens the histological course of HCV infection by increasing and accelerating the risk of cirrhosis or leading to rare but lethal fibrosing cholestatic hepatitis, according to the French research team at the Hopital Necker in Paris.

“Liver disease is now one of the leading causes of morbidity and mortality in co-infected patients, even if HAART and especially HIV protease inhibitors, may decrease the severity of the liver disease and the liver-related

mortality," according to the study authors. "Several non-exclusive pathogenic processes explain the increasing rate of liver complications associated with HCV-related liver disease," they conclude.

MedMira granted European patent for hepatitis C diagnostic system

<http://canadaeast.com/apps/pbcs.dll/article?AID=/20060104/TPMONEY08/601040316/-1/MONEY>

Medical diagnostic test maker MedMira Inc. said Tuesday it has been granted a patent for a key component of its rapid hepatitis C test as it plans to launch the product and a combination rapid test for the disease and HIV.

The European patent for the HCV Mosaic Antigen is MedMira's first major patent on its rapid diagnostic technology in Europe "and paves the way for the world's first combination HIV and hepatitis C instant rapid test," the company said in a release. MedMira's rapid HCV tests and HIV/HCV combination tests slated for market entry in 2007.

The HCV Mosaic Antigen is a highly immunoreactive mosaic antigen composition containing different antigenic peptides encoded from the core region of the HCV genome. The patent also describes a test kit using the antigen and a method for its use for the purpose of detecting antibodies to HCV in a test sample.

Liver Cancer, Hepatitis C Connection Gets Clearer

<http://www.forbes.com/lifestyle/health/feeds/hscout/2005/12/07/hscout529493.html>

Scientists have long noted a link between chronic hepatitis C infection and an increased risk for liver cancer, and a new study may help explain why.

"What we've found is that one of the hepatitis C virus proteins (NS5B) targets a cell protein (retinoblastoma) that is crucial for suppressing the development of tumors, interfering with its ability to control cell proliferation," senior author Dr. Stanley M. Lemon, of the University of Texas Medical Branch at Galveston, said in a prepared statement. "By knocking out this 'tumor suppressor' and promoting the proliferation of liver cells, this rival protein is setting up the liver for cancer," Lemon explained. The study appears this week in the early online edition of the journal *Proceedings of the National Academy of Sciences*.

It has long been known that hepatitis C infection can lead to liver cancer, but it wasn't known how the virus actually worked to promote liver cancer. "The way that NS5B docks with the retinoblastoma protein is biochemically almost identical to the way a protein made by human papilloma virus (HPV) does so to produce similar cancer-promoting results," Lemon said.

Experts consider HPV infection to be the leading cause of cervical cancer. The parallel is "interesting," Lemon said, "because the two viruses are so different -- HPV is a DNA virus, while hepatitis C is composed of RNA." These new findings may help in the development of improved treatments for people infected with hepatitis C in order to prevent liver cancer, he said.

Dr. Jack Kevorkian Losing Fight With Hepatitis C

<http://www.prnewswire.com/cgi-bin/stories.pl?ACCT=104&STORY=/www/story/12-06-2005/0004228994&EDATE=>

Attorney Mayer Morganroth said today that his client, Dr. Jack Kevorkian, telephoned him a short time ago with more bad news. Morganroth said Dr. Kevorkian told him that prison doctors informed Kevorkian that his liver enzymes are now triple of what is normal. "I'm alarmed," Morganroth said, "because it now appears that the Hepatitis C Dr. Kevorkian contacted while testing blood transfusions given to American soldiers during Vietnam is attacking his liver."

Dr. Kevorkian, 77, has been in a Michigan prison for the past six-and-a-half years after being found guilty on charges he assisted in a suicide. He is scheduled for release in 2007. "I'm fearful for Dr. Kevorkian because if his liver fails it leaves only two avenues," Morganroth said. "Either a liver transplant or death."

Dr. Kevorkian is in dire shape with multiple physical deterioration. Morganroth said, "Jack is suffering from dangerously high blood pressure, cardiovascular disease, temporal arteritis, peripheral arthritis, adrenal insufficiency, chronic pulmonary obstruction disease and cataracts."

Morganroth has asked Michigan Governor Jennifer Granholm to show compassion and grant a pardon and/or commutation of sentence for Dr. Jack Kevorkian even though she is opposed to assisted suicide.

New Insights Into Protein Synthesis And Hepatitis C Infections

<http://www.sciencedaily.com/releases/2005/12/051203122213.htm>

Scientists have uncovered key new information towards understanding the crucial first step in protein synthesis, the process by which the genetic code, harbored within DNA and copied into RNA, is translated into the production of proteins. This new information also helps to explain how viruses, such as Hepatitis C, are able to hijack protein synthesis machinery in humans for their own purposes.

Biochemist Jennifer Doudna and biophysicist Eva Nogales, both of whom hold joint appointments with the Lawrence Berkeley National Laboratory (Berkeley Lab), the University of California at Berkeley, and the Howard Hughes Medical Institute (HHMI), led a study in which cryo electron microscopy (cryo-EM) was used to create a 3-D model of the protein complex called eukaryotic translation initiation factor 3 (eIF3). The model showed that the eIF3 protein complex employs the same structural mechanics in the loading of either human or viral RNA to ribosomes, the complex machinery in living cells responsible for protein synthesis.

“This is the first insight into how the initiation mechanisms of protein synthesis work specifically for humans, and a step towards understanding at the molecular level what happens when a viral infection occurs,” said Doudna, a member of Berkeley Lab’s Physical Biosciences Division. “A better understanding of these mechanisms could open the door to new and improved therapies for viral infections.”

Said Nogales, also a member of Berkeley Lab’s Physical Biosciences Division, “Using cryo-EM, we can reconstruct images of the entire protein ensemble to study the molecular machinery behind the protein synthesis process. We now have the tools to see how the many different parts of the molecular machinery come together.”

The results of this study are in the December 2, 2005 issue of the journal *Science*, in a paper entitled *Structural Roles for Human Translation Factor eIF3 in Initiation of Protein Synthesis*. Co-authoring the paper with Doudna and Nogales were Bunpote Siridechadilok and Christopher Fraser of UC Berkeley, and Richard Hall of Berkeley Lab.

Proteins, the curiously-shaped macromolecules that serve as the basic construction material of all living cells, and also initiate and control nearly all cell chemistry, are assembled out of amino acids according to the instructions contained within the genes. These genetic instructions are carried from the DNA inside a cell’s nucleus out into the cell’s cytoplasm via messenger RNA (mRNA). There the information will be translated to a sequence of amino acids via the ribosome, an ancient organelle so highly conserved by evolution that its core components are pretty much the same for all forms of life.

Protein synthesis in mammalian cells begins with the loading of mRNA onto the small ribosome subunit, 40S, which is, in part, one of the responsibilities of the eIF3 complex. The eIF3 complex also interacts with other translation elements that bind at the start of the mRNA, prevents premature joining of the 40S and 60S ribosomal subunits, and helps assemble active ribosomes. Until now, the structural basis for eIF3’s multiple activities has been unknown.

At a resolution of 30 angstroms, the cryo-EM reconstructions of Doudna and Nogales and their collaborators show eIF3 to be a particle consisting of five lobes - analogous to a head, and a pair of arms and legs. The study shows that the left arm of the eIF3 complex binds to the eukaryotic protein complex that recognizes the methylated guanosine cap at the 5’-end of the eukaryotic mRNAs (mRNA consists of a coding region sandwiched between a 5’-end and a 3’-end). By drawing the mRNA’s 5’-end cap through the ribosome entry site and towards the exit, eIF3 ensures the mRNA is properly positioned for its genetic code to be translated.

Acting like a molecular wrestler, eIF3 will also wrap its arms and legs around a structural element of RNA for the hepatitis C virus (HVC), known as the internal ribosome entry site (IRES), and pin it to the exit site of the 40S ribosome subunit. The IRES leaves through the left arm of the eIF3 complex at the same location where interaction

with the human mRNA cap-binding complex takes place. “This might explain the amazing ability of the HVC IRES to hijack the human ribosome and its associated translation factors,” said Doudna.

Said Nogales, “The position of eIF3 in our models also provides a plausible explanation for its role in preventing premature joining of the 40S and 60S ribosome subunits.” Doudna and members of her research group are now working to improve the resolution of these models from 30 angstroms to about 10 angstroms. This would allow them to see secondary protein structures which would give them a better understanding of the chemistry behind eIF3’s structural mechanics.

Vertex Pharma launches midstage trial for hep C

<http://boston.bizjournals.com/boston/stories/2005/12/05/daily8.html>

Vertex Pharmaceuticals Inc. has launched a midstage human clinical trial for VX-950, its drug to treat hepatitis C.

The Cambridge, Mass., company announced on Monday that the midstage, or Phase II, trial would last 28 days and explore the drug's safety and effectiveness when combined with two other hepatitis C treatments. Vertex expects to launch multiple midstage trials for the compound in 2006.

North Carolina Hepatitis C/HIV Program Works to Meet Future Community Needs

<http://www.prweb.com/releases/2005/12/prweb317622.htm>

An innovative, three-year project to address Hepatitis C and HIV in the Durham, N.C. area has established groundbreaking programs that help people at risk, says Beth Stringfield, director of the Piedmont HIV Health Care Consortium. She spoke Wednesday to a meeting of partner organizations to present the results of the program and announce future plans.

“Resources for HIV care have been in place, but most people don’t know about the threat of Hepatitis C. Our PHICAS project has helped rally the testing programs, support groups, and community medical training for those co-infected with HIV and Hep C,” Stringfield said. “The PHICAS public service campaign on Hep C testing has raised awareness. People have access to resources through our website, www.phicas.org. It’s now time to build on that foundation to insure that these important services continue.”

The PHICAS project was established under a federal grant designed to coordinate health care services for the uninsured and underinsured. PHICAS partner agencies created a network to provide access to services in Durham, Franklin, Granville, Person, Vance and Warren Counties. As part of the project, a major public awareness campaign was launched in October to encourage people to get tested for Hep C.

“The measure of our success is here today,” Stringfield told the group. “Doctors, health professionals, social workers, educators – all have worked together to make sure that the most important people – our patients – receive the information and the care they need.”

PHICAS developed a managed information system to enable care providers to communicate and eliminate inefficiencies, Stringfield said. “This reduced the administrative burden on agencies and improved the continuity of care.” The program funded free Hep C screening at the Durham County Health Department and offered clinical education programs for medical providers.

One of the challenges the project faced was lack of information, Stringfield said. “Hep C is under-diagnosed, and it is not required to be reported to public health officials. One of our goals was to get a clearer idea of how many people in our target area are impacted, by raising awareness and encouraging testing.”

The culmination of the program will be a statewide symposium on Hepatitis C and HIV, scheduled for March 30 and 31, 2006 in Durham. It is sponsored by PHICAS, North Carolina Department of Health & Human Services HIV/STD Prevention and Care Branch HCV Program, and Wake Forest University.

Non-invasive markers of liver damage effective in HIV / hepatitis C co-infected patients

<http://www.aidsmap.com/en/news/E834FC18-ED93-4532-8092-353C620AD05D.asp>

Markers of liver damage due to hepatitis C infection that can be measured from blood samples are as effective in patients with and without HIV, according to the results of a study presented in the 15th December edition of *The Journal of Acquired Immune Deficiency Syndromes*. This suggests that non-invasive markers of liver damage could be used in HIV / hepatitis C co-infected patients in place of liver biopsies.

The current 'gold standard' for measuring the degree of liver damage or 'fibrosis' in patients with hepatitis C is to take a biopsy - a small sample of liver tissue - for analysis under the microscope. This procedure is expensive, risky and subject to errors caused by the sampling procedure, as well as human error by the person analysing the sample. It is also not feasible to carry out repeated biopsies on one patient to monitor liver disease or treatment.

A number of markers of liver fibrosis that can be measured in blood samples have been developed, but most have not been assessed in HIV-positive patients. Since HIV or its treatment could affect the levels of these markers, investigators wished to determine their effectiveness in HIV / hepatitis C co-infected patients.

The researchers, from Boston Medical Center, evaluated the fibrosis markers in 97 patients from the CHARM cohort, which consists of hepatitis C-infected injection drug users. Forty of the participants were co-infected with HIV and 57 were HIV-negative. Thirty-three of the HIV-positive patients were taking antiretroviral therapy.

All of the patients had a liver biopsy as part of their medical evaluation. The tissue samples were analysed by a single expert and graded on the 'Ishak scale'. This scale runs from zero to six, with higher numbers signifying more severe liver damage. Blood samples were taken within six months of the biopsy. The investigators then measured a range of markers that have been evaluated in HIV-negative patients, before comparing them to the biopsy results for each patient. The markers included the international normalised ratio (INR), platelet count, ratio of aspartate aminotransferase (AST) to alanine aminotransferase (ALT), AST platelet ratio index (APRI), Forns index, procollagen III N peptide, hyaluronic acid and YKL-40.

The researchers found that the correlations between the markers and the degree of fibrosis were similar in the HIV-positive and -negative patients. For example, the AST / ALT ratio did not predict the stage of fibrosis in either the HIV-positive patients ($p = 0.11$) or those without HIV ($p = 0.17$). In contrast, the Forns index, which is calculated from a range of biochemical measurements, was significantly linked to the stage of fibrosis in both groups ($p = 0.001$ and 0.003 , respectively). The investigators saw a trend for the markers to provide slightly better information on fibrosis stage in the HIV-co-infected patients. However, this may be due to the small sample size.

They also found that the markers were more useful in predicting the presence of severe liver damage or 'cirrhosis' than less serious damage. This difference was even more marked for the HIV co-infected patients. "Levels of almost all the markers tended to be more abnormal in the hepatitis C virus / HIV-co-infected group at the later stages of fibrosis," the investigators write. "We have shown that a variety of non-specific markers and markers of extracellular matrix metabolism perform similarly in HIV-positive and -negative populations and are probably valid in co-infected populations," the investigators conclude. "These tests may be of value for the clinical evaluation of hepatitis C virus / HIV-co-infected patients and warrant further study," they add.

Hepatitis C Is An Increasing Burden, Finds Report

<http://www.staffnurse.com/nursing-news-articles/hepatitis-c-is-an-increasing-burden-finds-report-1624.html>

Chronic hepatitis C infection has led to severe liver disease, including cirrhosis, liver failure and liver cancer, in 4,500 people living in England and Wales, according to figures published yesterday. This figure could rise to about 7,000 in five years' time, suggests a new report by the Health Protection Agency (HPA).

Dr Helen Harris of the HPA said: "Of the estimated 200,000 individuals who have a chronic hepatitis C infection a proportion will go on to develop severe liver damage." Most patients could be successfully treated, she said. "The success of treatment relies on people coming forward for testing.

"To enable this, local health services need to provide clear pathways of referral to enable these patients to access the necessary services and be diagnosed." Diagnoses of hepatitis C rose from 6,341 in 2003 to 7,902 in 2004. The increase is mainly due to injecting drug use, Dr Harris explained.

"Prevalence of hepatitis C among injecting drug users (IDUs) is high at around 40 per cent. The spread of infection can be prevented by reducing injecting drug use or encouraging current injectors to quit. If injecting cannot be avoided, injecting equipment should never be shared," she said.

Professor Pat Troop of the HPA added: "Our report shows that the burden hepatitis C places on the individual and on healthcare services is high and will rise in the future. "Public and professional awareness campaigns, such as 'FaCe It', being run by the Department of Health are vital."

SciClone Reports Results From First ZADAXIN Phase 3 Hepatitis C Trial

http://www.marketwire.com/mw/release_html_b1?release_id=103986

SciClone Pharmaceuticals, Inc. today announced top-line results from the first of its two phase 3 clinical trials using ZADAXIN® (thymalfasin) in combination with pegylated interferon alpha to treat patients with hepatitis C virus (HCV) who have failed previous interferon-based therapy. Treatment with ZADAXIN and pegylated interferon alpha did not demonstrate a statistically significant benefit compared to treatment with pegylated interferon alone in sustained viral response (SVR) or histologic improvement, the trial's co-primary endpoints. In this protocol, SVR was defined as the disappearance or absence of detectable HCV RNA in the bloodstream as measured by qualitative PCR test at the completion of a 48-week course of treatment and at week 72 the end of a 24-week observation period following completion of treatment. ZADAXIN was well tolerated with no treatment-related toxicities or side effects.

Although not statistically significant, a positive ZADAXIN treatment-related trend was observed in SVR. In addition, patients who received ZADAXIN therapy were less likely to relapse, an occurrence where the virus reappears after previously being undetectable at the end of 48 weeks of treatment.

"While all of us at SciClone are disappointed that this trial did not achieve statistical significance, there are several other important trials ongoing for ZADAXIN including the ongoing triple therapy HCV clinical trial as well as a phase 2 malignant melanoma trial, both trials being conducted in Europe," said Ira D. Lawrence, M.D., President and Chief Executive Officer of SciClone Pharmaceuticals, Inc. "We will evaluate the data from our HCV trial in greater detail as well as the second phase 3 trial results to determine and coordinate with Sigma-Tau, our European collaborator, the next steps regarding the development of ZADAXIN in hepatitis C therapy. Importantly, we expect the ongoing European HCV clinical trial evaluating the triple therapy combination of ZADAXIN, pegylated interferon alpha and ribavirin run by Sigma-Tau to provide further insight into ZADAXIN's potential in augmenting the current standard of care for hepatitis C patients."

SciClone expects that data from the second phase 3 clinical trial using ZADAXIN in combination with pegylated interferon alpha to treat non-responder HCV patients with early cirrhosis of the liver will be reported in May 2006.

About the U.S Hepatitis C Virus Phase 3 Trial

HCV patients in the first of two phase 3 clinical trials received a 48-week course of therapy of either ZADAXIN (1.6 mg, twice a week) and pegylated interferon alpha (180 mcg, once a week) or placebo and pegylated interferon alpha followed by a 24-week observation period. The primary endpoints of each U.S. HCV trial run by SciClone are the achievement of SVR and an improvement in the liver histological activity index assessed by liver biopsy at week 72.

Although not statistically significant, 4% (10/269) of patients treated with ZADAXIN plus pegylated interferon alpha achieved an SVR compared with only 2% (5/265) of patients treated with pegylated interferon alpha alone. No significant difference in histological improvement was observed between the patients treated with ZADAXIN plus pegylated interferon alpha and those patients treated with pegylated interferon alone.

All patients included in the trial had failed prior interferon-based treatment for hepatitis C virus, and had no cirrhosis of the liver. More than 75% of the patients enrolled in the trial were non-responders to the combination of interferon alpha (either regular or pegylated) and ribavirin, and were infected with the genotype 1 strain of the virus. Additionally, most patients in this trial had a high viral load, or greater than 850,000 copies per ml (or 5.93 log₁₀) of the hepatitis C virus.

About the HCV Triple Therapy Trial

SciClone's European partner Sigma-Tau is enrolling non-responder HCV patients in a 550-patient phase 3 HCV triple therapy trial evaluating the triple combination of ZADAXIN, pegylated interferon alpha and ribavirin. This trial is different from the two U.S. phase 3 hepatitis C trials in two important ways. First, patients in this trial will be treated with the anti-viral agent, ribavirin, in addition to ZADAXIN and pegylated interferon alpha, whereas patients enrolled in the two U.S. phase 3 trials were only treated with ZADAXIN plus pegylated interferon alpha. Second, patients enrolled in this trial are previous non-responders to the combination of pegylated interferon alpha plus ribavirin, whereas patients enrolled in the U.S. phase 3 trials were previous non-responders to any interferon-based therapy. SciClone and Sigma-Tau's objective for the European trial is to generate data on ZADAXIN's use as part of a triple therapy combination for hepatitis C patients.

ViRexx to Present Hepatitis C Vaccine Data at HepDART 2005

http://www.genengnews.com/news/bnitem.aspx?name=1124489XSL_NEWSML_TO_NEWSML_WEB.xml

ViRexx Medical Corp. a company focused on immunotherapy treatments for certain cancers, chronic hepatitis B & C and embolotherapy treatments for tumors, announced that an abstract relating to pre-clinical data from a hepatitis C Chimigen(TM) vaccine candidate will be presented at the HepDART 2005: Frontiers in Drug Development for Viral Hepatitis in Hawaii.

The conference is being held from December 11 to December 15 in the Kohala Coast, Hawaii at the Fairmont Orchid Hotel. Dr. Lorne Tyrrell, Chief Executive Officer and Dr. Rajan George, Vice President, Research and Development, Infectious Diseases at ViRexx Medical Corp. will be presenting an abstract entitled "A Novel Dendritic Cell-Targeted Chimeric Therapeutic Vaccine for the Treatment of Chronic C Infection".

"The Chimigen(TM) technology targets patients with chronic hepatitis B or hepatitis C. It is estimated that 170 million people worldwide suffer from chronic hepatitis C. The poster presentation reviews pre-clinical data from a hepatitis C vaccine," said Dr. Lorne Tyrrell, Chief Executive Officer of ViRexx. "As part of our ongoing clinical development program, we recently filed a Clinical Trial Application to initiate a Phase I hepatitis B Chimigen(TM) vaccine trial and intend to select a vaccine candidate for clinical development for hepatitis C."

Hepatitis B and C in the region and recent trends in diagnosis and management of the diseases," organisers told a press conference yesterday.

http://www.gulf-times.com/site/topics/article.asp?cu_no=2&item_no=64307&version=1&template_id=36&parent_id=16

Organising committee chairman Dr Nazeeh El Dweik, vice chairperson Dr Ajayeb al-Marri, secretary general and scientific co-ordinator Dr Moutaz Derbala, and HMC media department director Mohamed Jassim al-Jassim were present.

The symposium, under the patronage of National Health Authority chairperson Sheikha Dr Ghalia bint Mohamed al-Thani, is to be preceded by a satellite training programme on Wednesday and Thursday.

"We have speakers coming from countries including the US, the UK, Canada, Austria, Turkey, Libya, Germany, Egypt, and Saudi Arabia," the organisers said.

"All Arab countries are intermediate incidence area for hepatitis B with 2 to 7% cases, compared to the less than 2% figure in the West, and 20% cases in South East Asia," Dr El Dweik said. In the case of hepatitis C, Egypt has the highest incidence, at 20%, with the rest of the world having incidence rates between 0.2 and 2%.

"In Qatar, we are presently treating about 260 cases of hepatitis C, of whom only 10 to 15% are Qatari, and are sending two to three patients every year to China for liver transplantation," Dr Derbala said.

A majority of hepatitis C cases in Qatar are from the transfusion of infected blood, imported from Egypt and Florida, during the early 80s when there were no screening facilities, according to Dr El Dweik.

"We are trying to make guidelines for screening and treatment of hepatitis B and C, which could lead to liver cirrhosis and liver cancer if left uncared for," the doctors said.

Sirna Therapeutics Selects Development Candidate for Its Hepatitis C Antiviral Program

<http://biz.yahoo.com/prnews/051221/law030.html?v=42>

Sirna Therapeutics, Inc., a leading RNAi therapeutics company, announced today that it has selected Sirna-AV34, a systemically delivered, chemically modified short interfering RNA (siRNA) compound, as its candidate for advancement to human clinical testing against Hepatitis C virus. Sirna completed its preclinical evaluation of the efficacy of Sirna-AV34 and has begun cGMP manufacturing for its Phase I clinical studies. Sirna expects to initiate IND-enabling toxicology studies in the first quarter of 2006 followed by the filing of an Investigational New Drug (IND) application with the U.S. Food and Drug Administration (FDA) by the fourth quarter of 2006.

Valopicitabine Showing Continued Good Results in Hepatitis C: Presented at HEP DART

<http://www.docguide.com/news/content.nsf/news/8525697700573E18852570DC00473AE9>

The novel prodrug valopicitabine (NM283) continues to show promise in the treatment of hepatitis C in patients who have been refractory to standard HCV therapy, according to partial 24-week results from an ongoing phase 2b trial. Results from the trial show early virologic response (EVR) in up to 70% of patients who are taking high doses -- 400 to 800 mg daily -- of valopicitabine compared to 41% of controls on pegylated-interferon/ribavirin (peg-IFN/RBV) regimens, researchers reported here at the Frontiers in Drug Development for Viral Hepatitis HEP DART 2005 meeting.

"We are seeing statistically superior antiviral effect [with valopicitabine], and overall safety has been satisfactory to date," said Christopher O'Brien, MD, Clinical Associate Professor of Medicine, University of Miami, Miami, Florida, in a presentation on December 13th. "There have been no viral breakthroughs to date." The "very encouraging early data" prompted Dr. O'Brien and colleagues to extend the trial to 48 weeks.

The multicenter trial, which includes 178 patients, is interesting in several regards, Dr. O'Brien said. Stringent inclusion criteria require that participants be non-responders who have failed previous treatment "for efficacy, not for tolerability," he noted. For inclusion in the study, participants must have received at least 12 weeks of peg-IFN/ribavirin and at least 75% of the prescribed dose of both drugs. To remain in the current trial, patients also must meet mandatory response criteria at weeks 4, 12 and 24, a HCV RNA 0.5 log drop (1 IU/mL) by week 4, a 1.0 drop by week 12 and a 2.0 log drop by 24 weeks. "If patients did not meet the response criteria they were discontinued from the trial," Dr. O'Brien said.

Patients were randomised 1:2:2:2, to receive valopicitabine alone, valopicitabine plus peg-IFN (400 mg, 400-800 ramping dose and 800 mg) or peg-IFN plus ribavirin in the re-treatment control group. Dr. O'Brien explained that the study population is unusual in that it includes a large number of Asians, Middle Easterners and Indians. The best results, as measured by HCV RNA levels, were seen in the two high-dose valopicitabine groups, who achieved -3.8 and -3.5 log₁₀ copies/mL decreases, compared to 3 to 0.5 in the control arm. "We find these numbers encouraging because the drops appear to be continuing down from week 12 to 24," Dr. O'Brien said.

"The consistency of response seen in the individual patient data in the valopicitabine combination arms compared to the control arm suggests that the differential in viral load reductions may continue to widen in favor of the valopicitabine combination arms as treatment progresses," he added. Four percent of participants discontinued treatment for serious adverse events and there were no hematologic toxicities for valopicitabine monotherapy. Neutropenia and thrombocytopenia, as expected, occurred in all arms on peg-IFN, Dr. O'Brien said. Transient nausea and vomiting were common in patients on high doses of the study drug but not severe enough to warrant discontinuation, he said.

Science & Medicine | Mother-to-Child Hepatitis C Transmission Twice As Likely Among Infant Girls As Boys, Study Says

http://www.kaisernetwork.org/daily_reports/rep_index.cfm?DR_ID=34383

Pregnant women living with hepatitis C are about twice as likely to transmit the virus to an infant girl as they are to a boy, according to a study published in the Dec. 1 issue of the *Journal of Infectious Diseases*, *Reuters Health* reports. Pier-Angelo Tovo from the Universita degli Studi di Torino in Turin, Italy, and colleagues examined 1,787 pregnant women living with hepatitis C and their infants at 33 centers in Europe and recorded a mother-to-child transmission rate of 6.2%. The researchers also found that elective delivery by caesarean section did not prevent infants from contracting the virus. In addition, breastfeeding, maternal history of injection drug use and premature birth were not significantly associated with higher rates of vertical transmission of hepatitis C, according to the study (*Reuters Health*, 12/15). Women co-infected with HIV and hepatitis C had a higher hepatitis C transmission

rate -- 8.7% -- than the other women participating in the study -- 5.5% -- but the finding was not statistically significant (Tovo et al., *Journal of Infectious Diseases*, 12/1). The researchers said the higher rate of hepatitis C infection among infant girls suggests hormonal or genetic differences between girls and boys affect an infant's risk of contracting the virus. In an accompanying *JID* editorial, Palmer Beasley from the University of Texas School of Public Health said that the study's finding on gender differences is "interesting, provocative and worth further investigation." Beasley adds that the finding is consistent with recent observations regarding gender differences in vertical HIV transmission.

Schering-Plough Announces PEG-INTRON(R) and REBETOL(R) Approved in Japan for Expanded Use in Treating Chronic Hepatitis C

<http://www.prnewswire.com/cgi-bin/stories.pl?ACCT=104&STORY=/www/story/12-22-2005/0004238569&EDATE=>

Schering-Plough Corporation today announced that Schering-Plough K.K., the company's country operations in Japan, has received marketing approval for a new, additional indication for PEG-INTRON(R) (peginterferon alfa-2b) Powder for Injection in combination with REBETOL(R) (ribavirin) Capsules – the treatment of chronic hepatitis C in adult patients other than those with genotype 1 virus and high viral load. This expanded use represents approximately 40 percent of the patient population in Japan. With this approval, PEG-INTRON and REBETOL is indicated for the treatment of the vast majority of Japanese patients diagnosed with chronic hepatitis C virus (HCV)infection. The approval by the Ministry of Health, Labor and Welfare (MHLW) follows a priority review designation granted May 18, 2005. An estimated 1 to 2 million Japanese are chronically infected with hepatitis C.

PEG-INTRON and REBETOL was first approved in Japan in October 2004 for treating patients with genotype 1 virus (genotype 1a or 1b) and high viral load for a recommended duration of 48 weeks. With this new, expanded approval, the recommended duration of therapy for all other HCV indications is 24 weeks. This includes patients with genotype 2 or 3 virus and high viral load, as well as patients with genotype 1, 2 or 3 virus and low viral load who did not respond or who relapsed following treatment with interferon monotherapy. In the Japanese clinical study supporting this approval, a sustained virologic response (SVR)(1) rate of nearly 90 percent was achieved in these patients with 24 weeks of therapy.

"This expanded indication for PEG-INTRON and REBETOL combination therapy represents a significant advance in the treatment of chronic hepatitis C, a major public health problem in Japan," said Robert J. Spiegel, M.D., chief medical officer and senior vice president of medical affairs, Schering-Plough Research Institute. "This approval, and the supporting clinical data, further underscore the efficacy of individualized, weight-based PEG-INTRON used in combination with REBETOL in treating chronic hepatitis C."

PEG-INTRON and REBETOL is the only pegylated interferon-based combination therapy for hepatitis C approved in Japan. PEG-INTRON is administered once weekly in combination with REBETOL daily. Importantly, PEG-INTRON is the only peginterferon product approved in Japan for which a blood test is not required before every injection.

HCV genotype 1 is generally considered to be the most difficult-to-treat form of hepatitis C and is the most common form in Japan, accounting for approximately 70 percent of all HCV infections there. Hepatitis C is the leading cause in Japan of liver cancer, with more than 35,000 deaths occurring annually. Hepatitis C is the most common reason for liver transplant in major world markets, including Japan, according to the World Health Organization (WHO).

Saliva-based hepatitis C test developed

[http://www.scidev.net/gateways/index.cfm?fuseaction=readitem&rgwid=4&item=News&itemid=2560&language=](http://www.scidev.net/gateways/index.cfm?fuseaction=readitem&rgwid=4&item=News&itemid=2560&language=1)

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Israeli scientists have developed a saliva-based test to detect the hepatitis C virus, and say it could be appropriate for mass screening programmes in developing countries. Hepatitis C is common in the developing world, but the conventional method of detecting the virus in a blood sample is often inaccessible to poorer nations.

Current tests use a sample of the patient's serum, the liquid part of blood in which blood cells are suspended, and detect antibodies that the body produces in reaction to the virus. But such tests are costly, complicated and rely on an array of medical equipment and skilled personnel. Now researchers led by Arie Yaari of Soroka University Medical Center, Israel, have shown that saliva can be used instead of serum to detect the virus.

They carried out their study on 37 dialysis patients, people without kidney function whose blood must be passed through a machine to filter out waste products. Such patients have a high incidence of hepatitis C and may resemble ill people in developing countries in their immune response levels. Yaari and colleagues report 100 per cent success at detecting hepatitis C in the saliva of patients who had symptoms of the disease. This is comparable to the results of testing serum. In patients who had the virus but had yet to develop symptoms, the saliva test was accurate in 94 per cent of cases, while the conventional serum test detected only 63 per cent of infections.

Yaari's team say that as it is cheap and easy to obtain saliva samples, detecting hepatitis C infections using this technique might be economically and clinically important in developing nations. They add that as the research involved only 37 patients, a larger study is needed to confirm the results. This could focus on a different high-risk population, for example people in developing countries, say the researchers.

Medivir: Candidate Drug Designated within the Tibotec Collaboration

http://home.businesswire.com/portal/site/google/index.jsp?ndmViewId=news_view&newsId=20051228005381&newsLang=en

Hepatitis C Virus (HCV) collaboration with Tibotec Pharmaceuticals Ltd has recently designated a Candidate Drug (CD). The aim of the research collaboration is to identify and develop orally active inhibitors of the HCV protease NS3/4A. The collaboration was initiated in November 2004 and attaining a CD designation represents an important step on the way towards clinical development. Separately, the first milestone for preclinical development has been reached in the program, triggering a milestone payment to Medivir of EUR 5m.

"Hepatitis C is a highly interesting area for the development of new, innovative pharmaceuticals, and there is a huge need for new treatment principles. It is enormously satisfying that this project with joint resources and efforts has reached such an important development stage as the designation of a CD. We are extremely pleased with the collaboration and the pace it is progressing", says Medivir's VP Research Bertil Samuelsson.

"The designation of this Candidate Drug is the third in a row of protease-based CDs which we have achieved in less than two years. This further validates the productivity of our protease research engine. It enhances the prospects of entering clinical trials over the next few years with several protease inhibitor projects, targeting large patient populations", comments Medivir CEO Lars Adlersson.

Vertex hepatitis C drug will get fast track review

http://today.reuters.com/sponsoredby/amex/article.aspx?type=innovationNews&storyID=2005-12-08T133241Z_01_YUE848748_RTRUKOC_0_US-VERTEX.xml

Vertex Pharmaceuticals Inc. said on Thursday that U.S. regulators will review its experimental hepatitis C drug on an accelerated basis. The Cambridge, Massachusetts-based company said the U.S. Food and Drug Administration granted "fast track" status to the drug, VX-950, meaning the agency could reach a decision on whether to approve the drug six months after Vertex files for approval, rather than the normal 12-month period. The status is typically given to drugs designed to treat serious or life-threatening conditions. Vertex's drug is currently in early clinical trials.

Valeant Pharmaceuticals Agrees to Acquire Rights to Hep-C Drug Infergen® from InterMune

http://www.genengnews.com/news/bnitem.aspx?name=1114732XSL_NEWSML_TO_NEWSML_WEB.xml

Valeant Pharmaceuticals International today announced that it has signed a definitive agreement to acquire the United States and Canadian rights to the hepatitis C drug Infergen® (interferon alfacon-1) from InterMune, Inc. Valeant will pay InterMune \$113.5 million in cash upon closing, and subsequent milestone payments of up to approximately \$22.5 million. Valeant also will acquire an estimated \$6.5 million in inventory from InterMune. The transaction was approved by Valeant's board of directors and is expected to close following the expiration or early termination of the waiting period under the Hart-Scott-Rodino Antitrust Improvement Act of 1976, as amended. Closing is expected in late 2005.

"The acquisition of Infergen will have an immediate sales impact on Valeant and provide us with a valuable addition to one of our core therapeutic areas," said Timothy C. Tyson, Valeant's president and chief executive officer. "In addition, we intend to hire up to 50 of InterMune's sales and marketing force, which will help to provide Valeant with an immediate presence in the hepatitis C market and position us for the anticipated launch of Viramidine®." Viramidine, which is currently in Phase 3 clinical trials, is expected to be launched in 2007.

Infergen or consensus interferon, is a bio-optimized, selective and highly potent type 1 interferon alpha originally developed by Amgen and launched in the United States in 1997. It is currently indicated as monotherapy for the treatment of adult patients suffering from chronic hepatitis C viral infections with compensated liver disease and is dosed three times per week. Infergen is the only interferon with data in the label regarding use in patients following relapse or non-response to certain previous treatments. Infergen is being studied in ongoing clinical trials to establish additional labeling for daily use with ribavirin. Enrollment in the Phase 3 IHRC-001 (DIRECT) trial was completed in mid-2005 with 514 patients at 40 sites in the United States. The DIRECT trial, which should be completed in 2007, is evaluating the safety and efficacy of both 9mcg and 15mcg doses of daily Infergen in combination with ribavirin in non-responders. Management of the DIRECT trial will be transitioned from InterMune to Valeant following the closing of the transaction.

Sales of Infergen were \$22 million in 2004. For the first nine months of 2005, sales of Infergen increased by 79 percent to \$25.3 million compared to \$14.2 million for the first nine months of 2004. The acquisition of Infergen is expected to be neutral in 2005, excluding the impact of acquired in-process research and development, which is estimated to be approximately \$45 million, and modestly dilutive in 2006.

CLINICAL TRIALS, COHORT STUDIES, AND PILOT STUDIES

Similar compliance and effect of treatment in chronic hepatitis C resulting from intravenous drug use in comparison with other infection causes. Robaey G, et al. Eur J Gastroenterol Hepatol. 2006 Feb;18(2):159-166. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16394797&query_hl=11&itool=pubmed_docsum

OBJECTIVES: There is some reluctance to treat intravenous drug users (IVDUs) with chronic hepatitis C (CHC) because of presumed lower compliance and response to antiviral therapy. We intended to evaluate the compliance and response to antiviral treatment for CHC in IVDUs compared with non-IVDUs. **METHODS:** A retrospective cohort study - secondary analysis of the results of a treatment trial - was performed in Belgium and The Netherlands. A total of 406 previously untreated CHC patients, including 98 (24%) IVDUs, were studied for compliance (presentation at the end of treatment), complete response (alanine aminotransferase within normal limits and serum hepatitis C virus polymerase chain reaction negative) at the end of therapy and sustained virological response (SVR). **RESULTS:** Non-compliance (8.2%) in IVDUs was not different from non-IVDUs (6.8%) (relative risk=1.20; 95% confidence interval=0.55-2.62). Complete response after controlling for hepatitis C virus was similar (relative risk=1.19; 95% confidence interval=0.89-1.60). Controlling for treatment arm, age, sex, presence of cirrhosis or hepatitis C virus viral load before treatment did not change these results. There was a marginally significant difference in the sustained virological response between IVDUs (46.6%) and non-IVDUs (34.6%) (relative risk=1.35; 95% confidence interval=1.00-1.81), also disappearing after adjusting for genotype. No difference in compliance or sustained virological response was found between active and non-active IVDUs or between IVDU patients in or without a methadone maintenance program. **CONCLUSIONS:** In this group of Benelux patients, IVDUs showed similar compliance and response to treatment with interferon and ribavirin compared with other patients with CHC infection. Therefore, it is no longer justifiable to withhold treatment to chronic hepatitis C patients who use intravenous drugs.

Sustained virological response rate to pegylated interferon plus ribavirin for chronic hepatitis C in African Americans: results in treatment-naïve patients in a university liver clinic. Srivastava S, Bertagnolli M, Lewis JH. J Natl Med Assoc. 2005 Dec;97(12):1703-7. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16396063&query_hl=11&itool=pubmed_docsum

OBJECTIVE: The sustained virological response (SVR) to non-pegylated interferon-based regimens for chronic hepatitis-C virus (HCV) has been lower among African Americans compared to Caucasians, a finding attributed to the high proportion of genotype-1 infections in African Americans. To determine whether such a difference in SVR

is still present with pegylated interferon and ribavirin regimens, we analyzed SVR rates among treated racial groups according to genotype. **METHODS:** Consecutive treatment-naive patients of multiethnic and racial backgrounds attending a university liver clinic received either Peg alfa-2a or -2b plus ribavirin 1-1.2 g based on body weight for 24-48 weeks, depending on genotype. HCV RNA titers were analyzed at 0, six or 12 months, and six months posttreatment. **RESULTS:** Among the first 193 patients eligible for treatment, 73 received therapy [24 African Americans (genotype 1 in 88%); 49 non-African Americans (genotype 1 in 59%)]. Of the 120 patients not treated (33% African-American and 67% non-African-American), most either had mild hepatitis on biopsy, normal ALT values, an untreated psychiatric condition or had a low expectation of treatment efficacy. SVR results for the 73 patients who completed treatment indicate that African Americans and non-African Americans with genotype 1 have similarly low rates of SVR (19% in African Americans compared with 24% in non-African Americans, $p=NS$). **CONCLUSION:** Sustained viral response rates in our open-access liver clinic are similar for genotype-1 African Americans compared to non-African Americans receiving pegylated interferon and ribavirin. The predominance of genotype 1 among African-American patients likely accounts for the lower response rates, but genotype 1 in other racial groups is associated with a proportionately lower SVR as well as a risk for delayed relapse after SVR.

Pretreatment prediction of interferon-alfa efficacy in chronic hepatitis C patients.

Hayashida K, et al, Clin Gastroenterol Hepatol. 2005 Dec;3(12):1253-9..

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16361052&query_hl=3&itool=pubmed_DocSum

BACKGROUND & AIMS: Interferon has been used widely to treat patients with chronic hepatitis C infections. Prediction of interferon efficacy before treatment has been performed mainly by using viral information, such as viral load and genotype. This information has allowed the successful prediction of sustained responders (SR) and non-SRs, which includes transient responders (TR) and nonresponders (NR). In the current study we examined whether liver messenger RNA expression profiles also can be used to predict interferon efficacy. **METHODS:** RNA was isolated from 69 liver biopsy samples from patients receiving interferon monotherapy and was analyzed on a complementary DNA microarray. Of these 69 samples, 31 were used to develop an algorithm for predicting interferon efficacy, and 38 were used to validate the precision of the algorithm. We also applied our methodology to the prediction of the efficacy of interferon/ribavirin combination therapy using an additional 56 biopsy samples. **Results:** Our microarray analysis combined with the algorithm was 94% successful at predicting SR/TR and NR patients. A validation study confirmed that this algorithm can predict interferon efficacy with 95% accuracy and a P value of less than .00001. Similarly, we obtained a 93% prediction efficacy and a P value of less than .0001 for patients receiving combination therapy. **CONCLUSIONS:** By using only host data from the complementary DNA microarray we are able to successfully predict SR/TR and NR patients for interferon therapy. Therefore, this technique can help determine the appropriate treatment for hepatitis C patients.

Spontaneous elimination of hepatitis C virus RNA in individuals with persistent infection in a hyperendemic area of Japan . Uto H, et al. Hepatol Res. 2005 Dec 14; [Epub ahead of print]

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16360338&query_hl=3&itool=pubmed_DocSum

The natural course of hepatitis C virus (HCV) carriers is not well understood. We examined the clinical characteristics of individuals exhibiting spontaneous elimination of HCV as part of a cohort study of residents of a HCV hyperendemic area in Japan. In individuals who were judged to have persistent HCV infection in 1995, 302 had at least 4 annual ALT measurements between 1993 and 2000, and had not been treated with IFN. They were tested for the presence of HCV RNA in 2001 and/or 2002 and HCV RNA could not be detected in 20 of the 302 individuals. In these 20 individuals, 7 were confirmed to have detectable HCV RNA and 13 were not until 2000. Thus, 2.4% (7/289) were judged to have spontaneously eliminated the HCV infection during that 6-year period. Although there were no differences in age, sex, ALT levels, or serologically defined HCV genotype between individuals with and without exhibiting spontaneous elimination, there was a significant relationship between the elimination of HCV RNA and a low level of HCVcAg ($<20\text{pg/mL}$) ($P<0.001$) upon testing in 1995. These results suggest that spontaneous elimination of HCV RNA following persistent infection is rare and appears to be related to viral load.

Timing of interferon therapy and sources of infection in patients with acute hepatitis C.

Ogata K, et al. Hepatol Res. 2005 Dec 13; [Epub ahead of print]

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16359917&query_hl=3&itool=pubmed_DocSum

BACKGROUND/AIMS: Controversy over the selection of patients and optimum therapeutic method for acute hepatitis C has continued. The aims of this study were to investigate the source of infection, and to evaluate the timing of interferon (IFN) therapy in patients with acute hepatitis C in Japan. **METHODS:** The records of 102 patients from 12 facilities in Japan who developed acute hepatitis C after 1990 were investigated. In the patients treated with IFN, we performed multivariate analysis to investigate factors related to sustained virological response (SVR). **RESULTS:** Medical procedure was the most common source of infection, accounting for 32.4% in the 102 patients (33/102). Of 81 patients treated with IFN, 71 patients were followed after IFN therapy, and 57/71 (80.3%) had SVR. The SVR rate was significantly higher in patients treated with IFN within 24 weeks from onset of symptoms than the SVR rate in those treated after 25 weeks ($P=0.0016$). Multivariate analysis revealed that only the duration between onset of symptoms and initiation of IFN therapy (within 24 weeks) was related to SVR. **CONCLUSIONS:** Our multicenter cooperative survey revealed that medical procedure was the most frequent source of infection in acute hepatitis C. As concerns the therapy, interferon treatment should be initiated within 24 weeks after onset of symptoms.

Risk factors for perinatal transmission of hepatitis C virus (HCV) and the natural history of HCV infection acquired in infancy. Mast EE, et al. J Infect Dis. 2005 Dec 1;192(11):1880-9. Epub 2005 Oct 28.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16267758&query_hl=5&itool=pubmed_DocSum

BACKGROUND: The goal of the present study was to assess risk factors for perinatal hepatitis C virus (HCV) transmission and the natural history of infection among HCV-infected infants. **METHODS:** In a cohort study, 244 infants born to HCV-positive mothers were followed from birth until age $>$ or $=$ 12 months. Maternal serum was collected at enrollment and delivery; infant serum was collected at birth and at 8 well-child visits. Testing included detection of antibody to HCV, detection of HCV RNA (qualitative and quantitative), and genotyping. HCV-infected infants were followed annually until age 5 years. **RESULTS:** Overall, 9 of 190 (4.7% [95% confidence interval (CI), 2.3%-9.1%]) infants born to mothers who were HCV RNA positive at delivery became infected, compared with 0 of 54 infants born to HCV RNA-negative mothers ($P=.10$). Among HCV RNA-positive mothers, the rate of transmission was 3.8% (95% CI, 1.7%-8.1%) from the 182 who were human immunodeficiency virus (HIV) negative, compared with 25.0% (95% CI, 4.5%-64.4%) from the 8 who were HIV positive ($P<.05$). Three infected infants resolved their infection (i.e., became HCV RNA negative). In multivariate analysis restricted to HCV RNA-positive mothers, membrane rupture $>$ or $=$ 6 h (odds ratio [OR], 9.3 [95% CI, 1.5-179.7]) and internal fetal monitoring (OR, 6.7 [95% CI, 1.1-35.9]) were associated with transmission of HCV to infants.

CONCLUSION: If duration of membrane rupture and internal fetal monitoring are confirmed to be associated with transmission, interventions may be possible to decrease the risk of transmission.

Adiponectin and its receptors in patients with chronic hepatitis C. Jonsson JR, et al. J Hepatol. 2005 Dec;43(6):929-36. Epub 2005 Jul 1.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16139921&query_hl=5&itool=pubmed_DocSum

BACKGROUND/AIMS: There is increasing interest in the influence of excess body weight and associated metabolic factors on the liver. In patients with non-alcoholic steatohepatitis, lower levels of adiponectin were associated with higher grades of hepatic steatosis and necroinflammatory activity, suggesting a pathophysiological role for this adipokine in liver disease. **METHODS:** We studied 194 consecutive patients with untreated chronic HCV, to assess the relationship between adiponectin and its receptors and hepatic steatosis, fibrosis and inflammation. **RESULTS:** Significant negative correlations between serum adiponectin and male gender, body mass index and serum insulin were observed. However, there was no association between serum adiponectin and stage of fibrosis and lower levels of serum adiponectin were associated with the presence of steatosis in males only. In contrast, there was a significant increase in serum adiponectin and hepatic adiponectin immunoreactivity with increasing inflammation. The hepatic mRNA expression of the adiponectin receptors, AdipoR1 and AdipoR2, displayed significant but opposite associations with phosphoenolpyruvate carboxykinase (PEPCK) gene expression, a substitute marker of hepatic insulin sensitivity. **CONCLUSIONS:** In patients with chronic HCV, adiponectin was associated with steatosis only in males and was paradoxically increased with inflammation. Our results suggest that the role of adiponectin in chronic liver diseases may be linked to gender and etiology.

Th1 response during ribavirin and interferon-alpha combination therapy in chronic hepatitis C. Kobayashi K., et al. *Hepatology*. 2005 Dec 22; [Epub ahead of print].

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16377237&query_hl=2&itool=pubmed_DocSum

Ribavirin and interferon-alpha induce Th1 polarization of human CD4+ T cells. The study was conducted to investigate the whether cellular immune response during ribavirin/interferon-alpha therapy is associated with viral eradication by examining mRNA expression of molecules relevant to Th1 and Th2 polarization in CD4+ cells of 13 patients with chronic hepatitis C (seven patients with sustained viral response and six with transient response). Peripheral CD4+ T lymphocytes at 0, 4 and 24 weeks of treatment were tested. There were no significant differences in the mRNA levels at each point of time of the treatment between patients with sustained viral response and those with transient response. The percent increase in mRNA level of the IL-12R beta2 chain from the baseline to the end of the treatment was significantly higher in patients with sustained viral response (15.3+/-6.1%) than in those with transient response (-1.6+/-4.7%, $p < 0.05$). There was no significant difference in percent changes in level of IL-12R beta1 chain mRNA between the two groups. **In conclusion**, the results of this study indicate that the increase of Th1 response is related to the inflammatory activity in the liver and possibly to ribavirin and interferon-alpha therapy. It is also suggested that the measurement of Th1 response has the potential to distinguish patients with relapse from those with sustained virus response.

Efficacy of Interferon-alpha in the Treatment of Chronic Hepatitis C in Dialysis Patients: Two Therapeutic Protocols Compared. Grgurevic I, et al. *Nephron Clin Pract*. 2005 Dec 21;103(1):c8-c11 [Epub ahead of print].

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16374034&query_hl=2&itool=pubmed_DocSum

BACKGROUND: Data on the efficacy of particular therapeutic protocols of interferon-alpha (IFN-alpha) treatment for chronic hepatitis C in patients on hemodialysis (HD) vary. **Aim:** To compare the efficacy of two different therapeutic protocols for HD patients. **PATIENTS AND METHODS:** 15 hepatitis C virus (HCV)-positive patients on chronic HD at two dialysis centers: 8 patients treated with IFN-alpha 3 x 3 MU/week s.c. for 6 months (group A), and 7 patients treated with IFN-alpha 3 x 5 MU/week for 3 months, then 1 x 5 MU/week for another 3 months (group B). End of treatment response (ETR) and sustained virologic response (SVR) were evaluated by HCV-RNA determination. There was no statistically significant difference between the two patient groups according to age, sex, duration of HD and HCV infection. **RESULTS:** ETR was 87.5% (7/8) in group A and 28.5% (2/7) in group B, being statistically significant ($p < 0.05$). Although better SVR [50% (4/8) vs. 28.5% (2/7)] and lower drop-out rate [0% (0/8) vs. 28.5% (2/7)] were achieved in group A compared to group B, these differences did not reach statistical significance ($p > 0.05$). **CONCLUSION:** Therapy with IFN-alpha 3 x 3 MU/week s.c. for 6 months seems to be more appropriate for treatment of hepatitis C in HD patients, mostly due to better tolerability, i.e. lower drop-out rate. These differences could be attributed to different pharmacokinetic properties of the particular therapy protocol.

Kinetics of hepatitis C virus RNA load during pegylated interferon alpha-2a and ribavirin treatment in naive genotype 1 patients. Ouzan D, et al. *Comp Hepatol*. 2005 Dec 21;4(1):9 [Epub ahead of print]

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16371151&query_hl=2&itool=pubmed_DocSum

ABSTRACT: BACKGROUND: Pegylated interferon given for 24 or 48 weeks constitutes the most effective initial therapy for the treatment of chronic hepatitis C. It has been shown that viral load at week 2 appears the best time for predicting response to treatment. The objectives of this study were to assess whether the hepatitis C virus (HCV) RNA viral decline is predictive of sustained virological response (SVR) and to determine the best time for predicting complete response in our cohort of naive patients treated with pegylated interferon alpha-2a (Peg-IFN alpha-2a) and ribavirin. **RESULTS:** Twenty patients treated with Peg-IFN alpha-2a and ribavirin for 48 weeks were studied. Six months after the end of treatment, a SVR (negative HCV RNA measured by PCR six months after the end of therapy) was obtained in 9 patients. Samples were obtained before and at week 2, 4, 8, and 12. At the end of week 2, viral load decreased more than 1.39 log in 8 out of the 9 patients with SVR and in 1 out of the 11 other patients. When we considered the viral load reduction from baseline to each week of treatment, week 2 appeared to be the best point time for predicting SVR, with a sensitivity of 91% (95%CI: 59;99), a specificity of 89% (52;98), a positive predictive value of 91% (59;99) and a negative predictive value of 89% (57;98). **CONCLUSION:** During treatment with Peg-IFN alpha-2a plus ribavirin in genotype 1 patients, when the main objective of the treatment is

viral eradication, viral kinetics showed that week 2 appeared to be the best time point for predicting SVR. Our results must be further confirmed on a larger cohort.

BASIC AND APPLIED SCIENCE, PRE-CLINICAL STUDIES

Enhanced sensitivity of human hepatoma cells to 5-fluorouracil by small interfering RNA targeting Bcl-2.

Kanda T, et al. DNA Cell Biol. 2005 Dec;24(12):805-9.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16332177&query_hl=3&itool=pubmed_DocSum

This study was designed to reveal whether the apoptosis induced in human hepatocellular carcinoma (HCC) cell lines by 5-fluorouracil (5-FU) could be enhanced by transfecting Bcl-2 small interfering RNA (siRNA). Bcl-2 siRNA and control siRNA were transfected into cells following treatment with or without 5-FU. Suppression of Bcl-2 expression was confirmed by Western blotting; cell viability was evaluated by MTS assay, and the occurrence of apoptosis in cells was evaluated by apoptosis assay. Expression of Bcl-2 protein after transfection of 20 nM Bcl-2 siRNA was significantly lower than that of control. Incubation of all cell lines with Bcl-2 siRNA reduced cell viability 96 h after 5-FU treatment compared with all other controls: Huh-7 (P < 0.01), Huh-7 with hepatitis C replicon (P < 0.01), HepG2 (P < 0.01), HLE (P < 0.05). Moreover, the proportion of apoptosis in control siRNA, Bcl-2 siRNA, control siRNA prior to 5-FU treatment, and Bcl-2 siRNA prior to 5-FU treatment groups were (4.6 +/- 2.3)%, (7.5 +/- 0.5)%, (6.0 +/- 2.1)%, and (19.5 +/- 0.86)%, respectively. The Bcl-2 siRNA prior to 5-FU treatment group showed the strongest effect of inducing apoptosis. **In conclusion**, the combination Bcl-2 siRNA and 5-FU might represent a new therapeutic option for HCC.

Activation of V[gamma]9V[delta]2 T cells by non-peptidic antigens induces the inhibition of subgenomic HCV replication.

Agrati C, et al, Int Immunol. 2006 Jan;18(1):11-8. Epub 2005 Dec 16.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16361319&query_hl=3&itool=pubmed_DocSum

Hepatitis C virus (HCV) has evolved complex strategies to evade host immune responses and establish chronic infection. Since human Vgamma9Vdelta2 T lymphocytes play a critical role in the immune response against viruses, we analyzed their antiviral functions on Huh7 hepatoma cells carrying the subgenomic HCV replicon (Rep60 cells). In a transwell culture system, Rep60 cells were co-cultured with either PBMCs or highly purified gamma delta T cells stimulated by non-peptidic antigens. Vgamma9Vdelta2 T cell activation was associated with a dramatic reduction of HCV RNA levels. Neutralizing antibodies targeting IFN-gamma revealed a critical role for this cytokine in the inhibition of HCV replication. Interestingly, drugs already in clinical use, such as Phosphostim and Zoledronate, known to activate gamma delta T cells, were shown to induce the inhibition of HCV replication mediated by Vgamma9Vdelta2 T cells of HCV patients. **Our data suggest** that the therapeutic activation of Vgamma9Vdelta2 T lymphocytes may represent an additional strategy to inhibit HCV replication and to restore a T(h)1-oriented immune response in HCV-infected patients.

Chronic liver injury in rats and humans upregulates the novel enzyme angiotensin converting enzyme 2.

Paizis G, et al. Gut. 2005 Dec;54(12):1790-6. Epub 2005 Sep 15.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16166274&query_hl=5&itool=pubmed_DocSum

BACKGROUND: Angiotensin converting enzyme (ACE) 2 is a recently identified homologue of ACE that may counterregulate the actions of angiotensin (Ang) II by facilitating its breakdown to Ang 1-7. The renin-angiotensin system (RAS) has been implicated in the pathogenesis of cirrhosis but the role of ACE2 in liver disease is not known. **AIMS:** This study examined the effects of liver injury on ACE2 expression and activity in experimental hepatic fibrosis and human cirrhosis, and the effects of Ang 1-7 on vascular tone in cirrhotic rat aorta. **METHODS:** In sham operated and bile duct ligated (BDL) rats, quantitative reverse transcriptase-polymerase chain reaction was used to assess hepatic ACE2 mRNA, and western blotting and immunohistochemistry to quantify and localise ACE2 protein. ACE2 activity was quantified by quenched fluorescent substrate assay. Similar studies were performed in normal human liver and in hepatitis C cirrhosis. **RESULTS:** ACE2 mRNA was detectable at low levels in rat liver and increased following BDL (363-fold; p < 0.01). ACE2 protein increased after BDL (23.5-fold; p < 0.05) as did ACE2 activity (fourfold; p < 0.05). In human cirrhotic liver, gene (>30-fold), protein expression (97-fold), and activity of ACE2 (2.4 fold) were increased compared with controls (all p < 0.01). In healthy livers,

ACE2 was confined to endothelial cells, occasional bile ducts, and perivenular hepatocytes but in both BDL and human cirrhosis there was widespread parenchymal expression of ACE2 protein. Exposure of cultured human hepatocytes to hypoxia led to increased ACE2 expression. In precontracted rat aorta, Ang 1-7 alone did not affect vascular tone but it significantly enhanced acetylcholine mediated vasodilatation in cirrhotic vessels.
CONCLUSIONS: ACE2 expression is significantly increased in liver injury in both humans and rat, possibly in response to increasing hepatocellular hypoxia, and may modulate RAS activity in cirrhosis.

Partial reconstitution of hepatitis C virus RNA polymerization by heterologous expression of NS5B polymerase and template RNA in bacterial cell. Lee S, *Virus Res.* 2005 Dec;114(1-2):158-63. Epub 2005 Aug 11.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16099067&query_hl=5&itool=pubmed_DocSum

The hepatitis C virus (HCV) is a major etiological agent causing chronic hepatitis in humans. Since the virus does not grow in a cell culture, the direct measurement of viral replication is impossible. Therefore, the current study presents a surrogate model system using a viral polymerase and RNA template. A plasmid expressing the HCV NS5B polymerase was maintained with a plasmid containing a reporter gene in an *Escherichia coli* cell. The reporter construct contained the HCV 5' untranslated region (UTR) followed by a luciferase gene with a specific orientation so that a minus-sense transcript containing the luciferase fused to the 5' UTR was produced after the initial transcription. When the HCV NS5B polymerase was expressed in the same cell, the primary transcript was recognized by the polymerase due to the presence of the minus-sense 5' UTR, and a secondary transcript containing a plus-sense luciferase gene was produced. Thus, a simple luciferase assay was able to measure the HCV NS5B polymerase activity. The production of minus- and plus-sense transcripts was confirmed by an RT-PCR, while the production of HCV NS5B and expression of the reporter luciferase in the bacterial cell were confirmed by immunofluorescence microscopy. The polymerization occurred in the absence of any other viral/host factors. Accordingly, this would appear to be the first study to demonstrate that the heterologous expression of an animal viral RNA polymerase and its template in a bacterial cell can partially reconstitute the polymerization reaction.

Hepatitis C virus (HCV) core protein enhances the immunogenicity of a co-delivered DNA vaccine encoding HCV structural antigens in mice. Alvarez-Lajonchere L, et al. *Biotechnol Appl Biochem.* 2005 Dec 20; [Epub ahead of print].

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16367740&query_hl=2&itool=pubmed_DocSum

In the present work, recombinant hepatitis C virus (HCV) core proteins enhanced the immune response elicited by a co-delivered DNA vaccine encoding HCV core and envelope proteins. Particularly, the mixture of the plasmid pIDKE2 with Co.173, a protein comprising the first 173 aa of HCV core, induces strong humoral response, including antibodies that recognized peptides representing hypervariable region I from different viral isolates. Moreover, positive lymphoproliferative responses against the HCV structural proteins, encoded by the plasmid, were detected after 2 doses with this mixture. When the HCV core protein used in the mixture with pIDKE2 was Co.120, a protein comprising the first 120 aa of the viral antigen, strong humoral response and a positive lymphoproliferative response were also detected. The effectiveness of this formulation was tested *in vivo* by measuring the protection against infection with a recombinant vaccinia virus expressing HCV core protein. A 2 log reduction in vaccinia virus titer was observed in mice immunized with the mixture of pIDKE2-Co.120. Humoral and cellular immune responses elicited for the mixture of pIDKE2 with either Co.173 or Co.120 was stronger and more diverse than those generated by individual components. **In conclusion**, our results indicate that formulations comprising both DNA constructs and protein subunit vaccine candidates are able to elicit strong humoral and cellular immunity against several antigens. Particularly, HCV core protein might be used as a feasible vehicle/adjuvant for DNA vaccines.

HIV/HCV COINFECTION

Immunologic Response to Antiretroviral Therapy in Hepatitis C Virus-Coinfected Adults in a Population-Based HIV/AIDS Treatment Program. Braitstein P, et al. *J Infect Dis.* 2006 Jan 15;193(2):259-68. Epub 2005 Dec 7.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16362890&query_hl=2&itool=pubmed_DocSum

BACKGROUND: We sought to characterize the impact that hepatitis C virus (HCV) infection has on CD4 cells during the first 48 weeks of antiretroviral therapy (ART) in previously ART-naive human immunodeficiency virus (HIV)-infected patients. **METHODS:** The HIV/AIDS Drug Treatment Programme at the British Columbia Centre for Excellence in HIV/AIDS distributes all ART in this Canadian province. Eligible individuals were those whose first-ever ART included 2 nucleoside reverse transcriptase inhibitors and either a protease inhibitor or a nonnucleoside reverse transcriptase inhibitor and who had a documented positive result for HCV antibody testing. Outcomes were binary events (time to an increase of ≥ 75 CD4 cells/mm³) or an increase of $\geq 10\%$ in the percentage of CD4 cells in the total T cell population [CD4 cell fraction]) and continuous repeated measures. Statistical analyses used parametric and nonparametric methods, including multivariate mixed-effects linear regression analysis and Cox proportional hazards analysis. **RESULTS:** Of 1186 eligible patients, 606 (51%) were positive and 580 (49%) were negative for HCV antibodies. HCV antibody-positive patients were slower to have an absolute ($P < .001$) and a fraction ($P = .02$) CD4 cell event. In adjusted Cox proportional hazards analysis (controlling for age, sex, baseline absolute CD4 cell count, baseline pVL, type of ART initiated, AIDS diagnosis at baseline, adherence to ART regimen, and number of CD4 cell measurements), HCV antibody-positive patients were less likely to have an absolute CD4 cell event (adjusted hazard ratio [AHR], 0.84 [95% confidence interval {CI}, 0.72-0.98]) and somewhat less likely to have a CD4 cell fraction event (AHR, 0.89 [95% CI, 0.70-1.14]) than HCV antibody-negative patients. In multivariate mixed-effects linear regression analysis, HCV antibody-negative patients had increases of an average of 75 cells in the absolute CD4 cell count and 4.4% in the CD4 cell fraction, compared with 20 cells and 1.1% in HCV antibody-positive patients, during the first 48 weeks of ART, after adjustment for time-updated pVL, number of CD4 cell measurements, and other factors. **CONCLUSION:** HCV antibody-positive HIV-infected patients may have an altered immunologic response to ART.

Detection of HCV-RNA in Saliva of HIV-HCV Coinfected Patients. Eirea M, et al. AIDS Res Hum Retroviruses. 2005 Dec;21(12):1011-4.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16379604&query_hl=2&itool=pubmed_DocSum

The presence of HCV-RNA in saliva of patients with chronic hepatitis C provides a biological basis for the potential transmission of this virus. HCV viremia is particularly high in HCV-HIV-coinfected patients, which could favor the presence of HCV in their saliva. This study was designed to evaluate the prevalence of HCV in saliva of HCV-HIV-coinfected patients. Stimulated whole saliva was collected from 75 HCV-HIV-coinfected patients and 75 HCV controls. The presence of HCV-RNA in saliva was tested by a highly sensitive noncommercialized nested PCR, and analyzed in relation to demographic, clinical, and analytical variables. HCV RNA was detected in the saliva of 49 (65%) HCV-HIV-coinfected patients and 39 (52%) HCV controls. The presence of HCV in saliva was not related to any of the analyzed variables in HCV-HIV-coinfected patients. In the HCV control group a statistically significant relationship was demonstrated only between the detection of HCV-RNA in saliva and the viral load in peripheral blood ($p < 0.001$). **Our results indicate** that there is a trend toward a higher HCV-RNA prevalence in the saliva of HCV-HIV-coinfected patients.

Histological findings and clinical characteristics associated with hepatic steatosis in patients coinfecting with HIV and hepatitis C virus. Marks KM, et al. J Infect Dis. 2005 Dec 1;192(11):1943-9. Epub 2005 Nov 2.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16267765&query_hl=5&itool=pubmed_DocSum

BACKGROUND: Hepatic steatosis, a common histological finding in hepatitis C virus (HCV)-infected patients, is associated with severity of fibrosis. The prevalence and significance of steatosis in patients coinfecting with human immunodeficiency virus (HIV) and HCV are not well characterized. **METHODS:** To determine the prevalence and severity of steatosis, a single pathologist evaluated liver-biopsy samples from 106 patients coinfecting with HIV and HCV but without hepatitis B infection (negative results for hepatitis B surface antigen) for findings associated with steatosis or steatohepatitis and viral hepatitis. Medical records were reviewed retrospectively to elucidate risk factors for steatosis. **RESULTS:** Steatosis was present in 56% of biopsy samples, with moderate to severe grades in 9%. Severity of steatosis was associated with fibrosis (odds ratio [OR], 1.84 [95% confidence interval (CI), 1.06-3.20]; $P = .03$) but not with necroinflammation. In multivariate analysis, the severity of steatosis was associated with lower levels of high-density lipoprotein cholesterol (OR, 0.71 per 10-mg/dL increase [95% CI, 0.52-0.95]; $P = .02$), higher body-mass index (OR, 1.30 per kg/m² increase [95% CI, 1.13-1.49]; $P < .001$), and the presence of lipodystrophy (OR, 3.82 [95% CI, 1.13-12.88]; $P = .03$). There was a trend toward an association between the severity of steatosis and fibrosis in multivariate analysis (OR, 1.69 [95% CI, 0.91-3.16]; $P = .10$). **CONCLUSIONS:**

In patients coinfecting with HIV and HCV, hepatic steatosis is common and associated with more-advanced fibrosis. Lower levels of high-density lipoprotein cholesterol, higher body-mass index, and lipodystrophy are potentially modifiable risk factors associated with the severity of steatosis.

Hepatitis C-associated autoimmunity in patients coinfecting with HIV. Woitas RP, et al. Liver Int. 2005 Dec;25(6):1114-21.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16343060&query_hl=3&itool=pubmed_DocSum

BACKGROUND: Hepatitis C virus (HCV) infection is associated with multiple extrahepatic manifestations. It is unclear to what extent extrahepatic manifestations occur in HIV/HCV coinfection. **METHODS:** We prospectively assessed cross-sectional frequencies of autoimmune manifestations in HIV/HCV-coinfecting patients (n=98), HIV-mono-infected (n=45) and HCV-mono-infected patients (n=78). Diagnostic vasculitis scores, HCV and HIV loads, CD4 cell counts, thyroid-, cardiolipin-, non-organ-specific tissue antibodies (nuclear, smooth muscle, anti-liver-kidney-microsome, neutrophil-cytoplasmic) and cryoglobulins were determined. **RESULTS:** Synergistic effects of HCV and HIV infection were observed with respect to the prevalence of antibodies against thyroglobulin (HCV infection 15.4%, HIV infection 8.8%, HIV/HCV coinfection 30.6%; $P < 0.001$) and cardiolipin antibodies (HCV infection 9.0%, HIV infection 31%, HIV/HCV coinfection 46%; $P < 0.001$). Cryoglobulinemia type III, was significantly associated with HCV infection (HCV, 25.6%; HIV/HCV, 20.4%) but not with HIV infection (4.4%, $P < 0.05$). Rheumatoid factor was commonly detected in patients with HCV infection (48%), but occurred considerably less frequently in patients with HIV infection (4.4%) or HIV/HCV coinfection (9.5%, $P < 0.01$). **CONCLUSION:** HIV coinfection appears to differentially modulate the frequency of HCV-related autoimmunity. However, autoimmunity is rarely accompanied by clinical manifestations.

Do type and duration of antiretroviral therapy attenuate liver fibrosis in HIV-hepatitis C virus-coinfecting patients? Verma S, Clin Infect Dis. 2006 Jan 15;42(2):262-70. Epub 2005 Dec 2.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16355339&query_hl=3&itool=pubmed_DocSum

BACKGROUND: This study aimed to determine whether type and duration of therapy for human immunodeficiency virus (HIV) infection attenuates liver fibrosis in patients with HIV and hepatitis C virus (HCV) coinfection. **METHODS:** Patients with HCV mono-infection (group 1) and HIV-HCV coinfection were retrospectively selected; the latter patients were classified into the following 3 groups: group 2, patients who received no therapy or only nucleoside reverse-transcriptase inhibitors (NRTIs); group 3, those who received highly active antiretroviral therapy (HAART); and group 4, those who initially received NRTIs followed by HAART. Fibrosis stage (scale, 0-6) and necroinflammatory score (scale, 0-18) were assessed according to the Ishak system. Data are presented as mean +/- standard deviation. **RESULTS:** Three hundred eighty-one patients (296 HCV-mono-infected patients and 85 HIV-HCV-coinfecting patients) were recruited. The durations of HIV therapy before liver biopsy was performed for groups 2, 3, and 4 were 3.8 +/- 2.8, 3.3 +/- 1.8, and 6.6 +/- 2.2 years. The time from HIV diagnosis to HAART initiation was shorter for group 3 than for group 4 (9.1 +/- 7.3 vs. 34.1 +/- 13.1 months; $P < .0001$). Groups 1 and 3 had similar fibrosis stages (3.1 +/- 2 vs. 3.4 +/- 2.4), rates of fibrosis progression (0.13 +/- 0.09 vs. 0.16 +/- 0.11 per year), and necroinflammatory scores (6.1 +/- 1.8 vs. 6.1 +/- 2.0). Groups 2 and 4 had significantly more-advanced liver disease, as determined by fibrosis stage (4.6 +/- 1.8 vs. 4.3 +/- 2.0; $P < .0009$), rate of fibrosis progression (0.24 +/- 0.11 vs. 0.20 +/- 0.10 per year; $P < .0001$), and prevalence of cirrhosis (68% vs. 55%; $P < .006$), compared with group 1. **CONCLUSIONS:** HIV-HCV-coinfecting subjects who receive HAART as their sole form of therapy have liver histology findings comparable to those for HCV-mono-infected patients. A similar degree of benefit is not observed for HIV-HCV-coinfecting patients who receive no therapy, NRTIs, or HAART after NRTIs, despite having a longer duration of therapy.

COMPLEMENTARY AND ALTERNATIVE THERAPIES

Oxidative stress and hepatitis C viral infection. Koike K, Miyoshi H. Hepatol Res. 2005 Dec 16; [Epub ahead of print]

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16364681&query_hl=11&itool=pubmed_DocSum

The involvement of oxidative stress in the pathogenesis of hepatitis and hepatocellular carcinoma has been strongly suggested. Oxidative stress is produced by inflammatory processes that occur in hepatitis via immunological mechanisms. In addition, in hepatitis C virus (HCV) infectious disease, some role has been assigned to viral proteins in the induction of oxidative stress. In the presence of hepatic steatosis, insulin resistance and increased levels of some cytokines, all of which are also induced by viral protein expression, oxidative stress is enhanced in HCV infection. In this sense, the role of oxidative stress in the progression of chronic hepatitis and hepatocarcinogenesis is greater in hepatitis C than in other types of hepatitis such as hepatitis B or autoimmune hepatitis. The additive effects of oxidative stress caused by the inflammatory process and that induced by HCV proteins may, furthermore, exert synergistic effects with alterations in intracellular signaling systems such as mitogen-activated protein kinases (MAPK), which are also induced by HCV proteins. These synergistic effects may be responsible for rare characteristics, that is, the high incidence and multicentric nature of hepatocarcinogenesis in HCV infection.

Advancing patient care through innovative practice: the Clinical Partners Program.

Mehta BH, et al. Am J Health Syst Pharm. 2005 Dec 1;62(23):2501-7.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16303906&query_hl=2&itool=pubmed_docsum

PURPOSE: The development, implementation, and outcomes assessment of an innovative pharmacist-managed ambulatory care and community pharmacy practice clinic are described. **SUMMARY:** The Clinical Partners Program at The Ohio State University (OSU) provides an active learning environment for students and residents, offers a patient-focused practice model based on pharmaceutical care principles, and serves as an arena for applied research in pharmacy practice. The program offers multiple services, including anticoagulation management, diabetes self-management, cholesterol management, hepatitis C education, herbal product and dietary supplement consultations, medication management, smoking cessation, and wellness. The practice is currently staffed by two faculty members from the college of pharmacy, with a 0.8 full-time-equivalent (FTE) pharmacist and a 0.65 FTE community pharmacy resident. It has served as a training site for 17 pharmacy residents, 28 bachelor of science (B.S.) in pharmacy students, 30 post-B.S. doctor of pharmacy (Pharm.D.) students, and 132 entry-level Pharm.D. students at various levels of training. The most successful methods of reimbursement for programs have been contracted services with OSU Managed Health Care Systems, Inc., which serves OSU faculty and staff and fee-for-service billing, charged directly to non-OSU patients. Numerous studies have shown that Clinical Partners has consistently demonstrated improved therapeutic outcomes over those achieved in traditional practice. Faculty are exploring outreach services, including the development of advanced practice community sites for the college, establishing patient care services within physician offices, and providing disease management services for self-insured employers. **CONCLUSION:** The Clinical Partners Program has improved patient care and provided education and training opportunities for pharmacy students and residents.

MISCELLANEOUS

Behavior modification following a diagnosis of hepatitis C infection. Lindsey N, Reif JS, Bachand A, Seys SA. Am J Health Behav. 2005 Nov-Dec;29(6):512-9.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16336106&query_hl=11&itool=pubmed_DocSum

OBJECTIVES: To determine the extent of postdiagnosis counseling and to characterize behavior before and after diagnosis of hepatitis C infection. **METHODS:** We interviewed 133 persons diagnosed with hepatitis C in Wyoming from 1999 to 2001. **RESULTS:** Approximately two thirds of cases received counseling at the time of diagnosis. Older and symptomatic patients were more likely to receive counseling. Counseling was significantly associated with increases in condom use, wound covering, and hepatitis A and hepatitis B vaccination, but not with changes in addictive behaviors. **CONCLUSIONS:** Counseling was an effective strategy for promoting several desirable behavior changes among persons with hepatitis C infection.

Advances in digital quantification technique enhance discrimination between mild and advanced liver fibrosis in chronic hepatitis C. Lazzarini AL, Levine RA, Ploutz-Snyder RJ, Sanderson SO. Liver Int. 2005 Dec;25(6):1142-9.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16343064&query_hl=11&itool=pubmed_DocSum

BACKGROUND AND AIMS: The necessity of liver biopsy for staging fibrosis and its quantification in patients with chronic hepatitis C (CHC) remains controversial. Semiquantitative scoring of fibrosis is considered more subjective and less objective than digital quantification by image analysis. However, measurement of fibrosis using digital image analysis is thought to be less reliable in determining early stage fibrosis as compared with advanced fibrosis or cirrhosis. Our aims were to correlate all Ishak stages of fibrosis (0-6) with fibrosis percentage (%) using computerized digital image analysis, and thereby seek to improve discrimination between varying levels of liver fibrosis. **METHODS:** Fibrosis % data were obtained by image analysis on 164 trichrome-stained liver biopsies from untreated patients with CHC, representing all Ishak stages of fibrosis. **RESULTS:** Digital analysis of fibrosis % was highly correlated with Ishak scores of fibrosis (Kendall's tau-beta=0.86, P<0.001). Receiver-operator characteristic curves showed reliable discriminative capability of our digital image measurement of fibrosis when compared with semiquantitative assessments of fibrosis. Excellent interobserver reliability was found. **CONCLUSIONS:** Recent advances in digital quantification of fibrosis have resulted in improved discrimination between the varying stages of liver fibrosis, including mild fibrosis. This method is reproducible, can detect early as well as advanced fibrosis or cirrhosis, may prove to be the best assessment of mild fibrosis, and may be more precise than semiquantitative estimation of changes for monitoring fibrosis progression or regression during clinical therapeutic trials.

Prevalence of viral markers among first-time Arab blood donors in Kuwait. Ameen R, et al. Transfusion. 2005 Dec;45(12):1973-80.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16371052&query_hl=2&itool=pubmed_DocSum

BACKGROUND: The aim of this study was to assess the effect of blood donation modes on the prevalence of viral markers among Arab first-time blood donors in Kuwait. **STUDY DESIGN AND METHODS:** Donor ethnic background was classified as Kuwaiti nationals and non-Kuwaiti Arabs. A total of 26,874 donors were screened in 2002 for the following viral markers: hepatitis C virus antibody (anti-HCV), hepatitis B surface antigen (HBsAg), anti-hepatitis B core antigen (HBc), human immunodeficiency virus-1 and -2 antibody (anti-HIV-1 and -2), HIV p24, and human T lymphotropic virus-I and -II antibody (anti-HTLV I/II). All samples positive for the presence of anti-HBc were tested for anti-HBs. Among these donors, 12,798 were first-time donors of which 74 percent were replacement and 26 percent were volunteers. **RESULTS:** The prevalence of HCV among replacement donors was significantly higher than the volunteer group. The difference between the two modes of blood donations, however, was not significant for HBsAg. The prevalence of anti-HCV among Kuwaiti national and non-Kuwaiti Arab first-time donors was 0.8 and 5.4 percent, respectively, whereas the prevalence of HBsAg was 1.1 and 3.5 percent, respectively, with the difference being significant at a p level of <0.0001. The difference observed for prevalence of anti-HBc among Kuwaiti national and non-Kuwaiti Arab donors (17 and 33.3%, respectively) was significant (p < 0.0001). Among first-time donors, 13.7 percent were positive for the presence of anti-HBs, indicating that 13.7 percent of the total Arab donor population might have had a previous infection and possible immunity to hepatitis B virus (HBV). **CONCLUSION:** A high prevalence of HBV and HCV was found among non-Kuwaiti Arab donors. The prevalence of anti-HCV was only significantly higher among replacement versus volunteer first-time donors. Therefore, there is a need to develop a strategic plan that incorporates the diverse background of the blood donors living in Kuwait.

A general method for nested RT-PCR amplification and sequencing the complete HCV genotype 1 open reading frame. Yao E, Tavis JE, Virahep-C Study Group T. Virol J. 2005 Dec 1;2(1):88 [Epub ahead of print] http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16321149&query_hl=4&itool=pubmed_DocSum

BACKGROUND: Hepatitis C virus (HCV) is a pathogenic hepatic flavivirus with a single stranded RNA genome. It has a high genetic variability and is classified into six major genotypes. Genotype 1a and 1b cause the majority of infections in the USA. Viral genomic sequence information is needed to correlate viral variation with pathology or response to therapy. However, reverse transcription-polymerase chain reaction (RT-PCR) of the HCV genome must overcome low template concentration and high target sequence diversity. Amplification conditions must hence have both high sensitivity and specificity yet recognize a heterogeneous target population to permit general amplification with minimal bias. This places divergent demands of the amplification conditions that can be very difficult to reconcile. **RESULTS:** RT and nested PCR conditions were optimized independently and systematically for amplifying the complete open reading frame (ORF) from HCV genotype 1a and 1b using several overlapping amplicons. For each amplicon, multiple pairs of nested PCR primers were optimized. Using these primers, the

success rate (defined as the rate of production of sufficient DNA for sequencing with any one of the primer pairs for a given amplicon) for amplification of 72 genotype 1a and 1b patient plasma samples averaged over 95% for all amplicons. In addition, two sets of sequencing primers were optimized for each genotype 1a and 1b. Viral consensus sequences were determined by directly sequencing the amplicons. HCV ORFs from 72 patients have been sequenced using these primers. Sequencing errors were negligible because sequencing depth was over 4-fold and both strands were sequenced. Primer bias was controlled and monitored through careful primer design and control experiments. **CONCLUSIONS:** Optimized RT-PCR and sequencing conditions are useful for rapid and reliable amplification and sequencing of HCV genotype 1a and 1b ORFs.

Approach of primary care physicians to hepatitis C: an educational survey from a Southern Italian area.

Cozzolongo R, et al. *J Infect.* 2005 Dec;51(5):396-400. Epub 2005 Jan 21.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16321651&query_hl=3&itool=pubmed_DocSum

OBJECTIVES: To assess knowledge, attitudes and practices towards hepatitis C of primary care physicians (PCPs) working in a Southern Italian area. **METHODS:** A questionnaire exploring the basic knowledge on risk factors and the management of hepatitis C virus infection was administered in two occasions to a sample of PCPs before and 2 months later the presentation of the EASL guidelines on the management of HCV infection.

RESULTS: At the first survey, drug addiction, transfusion in 1982 and sexual contact with multiple partners were listed as the most common risk factors for acquiring HCV infection. As many as 27% of PCPs believed that blood transfusion after 1994 was still an important risk factor for this infection. Only 38% of PCPs would refer HCV positive subject with abnormal ALT levels to a gastroenterologist. Some points showed a definite improvement when first and second survey were compared: the more frequent use of qualitative instead of quantitative HCV-RNA testing for diagnostic purpose and the selection of IFN plus ribavirin as the regimen of choice for active disease. **CONCLUSIONS:** The general practice management of hepatitis C may be improved using educational activities involving directly and interactively PCPs.

Changes in risk behavior and dynamics of hepatitis C virus infections among young drug users in

Amsterdam, the Netherlands. van de Laar TJ, et al. *J Med Virol.* 2005 Dec;77(4):509-18.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16254983&query_hl=5&itool=pubmed_DocSum

To elucidate the character and magnitude of the hepatitis C virus (HCV) epidemic among drug users in Amsterdam, 197 young drug users from the period 2000 to 2004 were compared with 215 counterparts from 1985 to 1989. Although injection risk behavior and HCV seroprevalence decreased sharply over time, HCV seroprevalence remains high (44%) among young drug users who have ever injected. Phylogenetic analysis shows that current HCV infections originate from diversification of strains already circulating in the past, but also from the recent introduction of new subtypes. HCV subtypes 1a and 3a remain the most prevalent among drug users in Amsterdam, but other subtypes such as 4d and 2b have entered the population. In conclusion, both the unpopularity of injecting drug use and the success of prevention campaigns are likely to be responsible for the decline in the seroprevalence of HCV and increased median time to seroconversion. Treatment of those infected chronically, in combination with the continuation of prevention programs, might decrease future HCV transmission. Copyright (c) 2005 Wiley-Liss, inc.

Prevalence and correlates of hepatitis C infection among users of North America's first medically supervised safer injection facility.

Wood E, et al. *Public Health.* 2005 Dec;119(12):1111-5. Epub 2005 Oct 7.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16214189&query_hl=5&itool=pubmed_DocSum

BACKGROUND: North America's first medically supervised safer injection facility (SIF) for illicit drug users was opened in Vancouver, Canada on 22 September 2003. We examined the prevalence and correlates of hepatitis C (HCV) infection among a representative cohort of SIF users. **METHODS:** Users of the Vancouver SIF were selected at random and asked to enrol in the Scientific Evaluation of Supervised Injecting (SEOSI) cohort. At baseline, venous blood samples were collected and an interviewer-administered questionnaire was performed. Participants who were HCV-positive were compared with HCV-negative subjects using bivariate and logistic regression analyses. **RESULTS:** Between 1 December 2003 and 30 July 2004, 691 participants were enrolled into the SEOSI cohort, among whom 605 (87.6%) were HCV-positive at baseline. Factors independently associated with HCV infection in logistic regression analyses included: involvement with the sex trade [adjusted odds ratio

(AOR) 3.7, 95% confidence interval (CI) 2.1-6.1], history of borrowing syringes (AOR 1.8, 95%CI 1.1-2.9), and history of incarceration (AOR 2.6, 95%CI 1.5-4.4). Daily heroin use was protective against HCV infection (AOR 0.6, 95%CI 0.3-0.9). **CONCLUSION:** The SIF has attracted injection drug users with a high burden of HCV infection and a substantial proportion of uninfected individuals. Although cross-sectional, this study provides some insight into historical risks for HCV infection among this population, and prospective follow-up of this cohort will be useful to determine if use of the SIF is associated with reduced risk behaviour and HCV incidence.

What do patients consider when making decisions about treatment for hepatitis C? Fraenkel L, et al. Am J Med. 2005 Dec;118(12):1387-91.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16378783&query_hl=2&itool=pubmed_DocSum

PURPOSE: There are few data describing decision-making in chronic hepatitis C infection from the patient's perspective. In this study, we sought to investigate the factors that influence patients' decisions as they consider treatment for hepatitis C infection. **SUBJECTS:** Consecutive patients attending outpatient liver clinics were recruited. Purposeful sampling was employed to include patients who were currently being treated or had recently been treated for chronic hepatitis C infection with pegylated-interferon and ribavirin as well as patients who had refused therapy. **METHODS:** We conducted focus groups until thematic saturation was reached. All focus groups were facilitated by the same PhD-level senior research scientist, and constant comparative methods were used to analyze the data. **RESULTS:** A total of 40 patients (80% male) participated in 8 focus groups. The factors influencing patients' decision-making that emerged most frequently during the focus groups were consideration of risk benefit tradeoffs, protected values, heuristics, participants' conceptualization of hepatitis C infection, social issues, and physicians' recommendations. **CONCLUSION:** Ideally, complex decision-making is based on careful consideration of the tradeoffs related to available options. Our findings suggest that patients' treatment decisions are influenced by multiple factors besides the risks and benefits of interferon and ribavirin. By being aware of these factors physicians can improve decision-making in hepatitis C infection by 1) determining whether patients' decisions are biased by heuristics or protect values, 2) understanding how patients' conceptualization of their illness influences their attitudes toward therapy, and by 3) ensuring that patients understand that social responsibilities need not necessarily preclude treatment because therapy can be discontinued if adverse effects become intolerable.

Chronic Hepatitis C Virus Management: 2000-2005 Update (January). Hughes CA, Shafran SD. Ann Pharmacother. 2005 Dec 20; [Epub ahead of print]

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16368925&query_hl=2&itool=pubmed_DocSum

OBJECTIVE: To review recent advances that have significantly changed the management of chronic hepatitis C virus (HCV) infection. **DATA SOURCES:** A MEDLINE search (2000-July 2005) was conducted using key words such as hepatitis C, interferon, pegylated interferon, and therapy. **STUDY SELECTION AND DATA EXTRACTION:** All articles pertaining to treatment of chronic HCV infection were identified. Studies evaluating HCV treatment in treatment-naïve patients were considered for this review. **DATA SYNTHESIS:** Over the past several years, response to treatment for chronic HCV infection has significantly improved with the use of pegylated interferon and ribavirin therapy. Treatment response is influenced by HCV genotype and viral load, as well as patient-related factors, including adherence. **CONCLUSIONS:** Treatment of chronic HCV infection has improved, with overall response rates of approximately 55%. Identification and management of common adverse effects is important in maximizing adherence and response to therapy. Studies are needed to further delineate the optimum treatment of chronic HCV infection in specific patient populations.

APHA 2005 HCV – RELATED ABSTRACTS OF INTEREST

Abstract #100789

Intermediate harms and benefits of hepatitis C screening

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BACKGROUND: People with chronic hepatitis C develop cirrhosis slowly providing an opportunity for secondary prevention. This pilot study was designed to describe early harms and benefits of hepatitis C virus (HCV) screening among people who test anti-HCV positive.

METHODS: Hepatitis screening program records of clients testing anti-HCV positive between 4/1/01 and 10/31/03 at a health department-based program were abstracted to obtain risk factor, demographic, and immunization information. Eligible clients were interviewed over the phone using a standardized questionnaire, which included items pertaining to medical evaluation, behaviors to prevent liver damage and HCV transmission, and aversive consequences. **RESULTS:** According to the program's records, 109 of the 269 eligible clients were susceptible to hepatitis A or B, and 54 (50%) completed the hepatitis A or B vaccination series. Of the 269 clients, 56 (21%) were reached by phone, and 44 (79%) consented to the interview. Of these, 31 (70%) saw a physician regarding the test result. Among the 33 prior drinkers, 28 (85%) reported reducing alcohol use. All interviewed clients reported at least one positive step to protect their liver or prevent transmission to others. However, 51% reported at least one harm related to knowing their hepatitis C status, most commonly difficulty obtaining health insurance. Nevertheless, 86% reported that they were glad that they were tested. **CONCLUSIONS:** Results from this pilot study suggest that most clients who tested anti-HCV positive undertook at least one positive action to protect their livers, and most reported satisfaction with their decision to be tested.

Abstract #114702

Effects of hepatitis C-associated knowledge on risk behaviors among IDUs in Puerto Rico

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This study aimed to identify the effect of hepatitis C-associated knowledge on injection and sexual risk behaviors among a cohort of street-recruited injection drug users (IDUs). Participants underwent a structured interview at twelve-month intervals, HIV and hepatitis C virus (HCV) antibody testing, pretest and posttest counseling. The counseling sessions focused on how to prevent hepatitis infection, risk reduction, how to recognize hepatitis symptoms, alcohol consumption and disease progression. IDUs who reported at baseline that did not know their HCV status were reassessed at 12-months to detect possible behavioral changes after disclosure of their HCV status and hepatitis counseling. HCV-associated knowledge was assessed using a sixteen-item instrument based on CDC information. The prevalence of HCV infection at baseline was 78.2%. Of 212 IDUs that were reassessed at follow-up, 58% showed a high level of HCV-associated knowledge. After adjusting for sociodemographics, HIV status, depression symptoms, drug treatment experience and the corresponding behavior at baseline, IDUs did not show significant reductions in injection or sex risk behavior after disclosure of a positive HCV test result. Conversely, multivariate analyses results showed that those with a high level of HCV-associated knowledge were significantly more likely to reduce injection risk behaviors such as sharing the cooker, sharing rinse water and backloading during drug preparation. None of the tests showed a significant association between hepatitis knowledge and sex risk behaviors. Exposure to hepatitis information is crucial in the process of HCV status disclosure in order to effectively prevent the transmission of HCV infection and other blood-borne diseases.

Abstract #111316

Injection-related risk behaviors among cases of acute hepatitis C

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BACKGROUND: Injection drug use (IDU) is the primary risk factor for hepatitis C virus (HCV) infection in the United States. Understanding factors associated with infection among injectors is critical to designing appropriate prevention programs. **METHODS:** During 2001 to 2004, acute, symptomatic cases of hepatitis C were identified in six counties through Sentinel Surveillance. Cases were defined by an acute illness with discrete onset of symptoms; serum ALT levels >2.5 times upper limit of normal; and positive for HCV antibody or HCV RNA and negative for hepatitis A or B. Patients were extensively interviewed for risk factors for infection during the potential exposure period. **RESULTS:** A total of 111 cases were identified; 93 (83.8%) completed an interview. The most common risk factor was IDU, reported by 40 (43.0%) cases. Injectors were significantly younger than non-injectors (median 30 years vs. 39 years, respectively; $p < 0.001$). Among injectors, 45% reported initiation of injection in the previous year; 95% reported injecting heroin (62.5%), cocaine (87.5%), or methamphetamine (67.5%). Sharing injection equipment was reported by 80%, including needles (70%) or non-syringe paraphernalia (70%). Compared with injectors who reported not sharing, injectors who shared were significantly more likely to have injected for less than one year (53.1% vs. 12.5%, $p = 0.04$) and use heroin (75.0% vs. 12.5%, $p = 0.0013$). **CONCLUSIONS:** Almost half of injectors with acute hepatitis C reported initiating IDU in the previous year. Most injectors reported sharing injection equipment, particularly recent initiators. Hepatitis C prevention strategies should focus on preventing IDU and reducing injection-related risk behaviors.

Abstract #104073

Prevalence of hepatitis C in HIV-infected persons: Findings from an interview project

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BACKGROUND: An estimated 950,000 persons in the U.S. are infected with HIV and 3.9 million infected with hepatitis C virus (HCV). HIV/HCV co-infection can be high (e.g., in persons who ever injected drugs [IDU]) and can affect the progress and treatment of both diseases. We present self-reported prevalence of HCV and factors associated with HIV/HCV co-infection from the Supplement to HIV and AIDS Surveillance (SHAS) project.

METHODS: Data are from 19 sites that participated in SHAS (a behavioral interview study of HIV-infected adults age 18 and older) from May 2000 through December 2003. Chi square and logistic regression analyses identified factors associated with co-infection. **RESULTS:** Of 8129 HIV-positive persons, 14% (1135) reported a health care provider ever told them they had HCV. Individual factors significantly associated ($P < .001$) with HCV included ever IDU (46% vs. 6% never IDU), ever in jail (22% vs. 7% never in jail) and ≥ 10 lifetime sex partners (16% vs. 8% < 10 partners). In regression analyses among ever IDU, HCV was associated with ever sharing needles (adjusted odds ratio [AOR] 2.0, 95% confidence interval [CI] 1.5-2.6), ≥ 100 lifetime injections (AOR 1.9, CI 1.5-2.3), and ever in jail (AOR 1.4, CI 1.1-1.9). **CONCLUSIONS:** HCV co-infection was common in this HIV-infected population. Many HIV medication regimens are hepatotoxic; specific prevention messages should be targeted for those co-infected (i.e., hepatitis A vaccination, eliminating use of alcohol, risk of transmitting two viral diseases). Ascertaining HIV/HCV co-infection is an important consideration for individual treatment decisions, and for public health planning.

Abstract #118150

Barriers to seeking medical treatment for chronic hepatitis C (HCV) infection among young injecting drug users (IDUs) in metropolitan Chicago

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OBJECTIVE: To describe barriers to seeking treatment for chronic hepatitis C infection among Chicago IDUs participating in the NIDA-funded "Early natural history of HCV infection among young IDUs study (NAT_HCV)", 2002-2005. **METHODS:** To date, 116 HCV antibody-positive, young (median age=25), predominantly non-Hispanic white (58%), male (59%) IDUs have enrolled in NAT_HCV after referral from studies of street-recruited IDUs. Data were gathered using audio computer-assisted self-interview and person-to-person interviews.

RESULTS: Participants had relatively recent HCV infection (estimated median years of infection=2.5). We hypothesized that these participants would have better treatment responses than IDUs reported in the literature with more established chronic infection. Thus, those having a detectable HCV viral load were encouraged to consider liver disease evaluation and treatment ($n=83$, 72%). However, only 3 (4%) participants with medical insurance commenced treatment, while the remaining 70 encountered $\square 1$ obstacles. First, all 70 participants had no medical coverage. All were directed to the county hospital after 5 participants (7%) unsuccessfully applied for Medicaid. Seven participants (10%) attended an evaluation visit, but none commenced drug therapy. Participants not attending the evaluation visit cited $\square 1$ major barriers to obtaining treatment, including: 1) having to seek medical care at a county hospital (most of the study population were suburban residents); 2) requirement of drug use reduction/cessation; 3) fear of liver biopsy; 4) side-effects and/or rigor of treatment regimen. **CONCLUSION:** There are substantial barriers to accessing treatment among young IDUs with recent HCV infections. These include lack of health care coverage and a stringent treatment process.

Abstract #107560

Gaps in knowledge about hepatitis C among drug treatment program staff and administrators

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Drug treatment programs are uniquely situated to educate and test drug users for HCV, and facilitate their access to medical treatment when necessary. Drug treatment staff need to be well informed about HCV because their counsel can often influence patients' health-preserving behaviors. Because little is known about the level of HCV knowledge among drug treatment staff, this paper reports the results of a 36-item true-false HCV knowledge assessment among a convenience sample ($N=61$) of drug treatment staff and administrators attending a one-day professional conference in NY City. Scores ranged from 4 to 34 correct, with a mean of 22. Of special concern is that 10 of the 36 items were answered incorrectly by at least half of the respondents. For example, only 41% knew that IDUs are more likely to have HCV than HIV; only 23% knew that few people with HCV infection will develop

cirrhosis, and only 15% knew that some people exposed to HCV clear the virus spontaneously. Respondents answered significantly more items correctly if they had attended an HCV workshop as compared with those who had not (24 vs. 15, $p < .001$), and if they had been in the substance abuse treatment field for at least 3 years as compared with those with less experience (24 vs. 19, $p = .017$). These results underscore previous research findings of staff who perceived they needed HCV education yet few received such education at their drug treatment program. Results suggest the critical need for HCV staff training, especially those new to the field.

Abstract #111182

Unprotected Sexual Intercourse, Use of Drugs, and Prevalence of HIV, Other Sexually Transmitted Diseases, and Hepatitis C Among Young Men in California: Results from a Population-Based Survey

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OBJECTIVES: To assess risk behaviors and prevalence of HIV, gonorrhea, chlamydia, and hepatitis C among a population-based sample of men aged 18 to 35 years from 5 counties in northern California. **METHODS:** Blocks below the 10th percentile of median income within Alameda, Contra Costa, San Francisco, San Joaquin, and San Mateo counties were identified. Outreach teams recruited participants by going door-to-door in randomly-selected blocks. Selected characteristics and risk exposures within the last 6 months were assessed. Blood and urine samples were collected to assess disease outcomes. Results: Nearly half (49.0%) of 1,293 participants were Latino; 20.3% were African American, 12.6% were white; 48.6% were born outside of the United States. Thirty-five percent reported no or sporadic employment during the previous 6 months. Three-in-10 (30.4%) reported 2 or more sexual partners in the previous 6 months; no protection was reported for 62.6% of acts of vaginal intercourse during the past 6 months. Fifty-five (4.3%) men reported recent sex with men or transgender partners, but no protection was reported for 75.7% and 79.9% of acts of receptive and insertive anal intercourse, respectively. Cocaine and methamphetamine use during the past 6 months was 12.1% and 7.5%. Overall prevalence of HIV was 0.80%; gonorrhea, 0.40%; chlamydia, 4.05%; and hepatitis C, 1.33% **CONCLUSION:** A population-based, randomized sample of low-income young men from selected areas of California found very high levels of reported sexual risk, with respect to condom use, and in particular higher rates of unprotected intercourse with male compared with female partners.

Abstract #118073

Social network correlates of HCV-specific risk behaviors in injection drug users

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Injection drug use is the leading cause of hepatitis C virus (HCV) in the U.S. Although HCV and HIV share common transmission modes, evidence shows that HCV is acquired quicker after initiation of injection and more efficiently transmitted parenterally through low-dose percutaneous exposure, indicating different risk profiles of the two viruses. Compared to massive HIV research, few studies have intensively examined factors contributing to HCV infection especially in social contexts. This study applied social network methodology in a sample of inner-city injection drug users (IDUs). Data are collected as a part of the STEP-into-Action project, a network-oriented HIV/STDs prevention intervention among IDUs. A 3-dimensional HCV risk assessment survey characteristic to the drug injecting population is administered. Baseline data are analyzed exploring egocentric network correlates of HCV-specific risk behaviors, focusing on structure of, and the characteristics of the members of the drug network. Most of the current sample are African-American males. IDUs who have a large, low density drug network, have

more new injectors in network, or have more network members who inject cocaine are more likely to perform HCV-specific risk behaviors. Degree of overlap between injection network and sex network is also associated with level of HCV-specific risk behaviors. The expected whole sample is anticipated to be consistent with the current sample. As HCV-related chronic liver disease becomes a leading cause of hospital admissions and deaths among persons living with HIV/AIDS, this information may be useful in understanding HCV risk profile and promoting specific HIV/HCV combined intervention targeting high-risk IDUs.