

HCV ADVOCATE WEEKLY NEWS REVIEW

Review of HCV, HBV and HIV/HCV Coinfection Related News and Highlights

*Alan Franciscus
Editor-in-Chief*

Week Ending: May 17th 2008

In This Issue:

- [New theory suggests how hepatitis C may cause rare immune disease](#)
- [85 Now Identified With Hepatitis C in Las Vegas Investigation](#)
- [Hep C Drugs Slug It Out](#)
- [City clinic offers total care for hepatitis C](#)
- [HCV Common in Former Soviet Union Immigrants Living in NYC](#)
- [WARNING: Sulfasalazine for Rheumatoid Arthritis May Cause Severe Hepatotoxicity](#)
- [New treatment for hepatitis C](#)
- [Pharmasset Commences Dosing R7128 Cohorts 3 and 4 for the Treatment of Chronic Hepatitis C](#)
- [Students Bake Cookies For World Hepatitis Awareness Day](#)
- [Independent probe refused](#)
- [Acute Hepatitis C Virus Infections Attributed to Unsafe Injection Practices at an Endoscopy Clinic --- Nevada, 2007](#)
- [Silent disease an issue locally](#)
- [Warning issued that HIV drug can harm liver](#)
- [Hep C patients find hope](#)
- [A virus in hiding](#)
- [Hundreds Walk In Annual Hepatitis C Awareness Event](#)
- [Patient safety bill would publicize doctors' names](#)
- [Nexavar Significantly Improves Overall Survival by 47 Percent in Asia-Pacific Liver Cancer Study](#)
- [Schering-Plough Highlights PEGINTRON\(TM\) And Boceprevir Hepatitis C Data Presentations At Digestive Disease Week \(DDW\) Annual Meeting](#)

- [Higher LDL cholesterol levels mean better response to anti-HCV treatment in HIV/HCV coinfecting patients](#)

May 10th, 2008

New theory suggests how hepatitis C may cause rare immune disease

<http://www.news-medical.net>

Of the hepatitis alphabet, the C variant may be the nastiest. In 1990, researchers observed that most patients with hepatitis C also develop a rare autoimmune disease called **mixed cryoglobulinemia**, a condition that frequently leads to cancer, arthritis or both.

Now, researchers at Rockefeller University say that a decade-old explanation of how one disease causes the other is likely wrong, and instead offer a new - albeit controversial - theory of their own: that the pathogen causing the disease zeros in on a specific cellular target that has yet to be identified.

In persons infected with hepatitis C virus, the immune system initially ramps up the production of infection-fighting B cells, which make molecules called antibodies. As these B cells multiply, they make antibodies and release them into the blood where, under normal circumstances, they latch onto the invading pathogens and mark them for destruction. In mixed cryoglobulinemia, there is a problem: the B cells don't stop multiplying, sending the body into a tailspin of pathological conditions that follow a slow, smoldering course.

The uncanny association between hepatitis C and mixed cryoglobulinemia, ever since it was observed, perplexed researchers. Since hepatitis C infects the liver, not B cells, how does it trigger an immune disease? A popular theory proposed that a protein that peppers the outer coat of the virus binds to a receptor called CD81, which is found on the surface of almost every cell in the body, including B cells. If the viral protein directly latches onto the surface of a B cell, it can trigger uncontrolled B cell proliferation.

But scientists led by Lynn Dustin, an associate professor in Charles Rice's Laboratory of Virology and Infectious Disease, reveal that, test after test, the theory came up short. "If the theory were true, then you would expect all different kinds of B cells to be activated and proliferating abnormally - which is what you see in mixed cryoglobulinemia - because CD81 is everywhere," says Dustin. "Instead, every time we analyzed the blood of patients with hepatitis C and mixed cryoglobulinemia, we found that the same B cells were being activated."

In the immune system, billions of B cells are on guard. Each B cell can produce only one kind of antibody, which ordinarily can recognize and fight off only one specific pathogen. Since many of the B cells that Dustin and Edgar Charles, who is a Rockefeller University clinical scholar, isolated from these patients had remarkably similar antibodies as well as many other markers that were similar, the findings suggest that the virus doesn't activate B cells through the ubiquitous CD81 receptor. Otherwise, B cells with different antibody molecules and markers would be activated. "Already, there's a bias in terms of what antigen these B cells are seeing, which kind of rules out this idea that the virus is activating these B cells nonspecifically," says Dustin.

To confirm the findings, which appear in the February 1 edition of *Blood*, Dustin and Charles enrolled hepatitis C virus-infected patients at Rockefeller University Hospital and looked at their antibody genes, which were identical in the activated B cells from almost every mixed cryoglobulinemia patient. Dustin says this finding is all the more remarkable given that antibody genes must be chopped up and rearranged in order to diversify their repertoire of antibodies and accommodate the ever-growing number of microbes trying to break into the body. "The genes were all rearranged the same way, and the odds of that happening are on the order of one in a billion," says Dustin.

To date, technical obstacles and the nature of the disease prevent scientists from identifying the exact pathogen that triggers mixed cryoglobulinemia, but Dustin and Charles discovered another clue that could help them find the answer: That these antibodies are very similar to rheumatoid factors, which may provide insight into how they cause debilitating autoimmune disease.

In a way, says Charles, the findings signal good news for patients living with hepatitis C and mixed cryoglobulinemia - an estimated 100-170 million worldwide. "It suggests that the survival of these B cells depends on their seeing the pathogen. So finding this elusive pathogen may be the key to preventing these once beneficial B cells from becoming cancerous."

Blood 111(3): 1344-1356 (February 1, 2008)

<http://www.rockefeller.edu>

May 11th, 2008

85 Now Identified With Hepatitis C in Las Vegas Investigation

<http://www.injuryboard.com>

Jane Akre

The most expansive public health investigation in U.S. history has added more names to the list of patients who've contracted hepatitis C from the reuse of syringes and vials at Las Vegas area clinics.

Now health officials say 77 more people treated at the Endoscopy Center of Southern Nevada have been diagnosed with hepatitis C.

It's unclear how they were infected, though all have visited the center and none had hepatitis C or any risks factors before they were a patient there between March 2004 and January 11th of this year.

Risk factors for hepatitis C include IV drug use, sharing needles, an organ transplant or blood transfusion before 1992, dialysis for kidney failure or having sexual contact with a known carrier of hepatitis C.

The latest cases identified are among 400 former patients of the Endoscopy Center and another clinic on Shadow Lane who have recently tested positive.

The remaining may have had a risk factor for exposure. It's estimated about three to four percent of the population carries hepatitis C but is asymptomatic.

Brian Labus, senior epidemiologist for the Southern Nevada Health District tells the Las Vegas Review-Journal, "We can't say for certain that they got it at the clinic; however, the clinic is the obvious source of infection considering they had no other risk factors," Labus said.

Genetic testing can be useful to identify the source of the disease in clusters, but Labus says that the virus mutates rapidly making it difficult to identify the source.

Altogether there are now 85 confirmed cases of hepatitis C linked to the Endoscopy Center and the Desert Shadow Endoscopy Center also run by majority owner, Dr. Dipak Desai and his partner Dr. Eladio Carrera. The medical licenses of both men have been suspended pending a hearing by the Nevada State Board of Medical Examiners.

Health officials say at least 40,000 patients and thousands more of their exposed loved ones are being tested for hepatitis C, B and HIV. The original exposure at the clinic came through the reuse of syringes and single-use vials of sedative.

Reportedly, 10,000 former patients cannot be located.

There is no cure for hepatitis C, a blood-borne disease that can cause cirrhosis of the liver, liver cancer and death.

Last week, Dr. Desai was stopped by a car dealer from shipping his two Mercedes out of the country to Dubai.

The FBI, local police and State Attorney's office is also conducting criminal investigations into Dr. Desai who is alleged to have told his medical personnel to reuse syringes and other equipment in a cost-saving move.

Those inside the investigation say he also over-billed Medicaid for services.

Several hundred people have joined into class-action lawsuits against Dr. Desai and his clinic.

Lawyers for Dr. Desai want plaintiffs to fill out a 27-page questionnaire detailing information about their sex lives and drug use. Lawyers for plaintiffs say it is a designed to embarrass and humiliate those who have filed suit. Dr. Desai's lawyers believe it's necessary to determine whether those who are suing have any additional risk factors.

On Friday the Nevada State Board Medical Examiners refused to turn over to the District Attorney's office complaints against Dr. Desai.

Chief Deputy District Attorney Scott Mitchell told the Las Vegas Sun, "I think they are so far removed from what they're supposed to be doing that it hasn't occurred to them that they're protection for the public, not interference for the doctors."

Dr. Desai, one of the most prominent doctors in the state, was previously one of the nine board

member and many believe his friendships with other board members as well as Gov. Jim Gibbons is the only reason he is not in jail now.

The doctor has already paid the city \$500,000 in fines.

May 12th, 2008

Hep C Drugs Slug It Out

<http://www.fool.com>

By Brian Lawler

When a drug seems destined for approval, it's easy to get so excited about its prospects that you discount its competition. Last month, Vertex Pharmaceuticals (Nasdaq: VRTX) produced very strong study data on its lead antiviral hepatitis C drug, telaprevir, at the European Association for the Study of the Liver (EASL) annual meeting. But the resulting excitement may have blinded analysts and investors to an equally promising rival.

Digging through the data

The contender in question is boceprevir, a hepatitis C treatment from Schering-Plough (NYSE: SGP). Though Vertex's impressive results led EASL attendees to crown telaprevir the superior protease inhibitor, the data is not as clear-cut as it seems.

Patients treated with telaprevir in Vertex's PROVE-1 and PROVE-2 phase 2 studies experienced respective cure rates (what is known as a sustained virologic response, or SVR) of 61% and 68%. If its current results hold up, only 55% and 57% of patients in the two groups of Schering's phase 2 SPRINT-1 study have thus far achieved undetectable levels of hepatitis C virus 12 weeks after their boceprevir treatments ended.

So telaprevir's efficacy tops boceprevir's, right? Not yet. We'll first need to know how SPRINT-1's patients fared compared with the study's control group.

The population problem

Variables such as weight, initial viral count, and a patient's race can alter the effectiveness of hepatitis C treatments. Multiple studies have shown that for whatever genetic or virologic reason, African-American patients respond significantly worse to hepatitis C treatment than some other patient groups.

In the SPRINT-1 study, 16% of patients were African-American, compared to only 10% in PROVE-1, and less than 6% in PROVE-2. Unfortunately, the SPRINT-1 control group SVR data isn't out yet, so these demographics are the only way to judge which drug faced a potentially less-responsive patient population.

Interim study efficacy results do suggest that the SPRINT-1 study faced a rougher battle, even beyond patient characteristics. Only 34% of the SPRINT-1 control group patients were measured as having undetectable levels of hepatitis C in their blood after 12 weeks of treatment, compared to 39% of control patients in the PROVE-1 study, even though both control groups received similar standards of care (Pegasys and PEG-Intron).

This is important; this early viral response data is linked to the number of patients who will ultimately be declared cured. The data suggests that SPRINT-1's control group will yield lower cure rates than PROVE-1 and PROVE-2's did.

Interestingly, the studies' differing demographics could not only explain the apparent efficacy gap between boceprevir and telaprevir, but also the PROVE-2 study's higher cure rate than PROVE-1's. Both PROVE-1 and PROVE-2 produced cure rates 20 percentage points greater than those of their respective control groups. Once the SPRINT-1 control group's longer-term cure rate data is released, we'll be much better able to compare its effectiveness with the PROVE studies.

The comparisons don't end with efficacy

On the safety side of the equation, both drugs have prompted similar numbers of patients to drop out because of adverse events. SPRINT-1 dropout rates ranged between 11% and 15% in the study's various groups of boceprevir-treated patients, compared to 8% in the control group. PROVE-1 and PROVE-2 dropout rates were a combined 17% in telaprevir-treated patients, and 10% in the control groups.

Right now, telaprevir is ahead in the race to be the first antiviral hepatitis C agent on the market. Its efficacy and safety data -- which, as ViroPharma (Nasdaq: VPHM) has shown, are mighty important -- are also much better-known than boceprevir's because it has been tested in more patients and in a wider variety of studies. All things considered, telaprevir is a safer bet than boceprevir to reach the market at this point.

However, claiming that telaprevir is better than boceprevir, or superior to some of the polymerase and other protease inhibitors from InterMune (Nasdaq: ITMN), Johnson & Johnson (NYSE: JNJ) and Medivir, or Pharmasset (Nasdaq: VRUS), is a dangerous gamble -- at least until we learn how boceprevir's results in SPRINT-1 differed from those of its control group.

City clinic offers total care for hepatitis C

<http://news.guelphmercury.com>

Rob O'Flanagan

roflanagan@guelphmercury.com

A hepatitis C clinic in Guelph could soon become the first incorporated hepatitis C agency in Ontario, and perhaps the first in Canada.

Director Dr. Chris Steingart said patients need more than medical treatment for the debilitating virus, which affects the function of the liver. They also have housing needs, need assistance with mental health issues and often require addiction management services, he said.

The new Sanguen Health Centre, which is housed in the same building as Guelph's Masai Centre for Local, Regional and Global Health, and which opened last fall, is positioning itself to offer a totality of care.

"It is a tough treatment, and unless we address a lot of other issues, including non-health, social issues, it is difficult to successfully complete this treatment," said Steingart.

Slightly less than one per cent of the population the Wellington-Dufferin-Guelph area, roughly 1,000 residents, has hepatitis C. About 30 per cent of those are unaware they are infected.

Pamela Billings, 42, contracted hepatitis C more than 20 years ago. It took several years for the symptoms of the illness to show. Extreme fatigue alerted her that something was wrong. Until recently, she was not aware that the virus could potentially be cured.

She began a lengthy course of treatment at the Sanguen Health Centre, treatment that has a number of side-effects, including headaches, loss of appetite and nausea.

"You take two pills in the morning, two pills at night, and an injection once a week," said Billings, describing a treatment that lasts for nearly a year.

"I don't know if I would have been able to make it without Dr. Steingart," she said.

"No matter how hard the treatment was going to be, what I had to know and believe was that no matter where I was, no matter what time of day, if I needed support, I would be able to get it," Billings said.

There has been an absence of complete care for hep-C sufferers in the community, Steingart added.

"That is what prompted us to not just open this clinic, but to expand it and make it more than a clinic," he said, adding that he hopes the provincial government will provide funding for the clinic.

Currently there are no funded hep-C clinics or service agencies in the province, he said.

"As far as I know, we would be the first in Ontario, and maybe Canada," he said, adding that a satellite clinic is in the process of being established in Kitchener-Waterloo.

Existing health services for hepatitis C were overloaded before the clinic opened last fall, he added.

"We are trying to increase the availability of services for people in the more marginalized populations, who have hep C -- number one, to get them tested for hep C, and number two, to get them accessed and treated," he explained.

"Along with that, to try to help them with all these other issues that they have, so that we can be successful with treatment."

May 14th, 2008

HCV Common in Former Soviet Union Immigrants Living in NYC

<http://www.medscape.com>

NEW YORK (Reuters Health) May 07 - The prevalence of hepatitis C virus infection is high

among immigrants from the former Soviet Union residing in the New York City metropolitan area, a research shows.

While injection drug use is the most common cause of HCV transmission in the US, inadequately sterilized medical equipment and blood transfusions are the likely modes of HCV transmission in former Soviet Union immigrants, researchers say.

Dr. Steven Batash from New York University School of Medicine and colleagues conducted a 3-day community-based HCV screening program in Brooklyn and Queens - the two areas in New York with the highest density of former Soviet Union immigrants. "Russian cable television was used to invite subjects to come in for free HCV screening."

The overall prevalence of HCV infection among the 283 subjects screened was 28.3%, the team reports in the April issue of the *American Journal of Gastroenterology*. The prevalence was similar in men and women (30.3% and 26.5%, respectively) and was highest in people aged 70 years or older (35.0%).

HCV seropositivity was 11.1% in immigrants from Russia, 29.0% from Uzbekistan, 31.0% from Ukraine, and 36.8% from other regions.

In multivariable analysis, intramuscular injections (odds ratio, 9.1) and blood transfusions (OR, 3.2) were the only variables significantly associated with HCV infection.

"Given the high prevalence of HCV infection among immigrants from the former Soviet Union, our findings suggest that universal HCV testing should be strongly considered in this population," Dr. Batash and colleagues conclude.

Am J Gastroenterol 2008;103:922-927.

WARNING: Sulfasalazine for Rheumatoid Arthritis May Cause Severe Hepatotoxicity

www.medscape.com

NEW YORK (Reuters Health) May 06 - Potentially fatal hepatotoxicity can be triggered by **sulfasalazine** therapy for rheumatoid arthritis, according to a series of case reports investigated by UK researchers. This adverse effect seems particularly likely to occur in certain black patients.

"Serious hepatotoxicity, often associated with a skin rash and variably associated with evidence of an allergic reaction on blood tests - eosinophilia -- occurs within 6 weeks of starting sulfasalazine," lead investigator Dr. Paresh Jobanputra told Reuters Health. "Our experiences," he added, "indicate that such toxicity is likely to be missed by current recommendations for drug monitoring."

Liver failure in two patients prompted Dr. Jobanputra of the University of Birmingham and colleagues to set up a local reporting system for adverse events, to augment existing approaches.

Over a period of 7 years, 10 cases were identified, of which 8 occurred during the surveillance period, they report in the April 11th issue of *BMC Musculoskeletal Disorders*. Eight of the patients were hospitalized, two with hepatic failure, and one died following a liver transplant.

Seven patients had a skin rash, three had eosinophilia and one had interstitial nephritis. Five of the eight patients were black.

Dr. Jobanputra pointed out that "drug toxicity was particularly common in people of a Black British background or African or Caribbean descent."

"We estimate," he concluded, "that this drug reaction occurs in 1 of 250 patients treated with this drug. Although this risk frequency is regarded by convention as uncommon, the potential severity of reactions may make some patients and practitioners wary of sulfasalazine."

BMC Musculoskeletal Disorders 2008;9.

New treatment for hepatitis C

www.physorg.com

Researchers at the University of Oklahoma Health Sciences Center have found a new use for an old drug. Their findings appear online in the *American Journal of Gastroenterology*.

The drug, **Fluvastatin**, has been approved since 1993 by the U.S. Food and Drug Administration for the treatment of elevated cholesterol in adults. Millions of patients have taken Fluvastatin for cholesterol without difficulty.

In a study of 31 veterans at the Veteran's Administration Medical Center in Oklahoma City, researchers found that Fluvastatin significantly lowered the viral load, or levels of hepatitis C virus, for up to six weeks when used alone. Hepatitis C is the disease that claimed the life of Oklahoma and Yankee baseball great Mickey Mantle.

"This research is the first to demonstrate the antiviral activity of Fluvastatin in human beings infected with hepatitis C, most of whom were non-responders to the standard of care treatment," said Ted Bader, M.D., the principle investigator on the project and the director of liver diseases at the OU Health Sciences Center.

Since Fluvastatin will not completely clear the hepatitis C virus by itself, researchers have started a phase II randomized, controlled trial that combines Fluvastatin with the standard treatment of peg-interferon and ribavirin. They hope to use the combination of medicines to significantly improve the cure rate for hepatitis C. After further required testing and approval, the drug could be available as a new treatment for hepatitis C far sooner than any other anti-hepatitis C drug currently under research and development.

"We need additional drugs to add to this regimen to improve the cure rate," Bader said. "When patients are cured, they feel dramatically better, their health care costs plummet, their risk of liver cancer drops dramatically, and if they do not have cirrhosis, they will not need a liver

transplant. Moreover, they are no longer infectious.”

In the initial investigative study funded by the VA Research Foundation of Oklahoma City and Dr. Michael Bronze at the University of Oklahoma College of Medicine, veterans with chronic HCV were given oral doses of Fluvastatin daily for two to 12 weeks. Within a month, half of the patients showed a reduction of the virus. One patient’s viral load was about 50 times lower than before taking Fluvastatin.

Hepatitis C is a significant problem for Oklahoma. More than 80,000 Oklahomans have chronic hepatitis C (HCV), but less than 5 percent have been treated. HCV is the leading cause of liver-related deaths in our state and also is the cause for the majority of the 70 liver transplants performed in Oklahoma each year.

Nationwide, 2 percent of Americans (about 4 million) are infected with chronic hepatitis C, which is four times the number of patients infected with HIV. Chronic hepatitis C is often asymptomatic and can lead to progressive liver disease.

Most people with hepatitis C contracted the disease through blood transfusions before 1992 when a test was implemented to screen for the disease. You also can get the virus by injecting drugs with contaminated needles and, less commonly, from contaminated needles used in tattooing and body piercing.

Source: University of Oklahoma

Pharmasset Commences Dosing R7128 Cohorts 3 and 4 for the Treatment of Chronic Hepatitis C

<http://biz.yahoo.com>

- Two 4-week cohorts will evaluate R7128 1000mg BID in HCV genotype 1 treatment-naive patients and R7128 1500mg BID in HCV genotypes 2 or 3 treatment-experienced patients -

PRINCETON, New Jersey, May 14 /PRNewswire/ -- Pharmasset, Inc. (Nasdaq: VRUS - News) has commenced dosing two additional cohorts of a 4-week Phase 1 study of R7128 in combination with Pegasys® (peginterferon alfa-2a) plus Copegus® (ribavirin) in both treatment-naive and treatment-experienced patients chronically-infected with hepatitis C virus (HCV) genotypes 1, 2 and 3. R7128, a prodrug of PSI-6130, is a nucleoside analogue polymerase inhibitor of HCV that is being developed through Pharmasset's collaboration with Roche.

The purpose of this 4-week study is to evaluate the safety, tolerability, pharmacokinetics and antiviral activity of R7128 in the clinically-relevant setting of combination therapy for chronic HCV infection. The previously planned Cohort 3 will continue dose-exploration with administration of R7128 1000mg twice-daily (BID) in treatment-naive patients with HCV genotype 1. Cohort 4 will evaluate R7128 1500mg BID administered in combination with Pegasys plus Copegus in treatment-experienced patients with genotypes 2 or 3 who did not achieve a sustained virologic response (SVR) with previous interferon-based therapy.

There will be 25 patients in each dose cohort with 20 patients randomized to receive R7128 and

5 patients randomized to receive placebo. After completing 4 weeks of the triple combination regimen and a follow-up period of 4 weeks of Pegasys plus Copegus, patients will receive an additional 16 to 40 weeks of open-label dosing of Pegasys plus Copegus under a separate protocol to complete the standard of care regimen for each genotype. Preliminary safety and antiviral activity data from the 4-week combination treatment period are anticipated during the third quarter of 2008.

"Based on our pharmacokinetic modeling, we believe that the R7128 1000mg BID combination dosing regimen in Cohort 3 may be able to achieve similar antiviral responses as were demonstrated with R7128 1500mg BID in Cohort 2," stated Dr. Michelle Berrey, Pharmasset's Chief Medical Officer. "Cohort 4 will be the first administration of R7128 in patients with HCV genotypes 2 or 3, and thus will serve as proof-of-concept for this population who we believe represent an area of great unmet medical need. If R7128 shows activity in HCV genotype 2 or 3 patients, this would demonstrate a distinct clinical attribute of nucleoside polymerase inhibitors."

Please see www.clinicaltrials.gov or e-mail clinicaltrials@pharmasset.com for more information.

About R7128

R7128 is being developed for the treatment of chronic HCV infection. R7128 is a prodrug of PSI-6130, a cytidine nucleoside analog inhibitor of HCV RNA polymerase. A prodrug is a chemically modified form of a molecule designed to enhance the absorption, distribution and metabolic properties of that molecule. Results from a Phase 1 oral single ascending dose study of R7128 in 46 healthy male volunteers showed that R7128 was generally well tolerated with no serious adverse events in doses up to 9000 mg.

In a Phase 1 study, R7128 demonstrated potent, dose-dependent antiviral activity across four genotype 1 prior treatment-failure patient cohorts (n=40) receiving 750 mg or 1500 mg administered either once-daily or twice-daily for 14 days as monotherapy. The greatest mean decrease in HCV RNA from baseline was demonstrated in the patient cohort that received 1500 mg twice-daily, the highest dose of R7128 administered in the study. These patients demonstrated a mean 2.7 log₁₀ IU/mL (>99%) decrease in HCV RNA. There was no evidence of the development of viral resistance in any dose cohort after 14 days of dosing.

In a 4-week Phase 1 combination study that was conducted in 50 treatment-naive patients chronically infected with HCV genotype 1, R7128 demonstrated potent short-term antiviral activity and was generally safe and well tolerated. Eighty-five percent (85%) of patients receiving R7128 1500mg twice-daily (BID) with Pegasys plus Copegus for 4 weeks achieved undetectable HCV RNA levels with safety and tolerability comparable to placebo with Pegasys plus Copegus.

About Hepatitis C

Hepatitis C is a blood-borne infectious disease of the liver and is a leading cause of chronic liver disease and liver transplants. The WHO estimates that nearly 180 million people worldwide, or approximately 3% of the world's population, are infected with hepatitis C virus (HCV). The CDC has reported that almost four million people in the United States have been infected with HCV, of whom 2.7 million are chronically infected.

About Pharmasset

Pharmasset is a clinical-stage pharmaceutical company committed to discovering, developing and commercializing novel drugs to treat viral infections. Pharmasset's primary focus is on the development of oral therapeutics for the treatment of hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV).

Pharmasset is currently developing three product candidates. Clevudine, for the treatment of chronic HBV infection, is enrolling Phase 3 clinical trials for registration in North, Central and South America and Europe. Clevudine is already approved for HBV in South Korea and marketed by Bukwang Pharmaceuticals in South Korea under the brand name Levovir. R7128, an oral treatment for chronic HCV infection, is in a 4-week Phase 1 clinical trial in combination with Pegasys® plus Copegus® through a strategic collaboration with Roche. Racivir, which is being developed for the treatment of HIV in combination with other approved HIV drugs, has completed a Phase 2 clinical trial.

<http://www.pharmasset.com>

Students Bake Cookies For World Hepatitis Awareness Day

<http://www.wcsh6.com>

BANGOR (NEWS CENTER) -- Students at United Technologies Center in Bangor are "cooking up" viral hepatitis education. They hope to raise awareness of viral hepatitis testing and vaccinations here in Maine.

They are cooking gingerbread cookies and decorating them with the phrase "Am I number 12?" because one in 12 people worldwide are infected with viral hepatitis B or C. Also, because not everyone has symptoms, many people are unaware of their infection and do not receive proper treatment.

The students will deliver cookies to people potentially at risk around the Bangor area, including the homeless shelter, Eastern Maine Aids Network, and Riverstone in Brewer.

"Along with some materials to hand out to them about potentially at risk behaviors which would include ever had injected drugs, tattooing if you ever went to an unlicensed place, or if you share any blood or body fluids. Those are sort of, if not protected, at risk behaviors. So we want to raise awareness about what would make you at risk for contracting hepatitis," said Patty Hamilton, the Public Health Director for Bangor Health and Community Services.

For more information on where to get tested, click on the link to the right of the page or call the vaccination center at 1(800) 821-5821.

Independent probe refused

<http://www.sfgate.com>

Nevada Gov. Jim Gibbons says he won't name a special counsel to investigate doctors linked to a hepatitis C outbreak, saying the responsibility rests with the state Board of Medical Examiners.

In turn, two lawmakers who sought the independent investigation are now seeking assurances from the medical board's president that its probe will be thorough.

"We're just trying to keep the pressure on," said Assemblywoman Sheila Leslie, D-Reno.

In a letter to Dr. Javaid Anwar, the medical board president, Leslie and Senate Minority Leader Steven Horsford, D-Las Vegas, also said the board should "not impede" law enforcement agencies and other governmental entities looking into the public health crisis.

Their letter highlights the responsibilities of executive director Tony Clark under Nevada law and the overall duties of the board.

"We're on track to having the largest hepatitis C outbreak in the nation, and we have a medical board that doesn't want to cooperate with law enforcement," said Leslie, referring to Clark's refusal earlier this month to turn over to Las Vegas police any complaints filed against Dr. Dipak Desai, majority owner of the Endoscopy Center of Southern Nevada's Shadow Lane clinic. "This all seems like a bad dream."

Clark has since turned over the records, according to the lawmakers' letter, but not until the last day to comply with a grand jury subpoena.

Thousands of Endoscopy Center patients were notified to get tested for hepatitis and HIV viruses after health officials found unsafe injection practices there.

Leslie said the medical board has been slow to react to the health crisis, and she and other officials had criticized the medical board for what they saw as a response to concerns of physicians and not the public. That was a reason behind the request for a governor-appointed special counsel.

Leslie and Horsford sent Gibbons a letter April 25 urging an independent investigation into the 14 doctors who worked at the Endoscopy Center of Southern Nevada, where health officials think 84 people might have contracted hepatitis C.

Ben Kieckhefer, Gibbons' press secretary, said the governor did discuss the request with his legal counsel but felt he had already taken "very specific action" to ensure the public's trust in the medical board.

On April 2, Gibbons appointed three members to the medical board as replacements for Drs. Anwar, Sohail Anjum and Daniel McBride, who had recused themselves from matters related to the hepatitis C outbreak because they have relationships with Desai.

Information from: Las Vegas Review-Journal, www.lvrj.com

May 16th, 2008

Acute Hepatitis C Virus Infections Attributed to Unsafe Injection Practices at an Endoscopy Clinic --- Nevada, 2007

<http://www.cdc.gov>

MMWR Weekly

May 16, 2008 / 57(19);513-517

On January 2, 2008, the Nevada State Health Division (NSHD) contacted CDC concerning surveillance reports received by the Southern Nevada Health District (SNHD) regarding two persons recently diagnosed with acute hepatitis C. A third person with acute hepatitis C was reported the following day. This raised concerns about an outbreak because SNHD typically confirms four or fewer cases of acute hepatitis C per year. Initial inquiries found that all three persons with acute hepatitis C underwent procedures at the same endoscopy clinic (clinic A) within 35--90 days of illness onset. A joint investigation by SNHD, NSHD, and CDC was initiated on January 9, 2008. The epidemiologic and laboratory investigation revealed that hepatitis C virus (HCV) transmission likely resulted from reuse of syringes on individual patients and use of single-use medication vials on multiple patients at the clinic. Health officials advised clinic A to stop unsafe injection practices immediately, and approximately 40,000 patients of the clinic were notified about their potential risk for exposure to HCV and other bloodborne pathogens. This report focuses on the six cases of acute hepatitis C identified during the initial investigation, which is ongoing; additional cases of acute hepatitis C associated with exposures at clinic A might be identified. Comprehensive measures involving viral hepatitis surveillance, health-care provider education, public awareness, professional oversight, licensing, and improvements in medical devices can help detect and prevent transmission of HCV and other bloodborne pathogens in health-care settings.

The objectives of the investigation were to conduct case-finding and review health histories of infected persons, to determine the source of transmission and implement control measures, to identify other patients at risk for exposure, and to assist in development of recommendations to prevent HCV transmission in health-care settings. Persons with acute hepatitis C were interviewed, and blood samples were obtained after these persons gave oral consent. Blood samples were sent to CDC for testing for HCV genotype at the NS5b region and phylogenetic relatedness at the hypervariable 1 region (HVR1) to help determine whether a common source of transmission existed (1). Specimens also were tested for other bloodborne infections (hepatitis B virus [HBV]) and human immunodeficiency virus [HIV]). Case-finding activities included SNHD's review of acute hepatitis C surveillance records, cross-matching of local HCV laboratory records with clinic A procedure logs, review of medical records for patients who underwent procedures at clinic A on the same day as HCV-infected persons, and serologic HCV, HBV, and HIV testing of staff. An extensive review of the clinic practices and procedures also was conducted, including observation of several endoscopic procedures and endoscopic reprocessing, observation of anesthesia practices, and interviews with staff members regarding their infection-control practices.

For this investigation, a person was defined as having health-care--associated acute hepatitis C if he or she 1) had symptoms of acute hepatitis within 6 months of having a procedure performed at clinic A during July--December 2007; 2) had laboratory-confirmed HCV infection (antibodies to HCV [anti-HCV]) by enzyme immunoassay (EIA) and recombinant immunoblot assay (RIBA) or EIA with an appropriate signal-to-cutoff ratio for a given assay, or presence of HCV RNA by polymerase chain reaction (PCR) in the absence of acute hepatitis A virus (HAV); and 3) did not

have other risks for HCV infection.

In addition to the three persons identified initially, three other persons were determined to have health-care--associated acute hepatitis C, for a total of six cases diagnosed during July--December 2007. One of the three cases was identified by review of surveillance records, another by cross-matching local laboratory records with procedure records at clinic A, and the third by physician report after the start of the investigation. The six persons ranged in age from 37 to 72 years; four were female. All had signs and symptoms of acute hepatitis, including jaundice, abdominal discomfort, and laboratory evidence of liver inflammation with alanine aminotransferase (ALT) levels of 552--1,165 units/L.* Four of the six persons required hospitalization as a result of their HCV infection.

The six persons with acute hepatitis C had onset of symptoms in late October 2007 and November 2007, 35--90 days after undergoing procedures at clinic A (Figure 1) and within the typical incubation period of 15--160 days. None had significant risk factors for HCV infection and none had other common exposures. One of the procedures was performed in July 2007; the other five were performed on the same day in September 2007. Five persons (four with procedures on the same day) for whom blood specimens were available at the time of this report had HCV genotype 1a. The four who had procedures on the same day had viral sequences with 99%--100% genetic similarity at HVR1, pointing to a common source of infection. The viral sequence from the HCV-infected person who had the procedure in July 2007 was not genetically related to the other cluster, suggesting a separate transmission incident.

During the 2 days in which persons with health-care--associated hepatitis C had procedures at clinic A, 120 additional persons had procedures at the clinic. HCV test results for those persons are pending. Thirty-eight staff members at the clinic involved in direct patient care were available for testing during the investigation, and none had evidence of previous or current HCV infection. None of the persons with health-care--associated acute hepatitis C and none of the staff tested positive for HBV or HIV infections.

Inappropriate reuse of syringes on individual persons and use of medication vials intended for single-person use on multiple persons was identified through direct observation of infection-control practices at clinic A (Figure 2). Specifically, a clean needle and syringe were used to draw medication from a single-use vial of propofol, a short-acting intravenous anesthetic agent. The medication was injected directly through an intravenous catheter into the patient's arm. If a patient required more sedation, the needle was removed from the syringe and replaced with a new needle; the new needle with the old syringe was used to draw more medication. Backflow from the patient's intravenous catheter or from needle removal might have contaminated the syringe with HCV and subsequently contaminated the vial. Medication remaining in the vial was used to sedate the next patient.

As soon as improper injection practices were observed, health officials advised clinic A to stop these practices and educated staff about the risks. Clinic A is a free-standing private endoscopy clinic in southern Nevada that primarily performed upper endoscopies and colonoscopies (approximately 50--60 procedures a day, 5 days a week). For at least the 4 years that clinic A occupied its existing location, the unsafe injection practices had been commonly used among some staff members who administered anesthesia, according to those who were interviewed. On February 27, 2008, SNHD began notifying approximately 40,000 persons who underwent

procedures requiring anesthesia at the clinic from March 1, 2004, through January 11, 2008, via mail and through the media, to undergo screening for HCV, HBV, and HIV infections. Results of this screening are pending.

Reported by: B Labus, MPH, L Sands, DO, P Rowley, Southern Nevada Health District, Las Vegas; IA Azzam, MD, Nevada State Dept of Health and Human Svcs. SD Holmberg, MD, Div of Viral Hepatitis, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention; JF Perz, DrPH, PR Patel, MD, Div of Healthcare Quality Promotion, National Center for Preparedness, Detection, and Control of Infectious Diseases; GE Fischer, MD, M Schaefer, MD, EIS officers, CDC.

Editorial Note:

Although case-control studies have not indicated an increased risk for acquiring HCV from medical, surgical, or dental procedures in the United States (2), outbreaks of HCV in health-care settings have long been recognized (3). These outbreaks have been identified primarily through clusters of temporally related cases detected by routine viral hepatitis surveillance, a method that likely underestimates the magnitude of transmission. Surveillance for viral hepatitis typically is passive, with little or no capacity to investigate cases suggestive of transmission during health care and determine their cause (4). Among persons with acute HCV infections, 60%--70% are asymptomatic (2). Additionally, currently available laboratory tests cannot distinguish acute from chronic HCV infection, which makes identifying newly acquired cases difficult.

The investigation described in this report identified six cases of acute hepatitis C in persons who underwent procedures at clinic A 35--90 days before the onset of their illness. None of the persons had significant risk factors for HCV infection within the typical incubation period (15--160 days before onset of symptoms), and five of the cases had procedures on the same day (September 21, 2007). The genetic relatedness of the viruses from case patients who had procedures on September 21, 2007, supports the epidemiologic findings and points to a common source of infection. The lack of genetic relatedness to the patient seen in July 2007 suggests a separate transmission incident. The two distinct clusters suggest patient-to-patient transmission rather than staff-to-patient transmission.

Most outbreaks of health-care--associated HCV have involved patient-to-patient transmission attributed to unsafe injection practices (3,5). The reuse of syringes and needles or mishandling of medication vials usually have been implicated (6--8). In some situations, syringes or needles used on HCV-infected persons were directly reused on other persons. In other instances, syringes or needles used on HCV-infected persons were reused to draw medication from a vial from which medicine was then drawn and administered to multiple persons, as was found in this investigation.

When gross errors or high-risk infection-control breaches that could lead to bloodborne pathogen transmission are recognized, including unsafe injection practices, potentially exposed persons should be notified and tested, even if transmission has not been confirmed (9). Those persons who are found to be infected can then obtain proper medical care. In addition to approximately 40,000 notifications that occurred as a result of this outbreak, in unrelated incidents, unsafe injection practices at three other outpatient clinics in two states have resulted in approximately 28,000 patient notifications during the preceding year (CDC, unpublished data, 2008). These situations could have been avoided if standard infection-control precautions, which include basic

safe injection practices, had been followed (Box) (10).

This outbreak highlights the importance of surveillance and investigation in detecting viral hepatitis transmission in health-care settings. Prevention of transmission in these settings requires understanding and adherence to recommended infection-control practices. Medical and nursing school curricula and other health-care professional training, licensing, and continuing education requirements should include infection-control content, including the safe handling and administration of parenteral medications, as areas of competency. Although hospitals employ infection-control professionals and regularly evaluate infection-control practices, such oversight might be limited in outpatient settings that are not associated with hospitals. As use of these settings grows, appropriate methods will be needed to provide similar oversight for outpatient clinics. Better surveillance, education, and oversight are needed to detect and prevent bloodborne pathogen transmission in ambulatory and other health-care settings.

References

1. Patel PR, Larson AK, Castel AD, et al. Hepatitis C virus infections from a contaminated radiopharmaceutical used in myocardial perfusion studies. *JAMA* 2006;296:2005--11.
2. [CDC. Recommendations for prevention and control of hepatitis C virus \(HCV\) infection and HCV-related chronic disease. MMWR 1998;47\(No. RR-19\).](#)
3. Williams IT, Perz JF, Bell BP. Viral hepatitis transmission in ambulatory health care settings. *Clin Infect Dis* 2004;38:1592--8.
4. [CDC. Surveillance for acute viral hepatitis---United States, 2006. MMWR 2008;57\(No. SS-2\).](#)
5. Alter MJ. Healthcare should not be a vehicle for transmission of hepatitis C virus. *J Hepatol* 2008;48:2--4.
6. [CDC. Transmission of hepatitis B and C viruses in outpatient settings---New York, Oklahoma, and Nebraska, 2000--2002. MMWR 2003;52:901--6.](#)
7. Comstock RD, Mallonee S, Fox JL, et al. A large nosocomial outbreak of hepatitis C and hepatitis B among patients receiving pain remediation treatments. *Infect Control Hosp Epidemiol* 2004;25:576--83.
8. Krause G, Trepka MJ, Whisenhunt RS, et al. Noscomial transmission of hepatitis C virus associated with the use of multidose saline vials. *Infect Control Hosp Epidemiol* 2003;24:122--7.
9. CDC. Steps for evaluating an infection control breach. Atlanta, GA: US Department of Health and Human Services, CDC; 2007. Available at http://www.cdc.gov/ncidod/dhqp/bp_steps_for_eval_ic_breach1.html.
10. CDC. Guideline for isolation precautions: preventing transmission of infectious agents in healthcare settings 2007. Atlanta, GA: US Department of Health and Human Services, CDC; 2007. Available at http://www.cdc.gov/ncidod/dhqp/gl_isolation.html.

* The normal ALT range varies according to age, sex, and other factors. An upper limit of 28--55 units/L is generally considered normal.

FIGURE 1. Acute hepatitis C in six persons who underwent endoscopies at clinic A, by dates of procedures and onset of symptoms — Nevada, 2007

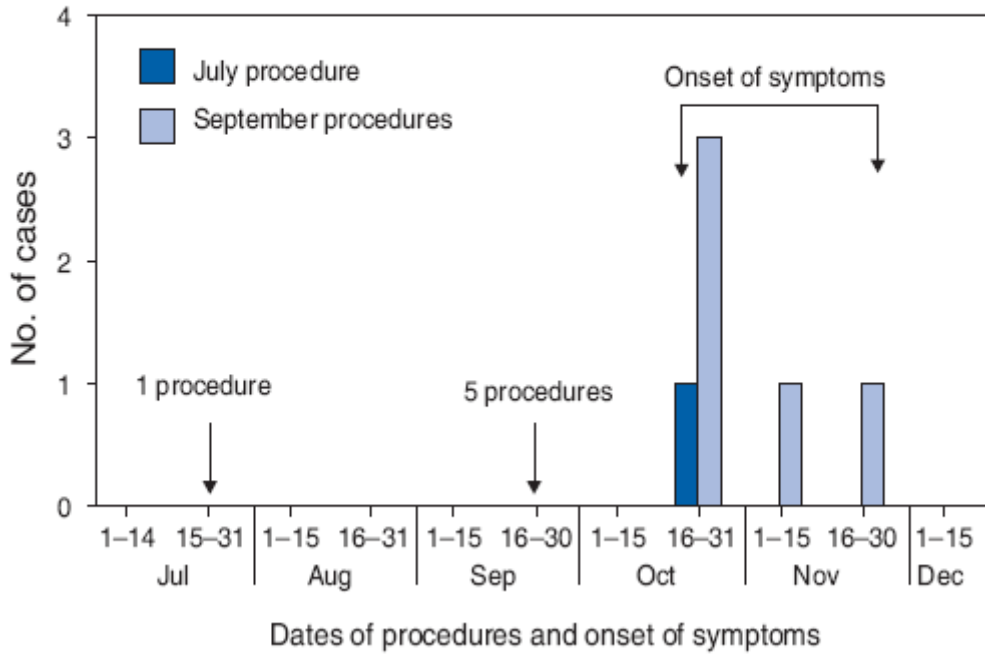
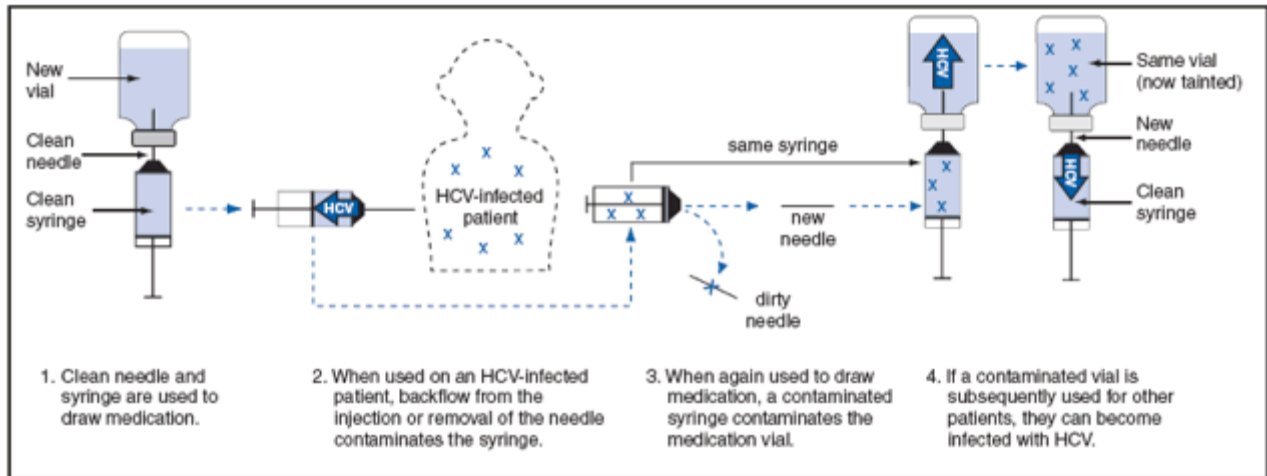


FIGURE 2. Unsafe injection practices and circumstances that likely resulted in transmission of hepatitis C virus (HCV) at clinic A — Nevada, 2007



BOX. Injection safety recommendations

- Never administer medications from the same syringe to more than one patient, even if the needle is changed.
- Consider a syringe or needle contaminated after it has been used to enter or connect to a patients' intravenous infusion bag or administration set.
- Do not enter a vial with a used syringe or needle.
- Never use medications packaged as single-use vials for more than one patient.
- Assign medications packaged as multi-use vials to a single patient whenever possible.
- Do not use bags or bottles of intravenous solution as a common source of supply for more than one patient.
- Follow proper infection-control practices during the preparation and administration of injected medications.

Adapted from: CDC. Guideline for isolation precautions: preventing transmission of infectious agents in healthcare settings 2007. Atlanta, GA: US Department of Health and Human Services, CDC; 2007. Available at http://www.cdc.gov/ncidod/dhqp/gl_isolation.html.

Silent disease an issue locally

<http://www.altoonamirror.com>

By Jimmy Mincin, jmincin@altoonamirror.com

Free hepatitis C screenings offered.

Hepatitis C is a disease many have — though few realize it.

It's been dubbed "the ghost virus" and the "silent stalker" because it evades media attention and even medical diagnosis, area medical practitioners say.

"It's a silent infection in that most people never know they've picked it up," said Dr. Ralph McKibbon, gastroenterologist at Altoona Regional Health System.

"Many people who have it have no recognizable symptoms. It often goes undiagnosed because it's unsuspected — if we don't look for it, we don't find it. That's why screening is so important," he said.

It also is the most prevalent cause of chronic liver disease.

In an effort to increase public awareness of the disease, Altoona Regional will provide a free and confidential hepatitis C blood screening from 4 to 7 p.m. Tuesday at 501 Howard Ave. (across from the Altoona Hospital Campus) in the B Building, Room 204.

Pre-registration is preferred but walk-ins will be accommodated as time permits.

“It’s a definite health problem in our area,” McKibbon said of the disease. “We have about 50 people under treatment right now at our offices. We’re screening it not just to identify it, but because there’s treatment for it. About 50 percent of people who undergo antiviral treatment will be cured. But the longer you wait, the harder it is to treat.”

Hepatitis C is a bloodborne, infectious disease caused by the hepatitis C virus (HCV), he said.

It attacks the liver, causing cirrhosis or scarring, liver failure and liver cancer, and is most often contracted through sharing of needles during intravenous drug use, tattoos and body piercing, and sharing razors with someone who is infected.

Others at an increased risk of exposure include those who had a blood transfusion before 1992 (before blood screening for HCV was implemented) and health care workers and medical emergency responders who are exposed to blood.

“People with tattoos and body piercings are particularly vulnerable, especially if you’ve had them done on vacation,” he said. “There’s some people out there who are less than honest about using new and fresh needles. They reuse needles to save money.”

Eighty percent of individuals exposed to hepatitis C will go on to have a chronic form of the disease, according to Kathy Henderson, community outreach coordinator at Home Nursing Agency, Altoona. Seventy-five percent of the liver may become damaged before a person shows any symptoms.

“Many individuals infected with HCV are not aware of their infection and are not clinically ill,” she said. “The consequences of chronic liver disease may not become apparent until 10 to 30 years after the initial infection.”

HCV is not spread through casual contact such as kissing, drinking or eating after someone or through coughing and sneezing, she said, adding that only 3 percent to 5 percent of cases are caused by sexual contact. But the virus is five times easier to contract than HIV and stands as the leading cause of liver cancer and the No. 1 reason for liver transplants in the United States. It affects one in 50 Americans, she said.

There are almost 5 million people with hepatitis C living in the U.S., according to the Centers for Disease Control and Prevention. Injection drug use is now responsible for the majority of new and existing cases of the disease. Seventy to 96 percent of long-term injectors have been exposed to hepatitis C, about half of them during their first year of injecting.

Blair County is fighting the spread of hepatitis C, Henderson said. She reports that Pennsylvania

is the first and only state to allocate money for the disease, and Blair is one of six counties in the state that has a hepatitis C testing program at local outpatient drug and alcohol treatment facilities.

“Blair County Drug and Alcohol Services sponsors this testing program and has been proactive in providing education about the risk of contracting hepatitis C during intravenous drug use,” she said.

Joe Noel, program director for the Altoona Hospital School of Medical Technology/Clinical Laboratory Science at Altoona Regional, said the jury is still out on the number of HCV’s long-term, and that’s also why it’s so important to get tested.

“We worry about the numbers because they’re going up — even in this area,” he said. “A person who tests positive needs to follow up. If left untreated, it can move on to a chronic phase, and that can lead to cirrhosis, cancer and other serious liver issues down the road.”

Most cases are treated with antiviral drugs such as interferon and ribavirin, he said.

“There isn’t yet a vaccine available for hepatitis C, like there is for hepatitis A and B — they’re still working on it,” he said. “Right now, there isn’t a whole lot we can do, except antiviral treatments.”

Mirror Staff Writer Jimmy Mincin is at 946-7460.

Warning issued that HIV drug can harm liver

<http://www.edmontonsun.com>

Serious side-effects

TORONTO -- Health Canada and pharmaceutical company Janssen-Ortho are warning people taking the HIV drug **Prezista** that the drug can cause serious liver side-effects.

Prezista, which is used in combination with another antiretroviral medication known as ritonavir, is used to treat adult patients in whom other HIV therapy has failed.

The warning says that in clinical trials, 0.5% of people who took the drug developed hepatitis or inflammation of the liver.

And since the drug has been brought to market, there have been 13 reports of patients who developed hepatitis, including two who died.

The warning says that between mid-2006 and the end of 2007 there were also 25 reports of patients who developed other liver problems; 14 of those patients died.

It's not clear if Prezista contributed to the adverse reactions and deaths or if they were due to other medical problems or medications the people were taking.

Health Canada notes the patients involved had advanced HIV disease and were taking other drugs as well, or had other illnesses such as hepatitis B or C infections.

People who have existing liver problems - such as hepatitis B or C - are at greater risk of side-effects from the drug, the warning says.

People on the drug should contact their doctor immediately if they have any of these symptoms: Dark urine, yellowing of the skin, abdominal pain (especially on the right side below the ribs), general itchiness, decreased appetite, nausea or vomiting or tiredness. People on the drug should not stop taking it without consulting a doctor or pharmacist.

*Prezista is the brand name for the drug **darunavir**.*

Hep C patients find hope

<http://www.canada.com/>

Rebecca Turcotte

Windsor Star

Hepatitis C is no longer a lifelong debilitating disease and can now be cured for more than half of patients, an expert on the disease said Thursday.

"Back in the early '90s we were really curing precious few -- no more than five or 10 per cent," said Dr. Stuart Gordon, the head of hepatology at Henry Ford Hospital in Detroit. "We're definitely making progress overall in curing hepatitis C."

Over the past decade drug companies have developed new drugs that more effectively control hepatitis C. Gordon is optimistic that with these medical advancements, more than 70 per cent of patients will be cured by 2010.

Gordon was in Windsor to speak to health care workers, community groups and patients at a conference organized by the Hepatitis C Network of Windsor and Essex County.

As many as 300,000 Canadians have the virus, which affects the liver. It is transmitted through blood-to-blood contact, such as receiving tainted blood transfusions, sharing needles and having medical treatments with unsterile equipment.

"There is still kind of a stigma about it," said Dan MacDougall, who was diagnosed in 1998. "When people find out they have it, there isn't enough information out there."

MacDougall, 57, helped start a support group for hepatitis C patients.

"Everybody needs a place where you can go to talk to people who are experiencing this and are at different stages of the disease," he said.

His illness is so advanced he needs a liver transplant. He is often fatigued, and has pain in his joints and muscles. But, the message he shares with those newly diagnosed is one of hope.

"This is not a death sentence," he said. "There are good things coming along, and the percentage of success is increasing exponentially."

A virus in hiding

<http://news.therecord.com>

Anne Kelly
Record Staff

As unlucky as George Oberholzer was to contract hepatitis C, he couldn't have been luckier when it came to treating it.

The Kitchener postal worker's infection was discovered by chance when he went to the doctor for an unrelated reason in September 2005.

After the first month of gruelling treatment, he was free of the virus. But he continued treatment for three months to be sure.

Like many people with hepatitis C, the 54-year-old went decades with no clue that he was infected. The virus eventually damages the liver and patients may develop cancer or need a liver transplant. But it can take 20 or 30 years for liver disease to become apparent.

Health Canada estimates 35 per cent of those who have chronic hepatitis C do not know they are infected. When initially infected, less than 25 per cent of people have symptoms.

"We have a reservoir of people who have this infection and continue to spread it," said Dr. Chris Steingart, medical director of infection prevention and control at Kitchener's two hospitals. "It is a continuing, growing health threat."

To meet the need for better care locally, Steingart opened the Sanguen Health Centre in Guelph last fall and will launch a Waterloo satellite next month.

Sanguen is the first community hepatitis C service organization in Ontario and possibly the first in Canada, said Steingart.

He treats the patients, his wife Michelle is the centre's co-ordinator and the provincial government's Hepatitis C Secretariat is funding a full-time nurse.

"This is a real coup for us," Steingart said of the funding. "The Hep C Secretariat expressed a lot of interest in what we're doing as a model for what other communities should be doing."

In 2004, it was estimated that about 3,000 Waterloo Region residents were infected with hepatitis C; there are an additional 1,200 in Guelph and Wellington County. The local prevalence rate is a bit lower than the provincial rate.

Risk factors include: current or past drug use by snorting or injecting with contaminated equipment; exposure to tainted blood products; having a body piercing or tattoo with unsterile equipment; having unprotected sex with an infected person; or having a medical or dental

procedure with unsterilized equipment.

Steingart said anyone in a risk group should be tested.

Oberholzer suspects he acquired the virus at age 17 when he and a friend shared a needle to inject speed. It was the only time he injected drugs, he said, but his friend, "was a real needle nut.

"That might be where I got it from. There's no other possible way."

A person doesn't have to be a repeat injection drug user to get hepatitis C. "It only takes once," Steingart said.

Symptoms may include fatigue, nausea, muscle and joint pain, trouble sleeping and weight loss.

Many people may not be aware treatment exists. Lasting 24 to 48 weeks or longer, it combines weekly self-injections and twice-daily pills. Most people have significant side effects, such as anemia, vomiting, severe fatigue and depression.

"You can't just give people a prescription and send them on their way," said Steingart. "You have to be there for them."

The doctor said it is difficult for local people to access specialists, especially the marginalized population that may have issues with housing, mental health or substance abuse.

Family doctors don't seem to know who to refer patients to, or which ones need to be referred to a specialist, he added.

"Hep C isn't something that should just be followed if the patient is feeling well. The virus can do significant damage even in the absence of symptoms."

Liver specialists called hepatologists typically locate in major cities, so most of the care locally falls to busy gastroenterologists.

The Public Health Agency of Canada predicts a doubling or tripling of disease conditions related to the infection in the future.

Recent research from Calgary showed a 400 per cent increase between 1994 and 2004 in the number of hospitalizations for serious complications, the number of deaths while in hospital and lengths of hospital stay.

Steingart got a sense of the challenges facing people with hepatitis C in his work with the Masai Centre for Local, Regional and Global Health in Guelph. The centre serves people with HIV/AIDS, some of whom also have hepatitis C.

While there is an established network to help HIV/AIDS patients with tasks like filling out drug coverage forms, nothing similar exists for patients with hepatitis C, he said.

Last year, Steingart was asked by the Hepatitis C Secretariat to help devise a regional strategy.

His wife Michelle interviewed local service organizations who deal with people who have the virus, but get no specific funding for them.

"What we heard over and over again, is 'what do we do with these people?' " he said.

Steingart opened the Sanguen Centre in the same building as the Masai Centre.

The organization will seek government funding, but also raise funds privately. It will co-ordinate care with dieticians, case workers, physiotherapy, massage and mental health services.

For patients who can be treated, there is a 50 per cent chance of cure, Steingart said.

The most common strain has a cure rate of 40 to 45 per cent; with some other strains, it is as high as 80 per cent.

Oberholzer, a father and grandfather, was fortunate his infection was the most curable.

He and his girlfriend of eight years, Bronwyn Rainbow, are grateful he is cured.

"Something like that is just amazing," said Rainbow.

"We would like to have really specialized care in our community so we don't have to send everybody to Toronto or London to see a liver specialist," added Steingart. "We will be on the leading edge of new treatment and hope eventually to be involved in clinical trials and research."

For more information on the Sanguen Health Centre, visit www.sanguen.com

HEPATITIS C STATISTICS

- 250,000 people are infected in Canada and about 120,000 in Ontario.
- 1,000 to 2,000 people die a year in Canada of hepatitis C related problems
- 3,200 to 5,000 Canadians are newly infected each year

Source: Health Canada

OPEN HOUSE

Saturday, May 24

Waterloo Memorial Recreation Complex, 101 Father David Bauer Dr., Waterloo
10 a.m. to 3 p.m.

Admission is free and registration is not necessary.

Program includes educational resources, guest speakers and representatives of organizations which help people deal with hepatitis C

Hundreds Walk In Annual Hepatitis C Awareness Event

<http://www.nyl.com>

Hundreds of New Yorkers walked from Battery Park to City Hall to raise awareness of Hepatitis C Thursday.

The Latino Organization for Liver Awareness held its fourth annual walk in Lower Manhattan to promote testing and treatment for the disease that affects one in every fifty New Yorkers.

"We want New Yorkers to know that testing is available and treatment is available. So this is really an awareness day," said Cathy Paykin of LOLA.

"This is a way of also showing the community that, you know what, Hepatitis C doesn't discriminate. It can affect anyone. A woman, a child, a teenager, a substance abuser or a doctor or a teacher. It's a universal, democratic virus," said Debbie Vega of LOLA. "So I think that this gathering here today shows all faces of anyone who could be at risk."

The group says Hepatitis C is the most common blood-borne infection in the country and the leading cause of liver transplants.

Patient safety bill would publicize doctors' names

<http://www.newsday.com>

BY RIDGELY OCHS | ridgely.ochs@newsday.com

Gov. David A. Paterson introduced a wide-ranging patient safety bill Wednesday that would give the state more authority in health investigations and, for the first time, make public names of doctors under scrutiny.

The bill follows the case of Dr. Harvey Finkelstein, a Long Island doctor whose poor infection control practices led to transmission of at least one case of hepatitis C.

"Our analysis of the Finkelstein case was that the action didn't go fast enough, so we asked 'How do we compress the time?'" said Health Commissioner Richard Daines.

Daines said the bill would give the state Department of Health a "crisper statement of authority" to speed up the investigation process and would ensure doctors are aware of infection control practices.

The health department came under fire in November after it was revealed that because of legal delays and complicated lab tests, it waited three years before telling the public that Finkelstein, a pain management doctor in Plainview, had infected at least one patient with hepatitis C by reusing syringes in multidose vials. More than 10,000 patients were notified of their possible exposure to tainted syringes.

Finkelstein also had had 10 malpractice settlements in a decade, which critics said should have triggered a probe by the Office of Professional Medical Conduct, the health department agency that investigates and sanctions doctors.

Under the governor's bill, for the first time the department would reveal the names of doctors being probed. Currently, unless and until a physician is found guilty, no one knows if a doctor

has been investigated.

The bill also requires that OPMC regularly review malpractice claims and payouts to see if a doctor should be investigated and would require that health plans report when they have terminated a contract with a doctor because of "impairment or misconduct."

The bill would also give the health department more power in conducting a public health investigation, authorizing it to order a physician to cease any practice deemed dangerous. And failure to provide records could lead to charges of professional medical conduct. The department can now subpoena records, an often lengthy process. "They are going to have to respond promptly and appropriately. It gives more teeth and authority to our request to review medical records," said health department spokeswoman Diane Mathis.

In addition, the bill would require every medical student to be trained in infection control, including training in preventing hepatitis C transmission, not just hepatitis B and HIV.

And the bill calls for the health department to study whether restricting use of multidose vials is viable and would improve infection control. In January, Daines wrote to the U.S. Food and Drug Administration calling for eliminating drugs in multidose vials. He said Wednesday he had not received a response from the FDA.

State Sen. Kemp Hannon (R-Garden City), who heads the Senate's health committee, said he had introduced a similar bill two weeks ago. "We'll negotiate," he said, referring to the governor. "It will be a top priority to get a bill this year."

Hannon's bill calls for an OPMC investigation to be triggered when a doctor has had five malpractice cases, a mandatory infection control curriculum with an emphasis on doctors in ambulatory care practices and getting rid of syringes that can be reused.

Assemb. Andrew Raia (R-East Northport), a member of the Assembly's health committee, praised Paterson's bill. "I got to tell you: I commend the governor. He's listened to the people."

Arthur Levin, head of the Center for Medical Consumers, called it "the most improvement in physician discipline" in more than a decade. "I hope this will pass without the legislature doing too much to it."

How doctors will view the bill was unclear. Dr. Michael Rosenberg, president of The Medical Society of the State of New York, which represents more than 25,000 doctors, made no specific reference to the bill in a statement yesterday, saying that the society "looked forward to working with the governor and legislature to achieve our shared objectives."

Nexavar Significantly Improves Overall Survival by 47 Percent in Asia-Pacific Liver Cancer Study

<http://www.therapeuticsdaily.com>

PR Newswire Europe (inc. UK Disclose) - May. 16, 2008

WAYNE, N.J. and EMERYVILLE, Calif., May 16 /PRNewswire-FirstCall/ -- Bayer HealthCare



Pharmaceuticals, Inc. and Onyx Pharmaceuticals, Inc. today announced that **Nexavar(R) (sorafenib)** tablets significantly improved overall survival by 47.3 percent (HR=0.68; p-value=0.014) in patients in the Asia-Pacific region with advanced hepatocellular carcinoma (HCC), or primary liver cancer versus those receiving placebo. Nexavar also significantly improved time to progression in these patients by 74 percent (HR=0.57; P=0.001). These data were presented at the 44th annual meeting of the American Society of Clinical Oncology (ASCO) and further confirm Nexavar's efficacy in liver cancer.

The international, Phase 3, randomized trial evaluated efficacy and safety of Nexavar versus placebo in 226 Asian patients with advanced HCC who had not received prior systemic therapy. The study was designed to compare overall survival, time to progression, time to symptomatic progression, response as defined by RECIST criteria and safety in patients receiving Nexavar versus placebo. Median overall survival was 6.5 months in patients treated with Nexavar versus 4.2 months for those taking placebo. The survival benefit was seen across multiple patient subsets analyzed, including age, extrahepatic spread and/or macroscopic vascular invasion.

"Liver cancer in the Asia-Pacific region continues to grow because of a high incidence of chronic hepatitis B viral infections, which now impact approximately 275 million people in the region," said Ann-Lii Cheng, MD, PhD, Department of Internal Medicine and Department of Oncology, National Taiwan University Hospital, Taipei, Taiwan and principal investigator of the trial. "Nexavar demonstrated a clear survival benefit in Asia-Pacific patients and had comparable results to last year's SHARP trial, despite these patients in the Asia-Pacific trial having poorer health status and more metastases."

Additional results from the trial are as follows:

- Median time to progression was 2.8 months in Nexavar-treated patients versus 1.4 months for those taking placebo.
- Median time to symptomatic progression was 3.5 months in patients treated with Nexavar versus 3.4 months for those taking placebo.
- Disease control rate (complete response + partial response + stable disease \geq 12 weeks) was 35 percent in Nexavar-treated patients versus 16 percent for those taking placebo.

Data from the study indicate that Nexavar was safe and well-tolerated in patients from the Asia-Pacific region. Adverse events were low to moderate in severity and treatment was well tolerated. The most common serious adverse events observed in the study were hand-foot-skin reaction, diarrhea, alopecia, fatigue, and rash/desquamation.

"These data provide further evidence that Nexavar is efficacious in liver cancer across multiple geographical regions and independent of disease characteristics and etiologies of underlying liver disease," said Susan Kelley, MD, Vice President, Therapeutic Area Oncology, Bayer HealthCare Pharmaceuticals. "Nexavar has quickly become the systemic standard of care for liver cancer, and is the only systemic therapy that has been shown to improve overall survival in Asian patients with liver cancer."

Hepatocellular carcinoma is the most common form of liver cancer and is responsible for about 90 percent of the primary malignant liver tumors in adults. Liver cancer is the sixth most common cancer in the world and the third leading cause of cancer-related deaths globally. More than 600,000 cases of liver cancer are diagnosed worldwide each year (more than 400,000 in

China, South Korea, Japan and Taiwan, 54,000 in the European Union, and 15,000 in the United States) and the incidence is increasing. In 2002, approximately 600,000 people died of liver cancer including approximately 370,000 in China, South Korea and Japan, 57,000 in the European Union, and 13,000 in the United States.(1,2)

In addition, chronic hepatitis B (HBV) and C (HCV) viral infections are the leading causes of primary liver cancer worldwide. In the Asia-Pacific region, more than eight percent of the general population is infected with HBV and between two and four percent is infected with HCV.(3,4)

Nexavar's Differentiated Mechanism

Nexavar targets both the tumor cell and tumor vasculature. In preclinical studies, Nexavar has been shown to target members of two classes of kinases known to be involved in both cell proliferation (growth) and angiogenesis (blood supply) -- two important processes that enable cancer growth. These kinases included Raf kinase, VEGFR-1, VEGFR-2, VEGFR-3, PDGFR-B, KIT, FLT-3 and RET.

Nexavar is currently approved in more than 40 countries for liver cancer and in more than 70 countries for the treatment of patients with advanced kidney cancer. Nexavar is also being evaluated by the companies, international study groups, government agencies and individual investigators as a single agent or combination treatment in a wide range of cancers, including metastatic melanoma, lung cancer, breast cancer and as an adjuvant therapy for kidney cancer.

Important Safety Considerations For Patients Taking Nexavar

Based on the currently approved U.S. package insert for the treatment of patients with unresectable hepatocellular carcinoma, hypertension may occur early in the course of therapy and blood pressure should be monitored weekly during the first six weeks of therapy and treated as needed. Bleeding with a fatal outcome from any site was reported in 2.4% for Nexavar and 4% in placebo. The incidence of treatment-emergent cardiac ischemia/infarction was 2.7% for Nexavar vs. 1.3% for placebo. Most common adverse events reported with Nexavar in patients with unresectable HCC were diarrhea, fatigue, abdominal pain, weight loss, anorexia, nausea and hand-foot skin reaction. Grade 3/4 adverse events were 45% for Nexavar vs. 32% for placebo. Women of child-bearing potential should be advised to avoid becoming pregnant and advised against breast-feeding. In cases of any severe or persistent side effects, temporary treatment interruption, dose modification or permanent discontinuation should be considered.

For information about Nexavar including U.S. Nexavar prescribing information, visit <http://www.nexavar.com/> or call 1.866.NEXAVAR (1.866.639.2827).

About Bayer HealthCare Pharmaceuticals Inc.

Bayer HealthCare Pharmaceuticals Inc. is the U.S.-based pharmaceuticals unit of Bayer HealthCare LLC, a division of Bayer AG. One of the world's leading, innovative companies in the healthcare and medical products industry, Bayer HealthCare combines the global activities of the Animal Health, Consumer Care, Diabetes Care, and Pharmaceuticals divisions. In the U.S., Bayer HealthCare Pharmaceuticals comprises the following business units: Women's Healthcare, Diagnostic Imaging, Specialized Therapeutics, Hematology/Cardiology and Oncology. The company's aim is to discover and manufacture products that will improve human health worldwide by diagnosing, preventing and treating diseases.

About Onyx Pharmaceuticals, Inc.

Onyx Pharmaceuticals, Inc. is a biopharmaceutical company committed to improving the lives of people with cancer. The company, in collaboration with Bayer HealthCare Pharmaceuticals, Inc., is developing and marketing Nexavar(R) (sorafenib) tablets, a small molecule drug. For more information about Onyx, visit the company's website at <http://www.onyx-pharm.com/>.

Schering-Plough Highlights PEGINTRON(TM) And Boceprevir Hepatitis C Data Presentations At Digestive Disease Week (DDW) Annual Meeting

<http://www.medicalnewstoday.com>

Schering-Plough Corporation (NYSE: SGP), a leader in advancing the science and treatment of chronic hepatitis C virus (HCV) infection, announced that data from several clinical studies with PEGINTRON(TM) (peginterferon alfa-2b) and REBETOL(R) (ribavirin, USP) combination therapy, as well as boceprevir, the company's investigational oral HCV protease inhibitor, will be presented at the 39th annual Digestive Disease Week (DDW) meeting to be held at the San Diego Convention Center, May 17-22.

Hepatitis C is the most common blood-borne infection in America and the most common form of liver disease, affecting nearly 5 million people in the United States and 200 million people worldwide. It is the leading cause of cirrhosis and liver cancer, and the number one reason for liver transplants in the United States.

Clinical investigators will present findings from several PEGINTRON studies evaluating patient response to therapy at important treatment milestones, an approach that is aimed at individualizing treatment for patients to help improve outcomes. In particular, Schering-Plough is exploring unique treatment strategies for patients with more difficult-to-treat forms of the disease, such as patients who were nonresponders to previous therapy.

Schering-Plough also is exploring novel therapeutic approaches to treating hepatitis C with boceprevir, its investigational oral HCV protease inhibitor currently in Phase II clinical development. The final results of a Phase II dose-finding study of boceprevir with or without ribavirin in patients who were "null" responders to previous peginterferon and ribavirin combination therapy will be presented.

Key Data Presentations at DDW

PEGINTRON

- Results from the EPIC3 Program: Platelet Counts Are Strong Predictors of Sustained Viral Response (SVR) in the Retreatment of Previous Interferon/Ribavirin Non-Responders (NR). Poynard, T. et al. Poster S1000, Abstract No. 442673, Sunday, May 18, 8:00 a.m. - 5:00 p.m., Sails Pavilion.
- Clearance of HCV at 5 Year Follow-Up for Peginterferon Alfa-2b with or without Ribavirin Is Predicted by Sustained Virologic Response at 24 Weeks Post-Treatment. Lindsay, K. et al. Poster S1001, Abstract No. 443097, Sunday, May 18, 8:00 a.m. - 5:00

p.m., Sails Pavilion.

- Sustained Virologic Response and Relapse Rates with Peginterferon Alfa-2b Plus Ribavirin in Clinical Trials Are Comparable to Those in Community-Based Studies. Manns, M. et al. Poster W1004, Abstract No. 441859, Wednesday, May 21, 8:00 a.m. - 5:00 p.m., Sails Pavilion.
- Rapid Virologic Response to Peginterferon Alfa and Ribavirin Treatment of Chronic Hepatitis C Predicts Sustained Virologic Response and Relapse. Poordad, F. et al. Poster W1007, Abstract No. 439219, Wednesday, May 21, 8:00 a.m. - 5:00 p.m., Sails Pavilion.

Boceprevir

- Role of Interferon Response During Re-Treatment of Null Responders with Boceprevir Combination Therapy: Results of Phase II Trial. Schiff, E. et al. Oral Presentation 162, Abstract No. 442360, Sunday, May 18, 4:30 p.m., Room 6DE.

Schering-Plough Supported CME Symposium

Defining the Course in the Management of HCV: A Case Based Approach Sunday, May 18, 6:30-9:30 p.m., San Diego Marriott Hotel and Marina, Hall 3-6. A world-renowned faculty will present and discuss recent data and how this information may impact clinical management decisions. Among the educational objectives of this program is to define the role of viral clearance as a predictor of HCV treatment response.

Schering-Plough Corporation

<http://www.schering-plough.com>

Higher LDL cholesterol levels mean better response to anti-HCV treatment in HIV/HCV coinfecting patients

www.aidsmap.com

Derek Thaczuk

HIV/HCV co-infected individuals with higher “bad” LDL cholesterol levels are more likely to respond successfully to anti-hepatitis C treatment than those with lower levels of LDL. While several previous studies had shown higher LDL to predict better treatment response in hepatitis C-monoinfected individuals, this retrospective study – reported in the May 11 issue of *AIDS* – is the first to show a similar effect in co-infected individuals.

In a growing number of studies in hepatitis C virus monoinfected patients, better response to pegylated interferon and ribavirin treatment has been seen in patients with high baseline serum levels of low-density lipoprotein cholesterol (LDL-C). It has been suggested that the cellular receptor for LDL cholesterol also functions as a receptor for hepatitis C, so that there is competition for binding, with higher LDL levels resulting in less attachment of hepatitis C to cells.

However, until now, this has not been studied in HIV/hepatitis C coinfecting patients, in whom lipid disorders are common and response to anti-hepatitis C therapy is relatively poor (27–49% show a sustained virologic response). (Other links have been found between coinfection and lipid disorders – for instance, lipid increases tend to be lower and less common in coinfecting individuals).

In this retrospective study, Spanish investigators assessed the relationship between baseline lipid levels and response to anti-hepatitis C therapy in 260 coinfecting patients treated with pegylated interferon and ribavirin. The study group was drawn from a cohort of 3564 coinfecting adult patients at ten Spanish hospitals, followed between October 2001 and February 2005. Of these, 339 received anti-hepatitis C treatment during follow-up, and 272 met inclusion criteria: available retrospective lipid profiles, first use of anti-hepatitis C therapy, and no use of lipid-lowering drugs during therapy or during the previous three months.

LDL cholesterol levels were not measured by direct assay, but estimated from total serum cholesterol, high density lipoprotein (HDL) cholesterol and triglyceride levels according to the formula: $LDL = \text{total cholesterol} - HDL \text{ cholesterol} - (\text{triglycerides}/5)$. In twelve patients, high triglyceride levels (> 400 mg/dl) made this estimate impossible, and they were excluded from analysis. This left 260 patients in the study group (80% of whom were male), with the following median characteristics: age 40 years, body mass index (BMI) 23, hepatitis C viral load 5.80 log₁₀, HIV viral load 80 copies/ml, CD4 cell count 520 cells/mm³, total serum cholesterol 166 mg/dl, LDL cholesterol 90 mg/dl, HDL cholesterol 44 mg/dl, triglycerides 128 mg/dl. One hundred and thirty-seven (53%) had the harder-to-treat hepatitis C genotype 1, one (0.4%) genotype 2, 100 (39%) genotype 2, and 21 (8%) genotype 4.

All patients were treated with pegylated interferon and ribavirin. Length of treatment was 48 weeks (or, for some patients with genotype 3, 24 weeks at the physician's discretion); treatment was discontinued early in nonresponders. Ribavirin doses were 800–1200 mg/day. Response was primarily measured by sustained virologic response at 24 weeks after completion of treatment; early virologic response at week 12 and end-of-treatment response were also evaluated.

SVR was achieved in 102 (39%) of patients overall: 38 (24%) of the 158 patients with genotypes 1 or 4, and 64 (63%) of the 101 with genotypes 2 or 3. Rates of sustained virological response were at least twice as high in patients with LDL cholesterol levels 100 mg/dl or more, independent of all other variables. In the study group overall, 49 patients (44%) patients with LDL cholesterol levels 100 mg/dl or more showed sustained virological response, compared with 53 (36%) with lower values (adjusted odds ratio [AOR]: 2.51; 95% confidence interval [CI]: 1.40–4.87; $p = 0.003$).

This association was independent of the remaining predictors of sustained virological response: genotypes 2–3, plasma hepatitis C viral load of 600 000 iu/ml or less, exposure to at least 80% of the planned therapy, and lack of concomitant antiretroviral therapy. No significant associations were found with other variables including other lipid levels, CD4 cell count, ribavirin dose, or degree of fibrosis/cirrhosis.

Higher rates of early virological response and end of treatment response were also seen at LDL cholesterol levels ≥ 100 mg/dl. In patients with genotype 1 only, the rate of sustained virological response was 31% for LDL cholesterol ≥ 100 mg/dl vs. 17% for LDL cholesterol < 100 mg/dl (AOR: 2.19; 95% CI: 1.04–4.66; $p=0.04$). For genotypes 2 and 3, the respective values were 73 and 58% (AOR: 2.71; 95% CI: 0.99–7.46; $p = 0.054$).

One possible confounder is that total and LDL cholesterol levels decline with increasing severity of liver disease, and treatment discontinuation rates may also increase with greater liver disease,

due to decreased tolerability. However, in this as in most other studies, sustained virological response rates were similar across all degrees of liver fibrosis and cirrhosis.

Despite the retrospective design of this study, the researchers conclude that they have demonstrated "for the first time that higher serum LDL cholesterol levels prior to therapy ... are associated with sustained virological response in HIV/hepatitis C-coinfected patients, as in hepatitis C virus monoinfection."

Reference:

del Valle J et al. Baseline serum low-density lipoprotein cholesterol levels predict response to hepatitis C therapy in HIV/hepatitis C virus coinfecting individuals. AIDS 22: 923-930, 2008.