

HCV ADVOCATE WEEKLY NEWS REVIEW

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

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May 10, 2009

Study: Doctors Show Lack of Knowledge about Hepatitis B

<http://www.kcbs.com>

SAN FRANCISCO (KCBS) -- Even though more than two million people in the United States have chronic Hepatitis B, a new study finds that not just patients, but a large number of doctors lack adequate knowledge about the disease.

Hepatitis B is known to cause up to 80 percent of liver cancers, but only occurs in the non-Asian population at rate of one person per every 1,000. But in the Asian population, the disease has been found to occur at a rate of 1 person for every 10. The study, by Stanford University's Asian Liver Center, found that doctors in the Bay Area were vague when it came to naming facts on Hepatitis B and were often not able to communicate and educate patients who didn't speak English.

Doctor Stephanie Choa, program officer at the center, says many cases start in childhood or birth.

"An infant born to a mom with chronic Hepatitis B has a 90 percent chance of developing the disease for the rest of their lives as well," she said.

Choa said their study, which also included OB/GYNs, found that most physicians showed a fundamental lack of knowledge about the disease.

"Overall the physician knowledge is pretty poor," she said.

Hepatitis B is easily cured in infants with a short series of shots, so Choa says it's doctors, as well as patients, who are now the primary targets for a public awareness campaign.

Ted Fang, director for the Hep B Free Campaign in San Francisco, tells residents that help is ready and available if they need it.

"We have a vaccine that works and we have treatments available even if you're already infected," said Fang.

Free screenings are provided by the campaign, but Fang says the goal is to get people at risk to have routine screenings by doctors, which he says would go a long way in winning the battle against Hep B.

May 11, 2009

Phase IIb Trial Will Further Assess Efficacy, Safety And Tolerability Of MK-7009 - For Patients With Chronic Hepatitis C

<http://www.medicalnewstoday.com>

Results from an ongoing Phase IIa study showed that **MK-7009**, Merck Sharp and Dohme's

(MSD) investigational oral hepatitis C virus (HCV) protease inhibitor, in combination therapy significantly improved rapid viral response, defined as viral suppression to undetectable levels within 28 days, compared to placebo in combination therapy in previously untreated (treatment-naïve) patients infected with chronic HCV genotype 1, one of the most difficult to treat genotypes of HCV ($p < 0.0001$). All patients received MK-7009 or placebo in combination with pegylated interferon and ribavirin (peg-IFN/RBV), the current standard of care for treatment of HCV infection. (Poster 2701) These findings were presented today at the 44th Annual European Association for the Study of the Liver (EASL) meeting in Copenhagen, Denmark.

According to the World Health Organization, an estimated 180 million people are infected with HCV worldwide, 130 million of whom are chronic HCV carriers at risk of developing liver cirrhosis and/or liver cancer. It is estimated that three to four million persons are infected each year.

"In this ongoing study, MK-7009 in combination therapy rapidly lowered and generally maintained the amount of virus in the blood to below detectable levels in previously untreated HCV patients," said Robin Isaacs, vice president and therapeutic head for Infectious Diseases, Merck Research Laboratories. "These preliminary results help us understand the efficacy and tolerability profile of MK-7009 and support the further development of MK-7009 for the treatment of HCV."

These findings are the primary analysis from an ongoing, randomized, placebo-controlled, double-blind study of MK-7009 in treatment-naïve, chronic HCV patients. In this study, 95 patients were randomized across five treatment arms with regimens of MK-7009 300 mg or 600 mg twice daily, MK-7009 600 mg or 800 mg once daily, or placebo, for 28 days. Patients in all treatment arms received standard doses of peg-IFN/RBV in combination with the MK-7009 or placebo regimens, and are continuing to receive peg-IFN/RBV for an additional 44 weeks. HCV RNA was measured by the HCV RNA PCR TaqMan 2.0 assay, which has a lower limit of detection (LLOD) of 10 IU/mL and a lower limit of quantification (LLOQ) of 25 IU/mL. The primary endpoint of the study was reduction in HCV RNA to undetectable levels (< 10 IU/mL) at day 28.

Suppression of viral load to undetectable levels by day 28

After 28 days of therapy, 69 to 82 percent of patients in the regimens containing MK-7009 ($n = 68$ included in the per-protocol analysis) versus 6 percent of patients in the placebo regimen ($n = 18$ included in the per-protocol analysis) achieved undetectable HCV RNA levels ($p < 0.0001$). More than 80 percent of patients in the regimens containing MK-7009 versus 11 percent of patients in the placebo regimen experienced viral suppression to below LLOQ (< 25 IU/mL) on day 28.

Viral suppression continued in the majority of patients following termination of MK-7009 treatment at day 28. At day 42, HCV RNA was undetectable in 77 to 94 percent of the patients in the regimens that had contained MK-7009 versus 12 percent of patients in the regimen that had contained placebo ($p < 0.0001$). Additionally, all subjects in the 600 mg twice daily regimen group achieved HCV RNA to below LLOQ (< 25 IU/ml) from Day 21 through Day 42.

Tolerability and safety profile of MK-7009

There were no serious adverse events and no discontinuations due to an adverse event during the

first 42 days of the study. The most commonly reported adverse experiences (> 20 percent in one or more treatment arms) in patients receiving MK-7009 versus patients receiving placebo, respectively, were nausea (28 to 40 percent versus 26 percent), headache (16 to 45 percent versus 37 percent), fatigue (5 to 35 percent versus 32 percent), flu-like symptoms (20 to 26 percent versus 16 percent), anorexia (5 to 25 percent versus 11 percent), diarrhea (6 to 25 percent versus 21 percent), indigestion (0 to 22 percent versus 21 percent), rash (10 to 17 percent versus 21 percent), and vomiting (0 to 40 percent versus 5 percent). The incidence of vomiting was higher in the treatment arm containing MK-7009 600 mg twice daily (40 percent) versus the treatment arm containing placebo (5 percent); vomiting did not require anti-emetic treatment and did not lead to discontinuation or dose reduction of MK-7009.

Phase IIb study to further assess efficacy, safety and tolerability of MK-7009

A Phase IIb study has been initiated to evaluate the safety, tolerability and efficacy of MK-7009 when administered concomitantly with peg-IFN/RBV to previously treated (treatment-experienced) patients with chronic hepatitis C genotype 1 infection. Patients will receive either placebo or MK-7009 at 300 mg or 600 mg twice daily in combination with standard doses of peg-IFN/RBV. The trial is a multicenter, partially double-blind, randomized, placebo-controlled trial that aims to enroll approximately 200 patients in multiple countries.

The study will measure the safety and tolerability of MK-7009 at all dose regimens as compared to placebo through 48 weeks. Additionally, the study will evaluate the proportion of patients in the MK-7009 600 mg treatment regimens achieving sustained viral response, i.e., undetectable viral load 24 weeks after the end of all study therapy, as compared to patients in the placebo regimen.

Source: Merck & Co., Inc.

Hep C virus genotype 1b is a risk factor for hepatocellular carcinoma

<http://www.gastrohep.com>

Hepatitis C virus genotype 1b as a risk factor for hepatocellular carcinoma development, finds the latest issue of the *Journal of Hepatology*.

However, whether the risk varies among patients infected with different Hepatitis C virus genotypes is still controversial.

Dr Sara Raimondi and colleagues from Italy performed a meta-analysis to clarify whether the genotype 1b is associated with a higher risk of hepatocellular carcinoma than other genotypes.

The team identified 57 relevant papers through a literature search to 2007 but.

Since age could represent a major confounder focused the meta-analysis on the 21 studies presenting age-adjusted risk estimates for Hepatitis C virus genotype 1b vs other genotypes.

The team used random-effects models with the DerSimonian–Laird method, and assessed heterogeneity between studies and publication bias.

“The team identified 57 relevant papers” --*Journal of Hepatology*

The researchers found patients infected with Hepatitis C virus genotype 1b have almost double the risk to develop hepatocellular carcinoma than those infected with other genotypes.

The pooled risk estimate was somewhat lower when we restricted the analysis to the eight studies conducted in patients with liver cirrhosis or considering the 36 studies presenting only crude data.

In 7 studies excluding patients with liver cirrhosis, the team noted that the relative risk increased to 2.5.

Dr Raimondi's team concluded, “This meta-analysis suggests that Hepatitis C virus genotype 1b plays an important role in hepatocellular carcinoma development, especially in patients with early stage liver disease.”

J Hepatol 2009; 50(6): 1142-54, 11 May 2009

Hepatitis - a matter of life or death

<http://www.newswire.ca/>

OTTAWA, May 11 /CNW Telbec/ - One in 12 people worldwide has hepatitis B or C - including 600,000 Canadians. Many don't even know it. They may have no obvious symptoms until serious liver damage has occurred. These are chronic, lifelong viral infections that can affect anyone from any walk of life. On May 19, World Hepatitis Day, Canada will join with groups around the world to raise public awareness about hepatitis.

Hepatitis B and C are sometimes linked to illicit drug use, unsafe sex, or alcoholism. Few people realize that virtually everyone is at risk. Transmission could come from something as simple as being nicked by a beauty parlour instrument that has previously cut someone who is infected. Sharing toothbrushes or razors is another potential source of infection.

Susan Kingston, 56, of Kemptville, Ontario, is suffering from cirrhosis of the liver and is hoping for a liver transplant. She was pricked with a needle while working as a laboratory technologist in the 1970s. She knew she had been infected with hepatitis B but didn't know that she had also been infected with the hepatitis C virus. Chronic hepatitis C causes inflammation and damage over time that can lead to cirrhosis, and Kingston's hep C went undetected for so long that the damage had been done by the time it was discovered.

Because her liver isn't functioning properly, Kingston suffers from ammonia build-up in her abdomen which affects the brain. She lives every day with pain and has to have her midsection drained regularly or the pain becomes unbearable. She is on a variety of medications while she waits for a compatible liver transplant. If an available liver isn't found soon, Susan has been told that she will be too sick to survive the transplant surgery.

In many cases, there are no symptoms for hepatitis C as the disease silently destroys the liver. Like any disease, the earlier it is found, the earlier it can be treated and the greater the possibility

of clearing the virus. Often the only outcome without treatment is eventual progression to cirrhosis, which can then lead to the need for a liver transplant or even death.

Hepatitis C is the leading cause of liver transplants in both Canada and the United States, but two-thirds of those on the waiting list will die waiting for a liver transplant because there are not enough donor organs to go around. Hepatitis C is almost five times more prevalent than HIV in North America.

The focus of this year's campaign is on raising public awareness. Everyone should learn about the risk factors involved in both forms of hepatitis and should talk to their health care provider about being tested if they think they have been infected. To find out more, visit:

<http://www.phac-aspc.gc.ca/hepc/index-eng.php>

www.whdcanada.ca

www.aminumber12.org

For further information: Maureen Johnson, World Hepatitis Day 2009 national coordinator, (613) 692-4236, mojo.3@sympatico.ca

Infected by teen addict, former foster mom wants compensation

<http://www.canada.com>

By Kent Spencer, Canwest News Service

VANCOUVER — Former foster mom Teresa Iezzi, who spent 22 years saving street kids, feels she's been tossed on the street by the provincial government.

Iezzi says she "lost everything" after being stabbed with an infected needle by a teenage drug user who was placed in her care by the government.

She blames the Ministry of Children and Family Development for contracting Hepatitis C, losing her foster parenting contract and her \$400,000 Burnaby home.

"I've been treated horribly. I want foster parents to know that when an accident happens the government does not take care of them," said Iezzi.

Over the course of her career, Iezzi and her husband took in hundreds of troubled street kids: drug addicts, car thieves and prostitutes.

The \$7,500 monthly gig was their main source of income.

In 1991, she was nominated for a lieutenant-governors' Foster Family Award.

But danger lurked around the corners of their six-bedroom group home.

Several times she was threatened. "I tried to cool the kids down and then called the police in those situations," she said.

But there was no time for a cool-down period on Feb. 3, 2001 when RCMP dropped off a girl, 17.

After shooting up heroin, the drugged-up teen accidentally stabbed Iezzi with a needle, infecting her with Hepatitis C, a sometimes-fatal liver disease.

Iezzi says the ministry did not warn her that the girl was a heroin addict or tell her she carried the highly infectious disease.

Things unravelled over the next four years. Her husband died and the ministry cancelled her foster parenting contract.

Iezzi, 65, suspects the contract was cancelled because the ministry discovered she had contracted Hep C.

She was forced to sell her home and survive on a small pension.

Iezzi's story is supported by records from police and her doctor. She wants an apology from the ministry and financial compensation.

A social worker, who requested anonymity because of employment concerns, called the case "tragic."

"The ministry pushed her out the back door with a life-threatening disease. It hurts," the worker said.

A spokeswoman for the ministry would not discuss the case.

Source: Vancouver Province

May 13, 2009

Pioneering Technique Using Microwaves Successful In Treatment Of Liver Tumors

<http://www.medicalnewstoday.com>

Leicester consultant surgeon who has developed a pioneering technique using microwaves to destroy liver tumours has treated more than 100 patients in the UK and other patients are now being treated internationally.

Worldwide, about one million people a year die of primary liver cancer, with another million dying with secondary liver cancer where the cancer has spread from other tumour sites such as cancer of the colon.

The incidence of primary liver cancer is gradually increasing in the Western world, but it is very common in Asia and the Far East where it is associated with endemic hepatitis. Most patients with liver cancer are deemed inoperable but with the development of this microwave equipment, literally thousands of patients worldwide could be offered curative treatment, even if they have

established liver cirrhosis.

Mr David M Lloyd, MBBS, MD, FRCS, a consultant surgeon with University Hospitals Leicester NHS Trust, is also acclaimed for his innovative work in keyhole surgery. The University of Leicester has awarded him an Honorary Senior Lectureship, and earlier this month he won the title of Honoured Citizen of the Year for the City of Leicester.

David Lloyd's research, in collaboration with Professor Nigel Cronin and Dr. Peter Clegg at the University of Bath, has led to the development and production of a microwave generator and probe, now being manufactured by Acculis Ltd, UK. The treatment of more than 100 patients with liver cancer has resulted in curing or extending life for many of them, whose life prognosis was less than twelve months. More than one third of the patients treated are still alive after three years and some have been, quite simply, pronounced cured and discharged.

The earliest patient to be discharged is one of David Lloyd's trial patients treated nine years ago. Several more are alive and well five years after receiving treatment.

The importance of this application of microwave technology is immense, as Mr Lloyd explained: "The technique will have a significant effect on liver cancers, because we are operating on people who have been declared inoperable. Someone with cirrhosis of the liver can't be operated on in a conventional way to remove a tumour, but we can place a microwave probe in by keyhole or percutaneous (through the skin) methods and can destroy these tumours."

Because of the pioneering research done at the University Hospitals Leicester, the microwave generator is being used as far afield as Hong Kong, Singapore, the USA and Australia. In particular, the microwave technology has been embraced by many of the top cancer hospitals in the US, including the Memorial Sloan-Kettering Cancer Institute in New York, The Johns Hopkins University in Baltimore, and the M D Anderson Cancer Centre in Texas. Mr Lloyd added: "We've placed several in France and Switzerland and many of the world's leading liver surgeons have now expressed an interest in using the generator.

Because David Lloyd was the only surgeon with this specialised equipment he was referred patients from all over the world for treatment. He is extremely pleased that more centres are now using the microwave device and, in the UK, there are now generators in major teaching hospitals in Liverpool, Manchester, Leeds, Basingstoke and Edinburgh. David Lloyd calculates that within a couple of years, every major liver centre in the UK will probably have a microwave generator.

The advantage the microwave technique has over other machines designed to destroy tumours, such as laser, ultrasound and radio-frequency (which is similar to an electric current) is that it is quick and produces cancer cell death with very few side effects.

Only tissue in the immediate field of the microwave energy is destroyed, David Lloyd explained, and not in other parts of the body, which is a danger with other methods, such as radio-frequency, where the electric current has to have an exit point from the body, with the risk of burning at that site.

"Microwaves don't cause collateral damage elsewhere in the body," he said. "They only heat up the tissue at the end of the probe and no energy is sent through the body. We can now treat very

large tumours up to 6-8 cms in diameter within 4-6 minutes. This makes it ideal for someone who may have multiple tumours, which by other techniques, might take several hours to treat.

"People have come to Leicester from all over the world," he added. "It has really put Leicester on the map, within this field. For the last ten years I have been invited to every world and European congress in liver surgery to talk about this development. There has been tremendous interest because of the frustration with other forms of energy which haven't delivered. Our system is safe, fast and reproducible and it does work.

"If it's used correctly there are no side effects, but because this is a very powerful device, it has to be used correctly. I tend to work in collaboration with a radiologist so that accurate placement of the microwave probe can be achieved. We have not seen significant side-effects so far."

Source: David M. Lloyd, University of Leicester

Hyperferritinemia is another surrogate marker of advanced liver disease

<http://www.scienceblog.com>

High serum ferritin, being a hallmark of hereditary hemochromatosis, is frequently found in chronic hepatitis C, alcoholic or non-alcoholic steatohepatitis and non-alcoholic fatty liver disease patients. A study in Italy has investigated the link between ferritin and steatosis in a non-obese cohort of non-alcoholic patients. In southern European populations, high ferritin levels, after exclusion of diagnosis of HH, represent a risk factor for steatosis and clinical relevance, being associated with low platelet count.

Patients with chronic hepatitis C virus (HCV) infection often have elevated serum iron indices, but these do not accurately reflect hepatic iron content, nor are they able to predict clinically important endpoints, such as progression of fibrosis and responsiveness to interferon-based regimens. Studies that attempt to link iron and the course of chronic hepatitis C have been inconclusive. In chronic hepatitis C, steatosis is a common histological finding, occurring in 30%-70% of such patients. The biological mechanism underlying steatosis in HCV infection is not definitively understood, and is considered to be multifactorial with metabolic mechanisms, including insulin resistance and iron overload.

A research article to be published on May 7, 2009 in the *World Journal of Gastroenterology* addresses this question. The research team led by Professor Licata from Gastroenterology and Hepatology Unit of Palermo University analyzed in a cross-sectional study, a cohort of non-obese, non-alcoholic patients with compensated chronic liver disease characterized by elevated serum ferritin levels, of varying etiology, excluding hemochromatosis, to reassess the link between hyperferritinemia and other markers of the metabolic syndrome, mainly steatosis. All data provide further evidence that hyperferritinemia might be another surrogate marker of advanced liver disease of any etiology.

May Is Hepatitis Awareness Month

<http://www.emaxhealth.com>

Interim Commissioner of Health Olivia D. Farrow joined with members of the Maryland Hepatitis Coalition and state and local officials to recognize national hepatitis awareness month. Free vaccinations were offered to children and at-risk adults as part of an effort to raise awareness of the health risks associated with hepatitis and reducing the spread of this potentially life-threatening disease.

Acute viral hepatitis most frequently is caused by infection with one of three viruses: hepatitis A virus (HAV), hepatitis B virus (HBV), and hepatitis C virus (HCV). Safe and effective vaccines are available for HAV and HBV. No vaccine exists against HCV. Most people become infected with the HCV virus by sharing needles to inject drugs.

“The Health Department actively promotes the prevention of hepatitis and substance abuse and encourages individuals to make healthy lifestyle choices,” said Interim Commissioner Farrow. “Getting young children and at-risk adults vaccinated for hepatitis A and B is an important step in stopping the spread of this endemic disease.”

The HAV vaccine first became available in 1995. In the last decade, Baltimore city has seen a significant drop in confirmed HAV cases – from 94 in 1999, to 4 in 2008. HBV vaccination rates for children age 19 to 35 months in Baltimore City remain historically high – 91 percent in 2006, the most recent data available. The Baltimore City Public Schools system requires students be fully vaccinated for hepatitis B before entering 9 grade.

The Health Department’s TIKE van offers free hepatitis immunizations for children and adults who do not have a medical provider.

Hepatitis C is a contagious liver disease. It can range in severity from a mild illness lasting a few weeks to a severe illness lasting several months. In chronic cases, it can cause death. HCV is transmitted through the exchange of bodily fluids. Most new confirmed cases stem from the sharing of intravenous needles, sex with an infected partner and (less commonly) through blood transfusions.

The Baltimore City Needle Exchange program seeks to reduce HIV, hepatitis C, and other infections by reducing the circulation of unclean syringes. The program provides testing for Syphilis, HIV, and hepatitis C. These services are provided in seventeen locations in the City of Baltimore. See our website for a list of hours and locations.

The MHC is a statewide coalition that advocates for people with hepatitis and works to eliminate hepatitis in Maryland.

Source: Baltimore Department Of Health

Hepatitis victim to testify law unfair

<http://www.lvrj.com>

by Paul Harasim

Bill would lift cap on pain, suffering damages

She says it's happened so many nights -- fear pulls Josephine Washington out of her sleep so she can see whether her husband is still breathing.

It is, she sighs, how you live life when a loved one's health continues to deteriorate from hepatitis.

"I really think I have to get counseling," the retired registered nurse said as she stood in the kitchen of her Henderson home Tuesday morning. "I'm afraid and depressed a lot. His liver is so swollen and he has cramps and so much pain. It's no way to live."

Michael Washington, her husband of 30 years, is one of nine people that public health officials say was infected at Las Vegas clinics where Dr. Dipak Desai was the majority owner. Authorities say more than 100 other hepatitis cases are possibly linked to the clinics.

Today, the 69-year-old retired Air Force veteran is scheduled to testify before the Senate Judiciary Committee, arguing on behalf of a bill that would remove the key element of the 2004 medical malpractice reform initiative: a \$350,000 cap on pain and suffering damages.

He says he will relate how acquiring both hepatitis B and hepatitis C worsened his diabetes to the point where he can no longer take oral medication to control it -- now he must have three insulin shots per day.

And, he said, he also will let legislators know that doctors have said that it was hepatitis that caused his glaucoma -- treated before with eye drops -- to become so severe that he has needed two eye operations.

He said his health is so compromised that doctors say it would be too risky for him to take the interferon treatments often used to fight hepatitis.

"Believe me," he said as he exchanged glances with his wife, "I'm not for frivolous lawsuits. But I am for fairness. The way my life has been changed is just terrible. I have to worry now all the time that I'm going to give this to someone else."

Washington has said health officials told him he was the first person to contract hepatitis C while undergoing a colonoscopy at the since-closed Endoscopy Center of Southern Nevada.

On July 25, 2007, records show that Desai, a registered nurse and a nurse anesthetist were in the operating room with Washington.

In 2008, city officials in a report said Desai ordered his nurses to reuse syringes and single-use medicine vials, and that investigators were told this approach was used to save money.

In all, health officials advised more than 50,000 patients of the clinics to get tested for infectious diseases.

What Washington expects to share with lawmakers, he said, is his belief that the current law is "simply unfair to the most vulnerable people in the community: children, homemakers and senior citizens."

The current bill allows for recovery of economic damages, including loss of future earnings and medical expenses, but Washington pointed out that seniors, stay-at-home moms and children don't have future earnings to calculate.

"Why should the most vulnerable be left with practically nothing when they're suffering and their lives are changed forever?" he said. "Aren't their lives worth something? Why do we want to protect bad doctors?"

As it stands now, malpractice awards for children, seniors and stay-at-home parents, and people who are injured but can still work essentially come out of the capped awards allocated for pain and suffering, a sum divvied up between the attorney and client.

Ed Bernstein, Washington's lawyer, said attorneys often have to pay more than \$100,000 for experts to prove a case that may take months or years. "Many attorneys will no longer take malpractice cases because it doesn't make economic sense," he said.

Doctors and insurance executives, who largely funded the 2004 initiative, argued that large payouts in Nevada -- often for pain and suffering -- caused medical malpractice rates to escalate dramatically. That, they said, was causing doctors to leave in droves.

Though the argument was found to be specious by the nation's General Accounting Office, it helped persuade Nevadans to vote for the initiative, which doctors say has helped their malpractice insurance rates drop by as much as 30 percent.

Desai, Washington noted, was the doctor who gave the most money -- \$25,000 -- to the malpractice reform initiative that became known as Keep Our Doctors In Nevada.

Now Washington's life has forever changed, he said.

"I don't cook any more because I'm afraid of cutting myself and giving it to others. When I go to someone's house, I always hope they have paper plates and cups that I can throw away."

Among his other medical issues, he has to deal with cramps in his abdomen.

Is Desai, he asked, "the kind of doctor we want to keep in Nevada?"

Contact reporter Paul Harasim at pharasim@reviewjournal.com or 702-387-2908.

May 14, 2009

Ask the Experts: The Inactive Carrier State in Chronic Hepatitis B Infection

www.medscape.com

Paul Martin, MD, FACP

Question

I have a 41-year-old patient who is hepatitis B e antigen (HBeAg)-negative/HBe antibody (HBeAb)-positive, with normal serum aminotransferases. He is also HBsAg-positive, HB core total Ab-positive, and HB core IgM-negative. What is your diagnosis?

Response from Paul Martin, MD, FACP

Professor of Medicine and Chief, Division of Hepatology, Center for Liver Disease, University of Miami School of Medicine, Miami, Florida

Despite advances in molecular biology, the routine diagnosis of hepatitis B virus (HBV) infection remains serologic. The presence of HBsAg indicates the patient is infected with HBV. The absence of IgM anti-core antibody implies that this patient has chronic rather than acute HBV infection. The patient is HBeAg negative with presence of antibody to e antigen (anti-HBe). In combination with the absence of e antigen, the patient's normal serum aminotransferases suggest an absence of viral replication and hepatic necroinflammatory activity. This patient can therefore be assumed to be in the inactive carrier state, or (in the older literature) a so-called "healthy carrier." However, there are a few important caveats. The term "healthy carrier" has fallen out of favor because chronic HBV infection, even in the absence of clinically overt liver disease, conveys an increased risk of hepatocellular carcinoma. Furthermore, reactivation of HBV replication, either spontaneously or iatrogenically induced by chemotherapy or immunosuppression, can lead to severe liver disease. Another important issue is whether this patient has detectable HBV DNA in serum. Although e antigen was for many years the conventional serum marker of HBV replication, it has become apparent that although many chronically infected patients shed e antigen in response to host immune pressure, they may have persistence of replication. This form of HBV, called e antigen chronic HBV, typically occurs after many years of infection. Recent literature has also drawn attention to the insensitivity of serum aminotransferases in excluding hepatic necroinflammatory activity. A number of reports have described extensive inflammatory changes and fibrosis in series of patients with chronic HBV infection and normal liver chemistries but persistent serum markers of replication, including HBV DNA.

Therefore, an important additional diagnostic test in this patient is a serum HBV DNA. If serum HBV DNA is absent, the patient is in the inactive carrier state. In contrast, if serum HBV DNA is detectable, particularly at a level of greater than 2000 IU/mL, the patient has e antigen chronic HBV infection. Irrespective of the presence or absence of detectable serum HBV DNA, this patient requires regular follow-up for surveillance for hepatocellular carcinoma and reactivation of HBV replication.[1]

In Chronic Viral Infection Immune Exhaustion Driven By Antigen

<http://www.medicalnewstoday.com>

One main reason why viruses such as HIV or hepatitis C persist despite a vigorous initial immune response is exhaustion. The T cells, or white blood cells, fighting a chronic infection eventually wear out.

Researchers at Emory Vaccine Center have demonstrated that exhaustion is driven by how the immune system detects infecting viruses.

To recognize the presence of a viral infection, T cells must be presented with bits of viral protein in a molecular frame supplied by other cells in the body -- called MHC (major histocompatibility complex) class I molecules.

In mice infected by lymphocytic choriomeningitis virus (LCMV), T cells became more or less exhausted depending on how much properly framed viral protein was available.

Insights from the research could guide efforts to revive the immune system in people with chronic viral infections. The results are published online this week in the *Proceedings of the National Academy of Sciences*.

Working with Vaccine Center director Rafi Ahmed, PhD, postdoctoral fellow Scott Mueller, PhD, examined the effects of limiting what kind of cells could display the viral antigens.

Ahmed is professor of microbiology and immunology at Emory University School of Medicine and a Georgia Research Alliance Eminent Scholar.

By performing bone marrow transplants on genetically engineered mice, Mueller created mice with MHC class I molecules on blood and immune system cells but missing from other cells such as nerve cells and connective tissue. LCMV infects both cells that come from bone marrow and cells that don't. But the roles each type of cell plays in communicating the infection to the immune system is different.

"We were trying to sort out which of several factors contribute to T cell exhaustion, such as viral antigen, inflammation and where the immune system encounters the virus," Mueller says. "What came out of these experiments allowed us to answer a broad question: the role of antigen in driving exhaustion."

When injected with LCMV, the altered mice had more energetic and responsive T cells early during the infection. But later, the altered mice had much higher levels of virus and more exhausted T cells. This contrast demonstrates how the level of antigen present is the motor behind immune exhaustion during the chronic infection.

"Early on, the T cells were healthier because they saw less antigen, and only saw it on cells that came from bone marrow," Mueller says. "But later, the immune system had trouble getting rid of the virus because the T cells couldn't recognize infection in cells that were not able to present the viral antigens."

The research was supported by the National Institutes of Health and the Gates Foundation.

Source: Holly Korschun, Emory University

Controlling Hepatitis C takes full public awareness

<http://www.bclocalnews.com>

By Gaeil Farrar - *Williams Lake Tribune*

Toni Pate, the community's new part-time prevention worker and fellow staff and patrons of the

NOOPA Youth Centre will be recognizing World Hepatitis Day this Tuesday, May 19 by handing out information material to the public.

Volunteers will be handing out information magnets and pamphlets along with a cookie, from 11 a.m. to about 2 p.m. at Boitano Mall, and if weather permits, at the corner of Third Avenue and Oliver Street, Pate says.

Pate says that world-wide, one in 12 people are living with chronic Hepatitis B or C, including 600,000 Canadians.

She says one per cent of the population in Canada has the HIV virus, and there are 5,000 new cases of Hepatitis C in B.C. every year, the majority of them among youth, and related to lifestyle.

And those are only the one's who have been diagnosed, Pate says.

"The problem is that many people don't even know it," Pate says.

In the Cariboo-Chilcotin she says a 2008 study indicated that 102 people in this region have Hepatitis C.

Hepatitis C is dangerous because it damages the liver and can lead to liver failure and liver cancer. Consumption of alcohol speeds up the progression of symptoms for those who have the virus.

There are vaccinations for Hepatitis A and B but not for Hepatitis C, Pate says.

According to information pamphlets about 20 per cent of people who are infected with Hepatitis C can get rid of the virus naturally.

While 20 per cent of people will show symptoms right away, for 80 per cent of people the virus continues as a chronic infection that may not be discovered until the liver is severely damaged. Between one and four per cent of infected people will develop liver cancer.

"When it comes to HIV and Hepatitis C ignorance is not bliss. These are infections we can protect ourselves from but we need to know how," Pate says.

Like HIV/AIDS she says Hepatitis C is transmitted through blood to blood contact through open wounds or by unprotected sex.

She says HIV can live in the vacuum of a needle for up to 72 hours.

Hepatitis C can live up to six weeks on a broken piece of glass.

Pate says it is safer to assume that any bodily fluid, needle or broken glass is infected with HIV or Hepatitis C than to assume that it is not infected.

Don't do tattoos, piercings, or brandings at home, she advises.

And if you do want a tattoo, go to a professional and make sure the artist is licensed and uses clean equipment and new ink every time.

She says it only takes one act of unprotected sex to get HIV or Hepatitis C if the partner is infected.

Sharing cocaine straws or crack pipes is also dangerous. People could have open sores on the lips or in the mouth through which the virus could be transferred by sharing a pipe.

Cocaine is like glass and breaks blood vessels in the nose which can release blood that will be passed from one user to another through a straw or rolled up bill, Pate says.

Never pick up a needle with bare hands that you may see in a public place.

Call her and someone will come and remove the needle. She says garbage may contain needles or glass that may be contaminated with Hepatitis C or HIV, which makes it unwise to push down garbage using hands.

“It is so easy to use these precautions to protect ourselves. I don’t want people to be afraid. I just want them to be aware,” Pate says.

Pate can be reached at 250-392-5730.

Student uses computers against hepatitis C

<http://www.sciencecentric.com>

Viruses are wily organisms, continually adapting and changing, while using a variety of ways to evade the immune system and cause damage.

University of Saskatchewan master's student Brett Trost has won a prestigious Vanier Canada Graduate Scholarship from the Natural Sciences and Engineering Research Council of Canada - worth \$50,000 a year for two years - that he hopes will help scientists stay one step ahead of viral evolution.

A U of S computer science grad, Trost is now working with supervisor Tony Kusalik to shed light on a recently discovered mechanism that viruses use to attack the body's cells and avoid detection.

It's known that certain viruses use small molecules of RNA (a chemical similar to DNA) called microRNA to prevent cells from producing proteins that could help defend the body against the virus.

If these microRNA molecules could be identified, it could help scientists answer important questions. What kinds of proteins do these microRNA molecules prevent the body from producing? How does this affect the body's response to the virus? Can we create drugs or therapies that can disable or destroy these microRNA molecules?

'Answering these questions will greatly enhance our understanding of viruses and will ultimately allow us to gain the upper hand in the fight against many viral diseases,' says Saskatoon native Trost. 'Unfortunately, the portions of the viral genome that encode these microRNA molecules are very difficult to locate. This is hampering efforts to identify and study them.'

His love of both computers and natural sciences led him to the exciting new field of bioinformatics - research that intersects biology, chemistry, computer science, mathematics, and statistics, enabling computer science techniques to be applied to biological problems such as virus mutation.

Trost's project will develop a computer program that uses statistical methods to accurately predict what portions of a viral genome encode microRNA molecules. Specifically, the program will be used to locate microRNA molecules in the hepatitis C virus, work that will then be verified at the U of S Vaccine and Infectious Disease Organisation.

Lab techniques commonly used to verify predicted microRNA are time-consuming and expensive, so accurate computational prediction techniques are extremely important in advancing this research.

'The chance to discover something that provides meaningful insight into the world around us - or find something that can improve people's lives - is what motivates me to do research,' says Trost.

Winning the scholarship allows Trost to pursue his studies without financial pressure.

'I really like research and teaching, so being a professor seems like the perfect career for me,' says Trost. 'To paraphrase my supervisor, it's a career in which you get paid to be curious. That seems perfect, doesn't it?'

Source: University of Saskatchewan

May 15, 2009

Ginger helps fight nausea from cancer treatment

www.reuters.com

By Maggie Fox, Health and Science Editor

WASHINGTON (Reuters) - Ginger, long used as a remedy for upset tummies, can help ease the nausea caused by cancer drugs, researchers reported on Thursday.

They found the lowest doses of ginger worked best.

"Patients ask all the time what else they can do to relieve their symptoms," Dr. Richard Schilsky, president of the American Society of Clinical Oncology and a blood cancer specialist at the University of Chicago, said in an interview.

"Ginger has been used for thousands of years for all types of stomach problems."

Dr. Julie Ryan and colleagues at the University of Rochester in New York tested 614 people with

various cancers who were being treated with chemotherapy and standard anti-nausea medications.

They got either a placebo or one of three doses of powdered ginger in a capsule.

"All of the doses of ginger were effective in reducing nausea," Schilsky said.

The lowest two doses -- half a gram and one gram of powdered ginger -- were more effective than 1.5 grams, Ryan's team reported.

Ryan said it was not exactly clear how ginger helps relieve nausea in these patients. "There is other research that shows it is a potent anti-inflammatory agent in the gut," she told reporters in a telephone briefing.

She said it might be possible to get the same effect by eating ginger cookies, depending on how much ginger is used.

More details of the study will be available at the oncology society's annual meeting later this month. A summary of the findings was released on Thursday.

(Additional reporting by Julie Steenhuysen in Chicago)

(Reporting by Maggie Fox; Editing by Xavier Briand)

ImQuest BioSciences and Arisyn Therapeutics Introduce Novel New HCV Therapeutic Agent at Hepatitis Conference

<http://sev.prnewswire.com>

FREDERICK, Md., May 14 /PRNewswire/ -- ImQuest Bio and Arisyn jointly presented important new results on ATI-0810 (Formerly PG301029), a novel late stage inhibitor of hepatitis C virus (HCV) replication, at the 13th ISVHLD meeting held last week in Washington D.C. The presentation highlighted the ability of PG301029 to potentially suppress the replication of HCV in vitro and defined its potential mechanism of antiviral action through the selection of a replicon resistant to the antiviral effects of the compound. Resistant HCV replicon sequences were selected in cell culture and resulted in mutations in the viral NS5A proximal to the NS5A-NS5B cleavage junction. The defined mutation would affect viral polyprotein processing at this site, or the interaction of NS5A, or the NS5A/5B polyprotein(s) with host cell factors involved in viral RNA replication, either of which presents a novel target for antiviral therapy. Todd B. Parsley, Ph.D., Director of Hepatitis Virus Research, presented the new findings which also included gene profiling patterns in compound treated and untreated cells. The studies included ImQuest co-authors Lu Yang, MD and Robert W. Buckheit, Jr., Ph.D.

"The data presented indicate that PG301029 has a unique mechanism of action as an inhibitor of hepatitis C virus replication," said the study's Principal Investigator, Dr. Parsley. "The genetic analysis suggests that PG301029 functions through a novel antiviral target, and we are excited about the prospects for exploiting this target for the development of new and potent anti-HCV

therapies."

The presentation represents a continuation of the research partnership between ImQuest and Arisyn for the development of Arisyn's portfolio of antiviral and anticancer products based on its platform technology involving targeting of RNA transcription. Funding for the study was obtained in part from a Small Business SBIR grant recently awarded to ImQuest by the NIH.

ImQuest BioSciences Inc., a privately held U.S. company located in Frederick, Maryland, is a leading provider of anti-infective therapeutic and microbicide development services to the biotechnology and pharmaceutical industry.

Arisyn Therapeutics Inc., a privately held virtual biotechnology company headquartered in Frederick, Maryland with a mission of identifying novel first in class inhibitors for infectious diseases and cancer and providing development resources for these agents through Phase 1 and 2 human clinical trials.

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Needles exchange program, becoming moral issue for Colo.

<http://www.denverpost.com>

By Karen Auge

The Denver Post

Andrew McClure, a member of the Denver Drug Strategy Commission, says that needle exchanges save taxpayers money. While Denver is studying such programs, they remain politically fraught.

Angie insisted her syringes were stolen.

Undeterred by what many would consider a weak demand for a drug user's tossed needles, she stuck by her story.

"I buried my red (syringe) box in the park and when I went back, somebody had stolen it," she said.

Angie, who injects cocaine multiple times a day, didn't hold up her end of the syringe-exchange bargain. Nevertheless, she got what she came for: a supply of clean, new syringes and a box for her used ones, free and completely illegal, from the Underground Syringe Exchange of Denver.

For more than a year, USED has been clandestinely conducting transactions its organizers say Colorado ought to bring into the open: syringe swaps meant to keep infection rates down by providing drug users with new syringes while taking used needles off the street.

Although 185 cities, including Boulder, now condone exchanges, that's not going to happen statewide in Colorado anytime soon. A legislative push this year to make legal exchanges possible was dead before arrival in the statehouse.

"The issue is more complex than it perhaps first appears," said Evan Dreyer, Gov. Bill Ritter's spokesman. "In fact, as they began to look at this proposal, law enforcement and the Colorado Department of Public Health and Environment both expressed serious reservations."

In any case, a coalition of public-health officials, treatment providers, advocates and a city commission have gingerly set their sights on Denver.

Nancy Steinfurth, executive director of the Hep C Connection, said her organization favors exchanges. An estimated 70 percent of hepatitis C cases and 10 percent of HIV infections come from sharing needles.

That's one reason Dr. Mark Thrun, director of HIV prevention for Denver Public Health, supports syringe exchanges.

"In the public-health community, it's very common-sense," he said. "It keeps them from getting these chronic, potentially fatal diseases; it gives us an opportunity to link them into treatment; and it lessens the economic burden on the already overburdened health care system."

In February, the 25-member Denver Drug Strategy Commission recommended that Mayor John Hickenlooper consider a pilot exchange program, said Karla Maraccini, the commission's director.

Hickenlooper called for more study, and that is happening, Maraccini said. The commission is checking out other programs, searching for a model.

Political risks daunting

Denver District Attorney Mitch Morrissey has concerns about a local program conflicting with state law, spokeswoman Lynn Kimbrough said.

"He can't simply choose to ignore state law," Kimbrough said.



State update

Twenty-seven states and the District of Columbia have at least one syringe-exchange program.

Alaska	1
California	22
Colorado	1
Connecticut	6
Georgia	1
Hawaii	1
Illinois	4
Indiana	1
Kansas	1
Louisiana	2
Maine	2
Massachusetts	3
Michigan	3
Minnesota	3
Missouri	1
New Jersey	1
New Mexico	17
New York	9
North Carolina	1
Oklahoma	1
Oregon	3
Pennsylvania	1
Texas	2
Utah	1
Vermont	3
Washington	15
Wisconsin	10
Washington, D.C.	1

In the meantime, the Hep C Connection is publicizing its "Drop to Stop" campaign this week, encouraging anybody with used syringes to drop them at one of several sites around Denver. They'll get no new needles, just the satisfaction of knowing their old ones are safely gone.

Maraccini was circumspect about what steps Denver might consider to get around state law, which makes possession of syringes without a prescription a crime. Hickenlooper's office was too.

"Anything in contradiction to city or state law would have to be carefully considered," Eric Brown, spokesman for the mayor, said in an e-mail. "We're just not there yet."

Needle exchanges are controversial propositions. They are also politically risky and invariably invite charges that they encourage or condone drug use.

Proponents say the drug use is happening already — and when it happens with dirty needles, it endangers everyone.

"I think it's unfortunate that people take a public-health issue and make it a moral issue," said Andrew McClure, a member of the Denver Drug Strategy Commission.

But even those who couldn't care less about drug users should consider the cost to taxpayers of treating HIV and hepatitis C, McClure said.

A year's course of treatment for hepatitis C averages about \$30,000, said Denver Health's Thrun. According to him, several studies refute the argument that exchange programs encourage or prolong drug use. Instead, he said, data show people in exchange programs are more likely to seek treatment.

A 2005 Centers for Disease Control and Prevention study found that 86 percent of exchange programs surveyed made referrals for treatment. In addition, more than 80 percent offered counseling and testing for HIV and hepatitis C.

The state health department estimates that nearly 80,000 Coloradans have been infected with hepatitis C. A 2005 survey of 500 Denver drug users found 52 percent had the hepatitis C virus.

"HIV is always a concern," said Monique Whalen, director of the Drop-In Center, which serves drug users. "But hep C in Colorado is much more of a concern than HIV. It's a virus that lives outside the human body. And people don't live in a vacuum. They are sharing syringes, having sex, sharing households."

Eliminating criminal penalties for carrying syringes has benefits, she said.

"Just the fear of being caught with one means people will leave them in hidden spaces, in the park or the dumpster or a public bathroom," Whalen said.

People like Angie.

Syringes and a scolding

Since what its staffers do is illegal, USED doesn't offer its services anywhere in particular. Rather, its 50 or so clients call a cellphone to set up meetings with volunteers.

USED orders syringes, alcohol and wipes online. Those and other expenses amount to \$700 or \$800 a month, said one of the group's volunteers, who asked to be identified only by an initial: S. Money for those supplies comes from donations and fundraisers at underground clubs, he said.

Each transaction is carefully recorded: for April, USED gave out 1,670 syringes, and got back 1,650.

As he logged miles walking downtown Denver on a drizzly Saturday, S. explained that Angie is an example of why, to him, exchanges are a good idea.

She's homeless, has tested positive for hepatitis C and is afraid of getting caught with syringes. So she buries them in a park, where thieves or dogs can dig them up and scatter them.

Eventually, S. gives Angie her new syringes and a scolding about losing her old ones.

Then, Angie and her friend, Leticia, pull scruffy daytimers out of backpacks that hold most of what they own and ask about services like health care or check-ups or meals. He gives them dates and times, which they carefully record.

He gently nags them about getting treatment for hepatitis C. But they know there isn't much treatment out there for them until they stop using.

And they're going to do that, they say. Soon.

Angie talks about cutting back on daily injections like a two-pack-a-day smoker who has cut back to one.

"I'm gaining weight, see?" She lifts up her sweatshirt and proudly pokes at a croissant-sized roll as evidence of her emerging health.

Leticia, who has two young children she can't see, says she's down to three heroin injections a day.

"I'm trying to wean myself down and off. We both are. And we're both healthier," she said.

The Drop-In Center's Whalen understands that the public might doubt whether anyone who injects drugs is really concerned about infections.

"Take my word for it: Having been an injector myself, I can say yes, they are."

Many are also concerned about their habit, said S.

Their desire to stop is real, he said.

"I still have a future," Angie said. "I just wish I'd pull my head out of my ass" and get on with it.

Novel Anti-HBV Vaccine May Prevent Hepatocellular Carcinoma

www.medscape.com

NEW YORK (Reuters Health) May 14 - A vaccine against hepatitis B virus (HBV), based on virus-like particles (VLP) loaded with multiepitope peptides, prevents hepatocellular carcinoma (HCC) in a mouse model, according to a report in the May *Hepatology*.

Fusion VLPs carrying multiepitope peptides could generate broader immune responses and lead to more powerful antitumor attack, the authors explain.

Dr. Fei-Xiang Ding and colleagues from The Second Military Medical University, Shanghai, China developed fusion hepatitis B core protein-VLPs inserted with four CTL epitopes derived from HBV X protein and the Th lymphocyte epitope PADRE, and investigated whether these particles could induce broad, specific immune responses and significant antitumor effects in vitro and in mice.

In vitro, VLP-pulsed dendritic cells elicited a broad repertoire of epitope-specific CTL responses, as well as a broad spectrum of specific CD8+ T cells, the authors report.

Primary cultured HCC cells from 6 patients were highly susceptible to lysis by autologous CTLs elicited by VLP-pulsed dendritic cells.

Splenocytes transferred from mice immunized with VLP-pulsed dendritic cells significantly inhibited the growth of hepatic tumor cells in nude mice, the researchers note. Furthermore, active immunization with the VLPs also had a significant inhibitory effect on tumor formation in this animal model of hepatocellular carcinoma.

"In light of the broad repertoire and strong magnitude of elicited CTL responses and significant antitumor effects in vitro and in vivo, our VLPs appear to be promising candidates for HBV-related HCC," the investigators conclude.

Hepatology 2009;49:1492-1502.