



## KY Hepatitis Connections

On behalf of the KY Adult Viral Hepatitis Program, we wish you and your loved ones a blessed and wonderful Thanksgiving holiday! We are pleased to share with you the November issue of *KY Hepatitis Connections*. The *KY Hepatitis Connections* provides current information, opportunities for viral Hepatitis continuing professional education and information about educational materials available.

Please feel free to forward and/or copy and distribute to other professionals in your network. Your knowledge and input are greatly valued, as we are committed to keeping you up to date on shared progress in the medical community on viral Hepatitis and its impact on our families throughout the Commonwealth. Join us on Facebook, KY Viral Hepatitis.

Kathy Sanders, RN MSN

## Inactivation of Hepatitis C Virus Infectivity by Human Breast Milk

### Abstract

**Background.** Hepatitis C virus (HCV) is spread through direct contact with blood, although alternative routes of transmission may contribute to the global burden. Perinatal infection occurs in up to 5% of HCV infected mothers and presence of HCV RNA in breast milk has been reported. We investigated the influence of breast milk on HCV infectiousness. **Methods/Results.** Human breast milk reduced HCV infectivity in a dose-dependent manner. This effect was species-specific since milk from various animals did not inhibit HCV infection. Treatment of HCV with human breast milk did not compromise integrity of viral RNA or capsids, but destroyed the lipid envelope. Fractionation of breast milk revealed that the antiviral activity is present in the cream fraction containing the fat. Proteolytic digestion of milk proteins had no influence on its antiviral activity whereas prolonged storage at 4°C increased antiviral activity. Notably, pretreatment with a lipase inhibitor ablated the antiviral activity and specific free fatty acids of breast milk were antiviral. **Conclusion.** The antiviral activity of breast milk is linked to endogenous lipase-dependent generation of free fatty acids which destroy the viral lipid envelope. Therefore, nursing by HCV-positive mothers is unlikely to play a major role in vertical transmission.

<http://www.ncbi.nlm.nih.gov/pubmed/24068703>

## Syndromes and conditions linked to hepatitis C

Hepatitis C virus (HCV) is an infectious disease that often remains asymptomatic and unrecognised until complications of the virus arise. These often include extrahepatic manifestations of the virus, which first bring patients into contact with the medical profession. First recognised in the 1990s several syndromes and conditions have now been linked to hepatitis C, while others are still emerging. In some patients, extrahepatic manifestations can be the dominant feature, while hepatic disease is mild. Some conditions have an established association with the virus with a proven pathophysiological and epidemiology, such as cryoglobulinaemia. Others have consistently been found to be seen in patients with HCV, but the underlying cause of these conditions is not clearly understood. These include porphyria cutanea tarda. Many other autoimmune conditions are commonly seen in the patients with HCV as well as nephropathies, but the exact interplay between virus and resulting clinical condition is not clear. Clinicians have to have a high index of suspicion and a knowledge of the extrahepatic manifestations of HCV in order to not only treat the manifestation but also in initiated timely therapies for the underlying HCV.

<http://hepatitisnewdrugresearch.com/syndromes-and-conditions-linked-to-hepatitis-c.html>



## Emerging resistance using sequential direct-acting antiviral agents for Hepatitis C

A translational study published in the latest issue of the American Journal of Gastroenterology investigates resistance emergence using sequential direct-acting antiviral agents for Hepatitis C using ultra-deep sequencing.

Direct-acting antiviral agents against hepatitis C virus (HCV) have recently been developed and are ultimately hoped to replace interferon-based therapy.

However, direct-acting antiviral agents monotherapy results in rapid emergence of resistant strains and direct-acting antiviral agents must be used in combinations that present a high genetic barrier to resistance, although viral kinetics of multidrug-resistant strains remain poorly characterized.

Dr **Kazuaki Chayama** and colleagues from Japan studied the emergence and fitness of resistance using combinations of telaprevir and NS5A or NS5B inhibitors with genotype 1b clones.

HCV-infected chimeric mice were treated with direct-acting antiviral agents, and resistance was monitored using direct and ultra-deep sequencing.

<http://www.gastrohep.com/news/news.asp?id=109930>

## Medivir: Simeprevir data from COSMOS study in Hepatitis C patients will be presented as late-breaking presentation at AASLD

Stockholm, Sweden - Medivir AB (OMX: MVIR) announced that data from the phase IIa COSMOS study (Combination Of SiMeprevir and sOfosbuvir in HCV genotype 1 infected patients) of the investigational protease inhibitor simeprevir (TMC435) administered once daily with Gilead's investigational nucleotide inhibitor sofosbuvir (GS-7977), with and without ribavirin, in genotype 1 chronic hepatitis C adult patients with compensated liver disease has been accepted as a late-breaking oral presentation at the upcoming Annual Meeting of the American Association for the Study of Liver Diseases (AASLD). AASLD will take place November 1 to 5 in Washington, D.C.

The COSMOS data will be presented during the late-breaking oral session on Monday, November 4, 2:45-4:30 p.m. (EST) in Hall E: SVR results of a once-daily regimen of simeprevir (TMC435) plus sofosbuvir (GS-7977) with or without ribavirin in cirrhotic and non-cirrhotic HCV genotype 1 treatment-naïve and prior null responder patients: The COSMOS study.

<http://www.swedishwire.com/press-releases/18396-medivir-simeprevir-data-from-cosmos-study-in-hepatitis-c-patients-will-be-presented-as-late-breaking-presentation-at-aasld>

## Janssen Acquires Investigational NS5A Inhibitor for the Treatment of Hepatitis C from GlaxoSmithKline

TITUSVILLE, N.J., Oct. 8, 2013 /PRNewswire/ -- Janssen Pharmaceuticals, Inc. (Janssen) announced today the acquisition of the investigational compound GSK2336805, an NS5a replication complex inhibitor in Phase 2 development for the treatment of chronic hepatitis C, from an affiliate of GlaxoSmithKline plc. Janssen has acquired all rights to develop and commercialize GSK2336805, including in combination with other drugs. Financial details of the agreement have not been disclosed.

Janssen plans to initiate Phase 2 studies to evaluate the use of GSK2336805 in interferon-free combinations with the investigational protease inhibitor simeprevir (TMC435) and TMC647055, Janssen's non-nucleoside polymerase inhibitor, for the treatment of chronic hepatitis C in adult patients with compensated liver disease.

"We're excited to add GSK2336805 to our existing portfolio of direct-acting antivirals (DAAs). This addition will broaden our clinical development program as we continue to look for new investigational interferon-free treatment combinations to combat the hepatitis C virus," said Gaston Picchio, Hepatitis Disease Area Leader, Janssen. "Janssen is dedicated to working with the hepatitis C community to investigate our portfolio of DAAs in a number of different treatment combinations and hepatitis C patient populations."



## HCV transmitted from organ donor with negative nucleic acid test

SAN FRANCISCO — Two recipients of organs from a single donor developed hepatitis C infection that was traced back to the donor, who was negative for the disease by nucleic acid testing, according to research presented here at IDWeek 2013.

"Antibody detection of hepatitis C typically takes 7 to 10 weeks, and RNA detection with nucleic acid testing takes 3 to 7 days, but this may vary by test sensitivity and hemodilution of specimen," **Emily Blumberg, MD**, professor of medicine at Perelman School of Medicine at the University of Pennsylvania, said during her presentation. "In 2013, the US Public Health Service updated their guidelines, recommending that [HCV](#) antibody and nucleic acid testing be performed on all organ donors."

Two organ recipients were reported to the CDC in March 2012 with newly-diagnosed HCV infections identified by routine, post-transplantation nucleic acid testing and screening. In December 2011, both had received organs — heart and left kidney — from one donor, an active [injection drug user](#) who had undetectable HCV by polymerase chain reaction.

<http://www.healio.com/infectious-disease/hepatitis-resource-center-2013/hcv-transmitted-from-organ-donor-with-negative-nucleic-acid-test>

## **IDWeek 2013: Tenofovir May Help Prevent Mother-to-child Hepatitis B Transmission**

Taking tenofovir (Viread) during the final months of pregnancy may provide extra protection against perinatal transmission of hepatitis B virus (HBV), along with immunization of the infant, according to a late-breaker presentation at the Second IDWeek conference last week in San Francisco.

In countries where hepatitis B is endemic -- including much of Asia, the Middle East, and Africa -- HBV is often transmitted from mother to child during pregnancy or delivery. Immediate vaccination of infants and administration of an antibody preparation, hepatitis B immune globulin (HBIG), dramatically reduces transmission risk, but it can still occur if the mother has a high HBV viral load.

Alper Gunduz and colleagues from Hamidiye Sisli Etfal Education and Research Hospital in Istanbul evaluated the safety and efficacy of tenofovir taken during the last trimester of pregnancy, along with HBV immunization, to reduce perinatal HBV transmission from hepatitis B "e" antigen (HBeAg) positive women with high viral load. Prior research indicates that 10% to 30% of babies born to such women develop chronic hepatitis B despite standard prophylaxis.

## **Interferon-free regimen safe, effective for patients with HCV genotype 1**

SAN FRANCISCO – A regimen of daclatasvir, asunaprevir, and a non-nucleoside NS5B inhibitor yielded high sustained virologic response rates among patients with hepatitis C genotype 1 in a study presented at ID Week 2013.

Gregory T. Everson, MD, University of Colorado Denver in Aurora, Colo., and colleagues randomly assigned 32 noncirrhotic, treatment-naive patients with hepatitis C genotype 1 to 60 mg NS5A inhibitor daclatasvir (DCV) once daily and 200 mg protease inhibitor asunaprevir (ASV) and 75 mg non-nucleoside NS5B inhibitor BMS-791325 twice daily for 24 (group 1; n=16) or 12 weeks (group 2; n=16). An additional 34 patients then were randomly assigned 60 mg DCV once daily and 200 mg ASV and 150 mg BMS-791325 twice daily for 24 (group 3; n=16) or 12 weeks (group 4; n=18).

Across the groups, all but two patients achieved HCV RNA below 25 IU/mL at 4 weeks of treatment, with 92% of evaluable patients achieving sustained virologic response at 4 weeks and 94% at 12 and 24 weeks. Rate of virologic response did not differ significantly between those who received 12 or 24 weeks of therapy. <http://www.healio.com/infectious-disease/hepatitis-resource-center-2013/interferon-free-regimen-safe-effective-for-patients-with-hcv-genotype-1>

## Will Evolving Hepatitis C Therapies Reduce the Need for Specialized Care?

### Enter the Nonspecialist: Will Evolving Hepatitis C Therapies Reduce the Need for Specialized Care?

When I first started treating hepatitis C, therapy was complicated primarily by interferon-associated adverse events such as flulike symptoms, thrombocytopenia, neutropenia, depression, and thyroiditis requiring a specialist to manage treatment. These specialists learned how to anticipate, manage, and work around these predictable adverse events to maximize adherence and outcomes. The addition of ribavirin and the anemia associated with its use resulted in hepatitis C treatment remaining firmly in the hands of specialists with experience in managing the complications of therapy. Nor did the availability of peg interferon alter the need for hepatitis C therapy to remain the purview of hepatologists, gastroenterologists, and infectious disease specialists. For the better part of 10 years, this standard of care remained unchanged.

In 2011, our field underwent an evolutionary leap forward with the introduction of the first DAAs, boceprevir and telaprevir. The addition of these new protease inhibitors to peginterferon and ribavirin finally allowed us to attack the virus directly and deliver to patients (at least those infected with genotype 1 hepatitis C) significant increases in sustained virologic response. However, the realities of adverse events, especially anemia, have persisted and nothing about the new protease inhibitor-based regimens have made treating patients any easier or less complex.

<http://hepatitisnewdrugs.blogspot.com/2013/10/will-evolving-hepatitis-c-therapies.html?spref=fb>

## Rapid Hepatitis C Virus Testing: An Innovative Pilot Study for Testing and Linking High Risk Populations from a Mobile Healthcare Clinic

**Session:** Poster Abstract Session: Viral Infections; Pathogenesis and Epidemiology  
*Saturday, October 5, 2013*

**Background:** After recent release of effective HCV treatments, CDC guidelines aim to increase HCV testing and linkage to treatment for certain high-risk populations. This approach has not, however, been empirically tested using rapid HCV testing strategies.

**Methods:** An innovative rapid HCV testing campaign was deployed from a mobile medical clinic (MMC) in New Haven, CT using routine medical intake information. Clients could select rapid versus traditional phlebotomy testing. Traditional testing included phlebotomy for other medical co-morbidities, including syphilis, hepatitis B, and chronic medical conditions. Independent correlates of: 1) type of HCV testing strategy; and 2) reactive HCV antibody results were assessed. Linkage to HCV care was defined as completing one follow-up clinical visit in person with confirmatory HCV testing.

**Results:** All of 190 clients approached from March 2012 to March 2013 accepted HCV testing; 154 (81.1%) chose rapid HCV testing. Overall, 17 (8.9%) were HCV+, with 13 (8.4%) in the rapid and 4 (11.1%) in the traditional group. Generally, participants were mean age 35.9 years, previously incarcerated (51.1%), had >15 lifetime sexual partners (81.6%), were US-born (84.7%), had used illicit drugs (75.3%), and previously tattooed (64.2%). Of the 60 (31.6%) people who inject drugs (PWID), only 9 (15.0%) were within the “baby boomer” cohort.

Independent correlates of choosing rapid HCV testing over phlebotomy were non-PWID (AOR 25.0;  $p=0.027$ ) and less than 15 lifetime sexual partners (marginal effect 0.17;  $p=0.003$ ). Independent correlates of being HCV+ were being non-Hispanic White (AOR 15.2;  $p=0.002$ ), reported sex with a known HCV+ partner (AOR 33.0;  $p<0.001$ ), and increasing age (AOR 1.08;  $p=0.003$ ). Among the 17 HCV+ patients, only 7 (53.8%) were within the “baby boomer” cohort, and 12 (70.6%) were successfully linked to HCV care.

**Conclusion:** The majority of individuals prefer rapid HCV testing, yet higher risk individuals opted for traditional phlebotomy testing, perhaps to identify other comorbid conditions. Rapid testing, however, identified the majority of new HCV infections, using an innovative MMC model which successfully engaged individuals who might otherwise not have been tested in traditional healthcare settings. Risk-based testing thus necessarily augments the “baby boomer” HCV screening age category.

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## **Incident Hepatitis C Virus Infection in Men Who Have Sex With Men: A Prospective Cohort Analysis, 1984-2011 'HIV-infection (6-fold), unprotected receptive anal intercourse (3-fold) increase risk for HCV acquisition, low CD4, syphilis'**

**Background.** Prospective characterization of hepatitis C virus (HCV) transmission in both human immunodeficiency virus (HIV)–infected and –uninfected men who have sex with men (MSM) over the entire HIV epidemic has not been comprehensively conducted.

**Methods.** To determine the trends in and risk factors associated with incident HCV in MSM since 1984, 5310 HCV antibody (anti-HCV)–negative MSM in the Multicenter AIDS Cohort Study were prospectively followed during 1984–2011 for anti-HCV seroconversion.

**Results.** During 55 343 person-years (PYs) of follow-up, there were 115 incident HCV infections (incidence rate, 2.08/1000 PYs) scattered throughout the study period. In a multivariable analysis with time-varying covariates, older age (incidence rate ratio [IRR], 1.40/10 years,  $P < .001$ ), enrollment in the

later (2001–2003) recruitment period (IRR, 3.80,  $P = .001$ ), HIV infection (IRR, 5.98,  $P < .001$ ), drinking >13 alcoholic drinks per week (IRR, 1.68,  $P < .001$ ), hepatitis B surface antigen positivity (IRR, 1.68,  $P < .001$ ), syphilis (IRR, 2.95,  $P < .001$ ), and unprotected receptive anal intercourse with >1 male partner (IRR, 3.37,  $P < .001$ ) were independently associated with incident HCV. Among HIV-infected subjects, every 100 cell/mm<sup>3</sup> increase in CD4 count was associated with a 7% ( $P = .002$ ) decrease in the HCV incidence rate up to a CD4 count of 500 cells/mm<sup>3</sup>, whereas there was no association with highly active antiretroviral therapy.

**Conclusions.** The spread of HCV among both HIV-infected and -uninfected MSM in the United States has been ongoing since the beginning of the HIV epidemic. In HIV



## **Advisory Issued for Dietary Supplement Linked to Hepatitis, Liver Failure**

**FRANKFORT, Ky. (Oct. 17, 2013)** – The Kentucky Department for Public Health is advising consumers and retailers concerning a Centers for Disease Control and Prevention (CDC) Health Advisory that was issued on Oct. 8. regarding acute hepatitis and liver failure linked to the reported use of a dietary supplement intended for weight loss or muscle building.

The CDC issued the advisory following an ongoing investigation by the Hawaii Department of Health (DOH) into a number of previously healthy individuals who developed acute hepatitis and sudden liver failure of unknown cause after using a dietary supplement. In all, 29 cases have been confirmed in Hawaii, with 83 percent reporting use of a product marketed as OxyELITEPro, a dietary supplement for weight loss and muscle gain, prior to illness onset.

The CDC, in collaboration with state health departments, is collecting additional clinical and epidemiologic information to determine if this outbreak is national in scope. The CDC has also issued



guidance to clinicians who evaluate patients presenting with symptoms consistent with acute hepatitis to ask about consumption of dietary supplements and report any patients with these symptoms to the local or state health department. The CDC is recommending that people using dietary supplements for weight loss or muscle gain should do so with caution and under a medical provider's close supervision.

Although there has been no official recall of the product, USPLabs LLC, the distributor of OxyElitePro, is cooperating with health officials and has agreed to halt distribution of the product until the investigation is complete. No illnesses associated with the use of this product have been reported in Kentucky. For more information on the advisory visit: <http://emergency.cdc.gov/HAN/han00356.asp>.

## **HCV Conference for Primary Care Providers**

The KY Adult Viral Hepatitis Prevention Program and the University of Louisville are partnering to coordinate an Annual Hepatitis C Conference targeting primary care providers and clinicians throughout the Commonwealth. We are in need of your assistance; please take the following survey to assist us in planning this conference. The survey will be open thru November 15<sup>th</sup>. Your feedback is vital to the success of this conference.

To take the survey, click on: <http://www.surveymonkey.com/s/HCVKYPrimaryCareClinicianConference>

## **EDUCATION**

### **Viral Hepatitis Updates from CDC**

#### **Online Serology Training**

The course is comprised of six animated tutorials with voiceovers and eight case studies. The tutorials and case studies combine to teach the course objectives.

<http://www.cdc.gov/hepatitis/Resources/Professionals/training/Serology/training.htm>

#### **Hepatitis C Online Course: Management of Cirrhosis–Related Complications**

Module 3: [Management of Cirrhosis-Related Complications](#) has been added to a self-study, interactive course for medical providers on Hepatitis C infection. Module 1: Screening and Diagnosis of Hepatitis C Infection and Module 2: Evaluation, Staging, and Monitoring of Chronic Hepatitis C are also active. New features include Color Coded Master Bibliography, Embedded Video, and Clinical Calculators. The project is brought to you by the University of Washington in collaboration with the International Antiviral Society-USA (IAS-USA). Free CME credit and free CNE credit are available. Funded by a grant from the Centers for Disease Control and Prevention. <http://hepatitisc.uw.edu/index.php>

## **Medscape Hepatitis C Continuing Medical Education Credits:**

<http://search.medscape.com/education-search?newSearchHeader=1&queryText=hepatitis+C>

### **KnowHepatitis.org Training**

The National Training Center provides training to frontline workers in community based organizations and clinics on hepatitis prevention, diagnosis, management, treatment and integration. Hepatitis, STDs and HIV are preventable diseases. Despite this it is estimated that up to 5 million people nationwide are chronically infected with hepatitis B or C and many of them do not know it. Concurrently, it is estimated that in 2006 that there were 36,828 new cases of AIDS, approximately 436,693 people living with AIDS and up 1.2 million people who are infected with HIV and do not know it. Approximately, 25% to 35% of all the people living with AIDS are also co-infected with HCV and chronic HCV infection is now a leading cause of death among people with AIDS.

<http://www.knowhepatitis.org/>

## **Save the Date:**

***The Webinar: “What Every Woman Needs to Know about Hepatitis B and C”***

**Thursday, November 7, 2013**

**2:30 PM - 4:00 PM EST**

Co-hosted by the Office of Women’s Health and the Office of HIV/AIDS and Infectious Disease Policy,  
U.S. Department of Health and Human Services

To register for this event:

1. Go to the URL listed below and choose Web RSVP under Join Events.
2. Enter the conference number and pass-code.
3. Provide your information for the event leader and then click submit

[https://www.mymeetings.com/emeet/rsvp/index.jsp?customHeader=mymeetings&Conference\\_ID=5488150&passcode=7608129](https://www.mymeetings.com/emeet/rsvp/index.jsp?customHeader=mymeetings&Conference_ID=5488150&passcode=7608129)

Conference number: 5488150 and Pass-code: 7608129

## FDA Advisory Committee Supports Approval of Gilead's Sofosbuvir for Chronic Hepatitis C Infection

FOSTER CITY, Calif.--(BUSINESS WIRE)--Oct. 25, 2013-- Gilead Sciences, Inc. (Nasdaq: GILD) today announced that the Antiviral Drugs Advisory Committee of the U.S. Food and Drug Administration (FDA) has voted unanimously (15-0) that the available data support approval of the once-daily nucleotide analogue sofosbuvir in combination with ribavirin for the treatment of chronic hepatitis C in adult patients with genotype 2 and 3 infection. Committee members also voted unanimously (15-0) that the available data support approval of sofosbuvir in combination with pegylated interferon and ribavirin for the treatment of chronic hepatitis C in treatment-naïve adult patients with genotype 1 and 4 infection.

The recommendations of the Advisory Committee are not binding, but will be considered by FDA as the agency completes its review of Gilead's New Drug Application (NDA) for sofosbuvir. Gilead submitted the NDA on April 8, 2013 and was granted a priority review. The FDA also granted sofosbuvir a Breakthrough Therapy designation. The FDA grants Breakthrough Therapy designation and priority review status to drug candidates that may offer major advances in treatment over existing options. A target review date of December 8, 2013 has been set under the Prescription Drug User Fee Act (PDUFA). Applications for marketing approval of sofosbuvir are also pending in the European Union, Australia, Canada, New Zealand, Switzerland and Turkey.

-See more at: <http://www.gilead.com/news/press-releases/2013/10/fda-advisory-committee-supports-approval-of-gileads-sofosbuvir-for-chronic-hepatitis-c-infection#sthash.codSqwbO.dpuf>



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