

HCV ADVOCATE WEEKLY NEWS REVIEW

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

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Editor-in-Chief*

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Screening Tool for Hepatitis C Virus Risk May Guide Serologic Screening

www.medscape.com

Laurie Barclay, MD

October 13, 2008 — A screening tool for hepatitis C virus (HCV) effectively identifies patients at high risk for the infection, according to the results of a prospective study reported in the October 13 issue of the *Archives of Internal Medicine*.

"Although...HCV has an estimated national prevalence of 1.8%, testing rates are lower than those recommended by guidelines, particularly in primary care," write Thomas McGinn, MD, MPH, from Mount Sinai School of Medicine in New York, NY, and colleagues. "A critical step is the ability to identify patients at increased risk who should be screened. We sought to prospectively derive and validate a clinical predication tool to assist primary care providers in identifying patients who should be tested for HCV antibodies."

At an inner-city primary care clinic, 1000 randomly selected patients completed a 27-item questionnaire evaluating 5 HCV risk factor domains: work, medical, exposure, personal care, and social history. They subsequently underwent HCV antibody testing, and risk factors associated with HCV antibodies were identified with use of multivariable logistic regression analysis.

The prevalence of HCV antibodies was 8.3% (95% confidence interval, 6.7% - 10.2%). Patients who tested positive for HCV antibody were more likely to be men, older, and insured by Medicaid ($P \leq .02$). A positive test for HCV-antibody was more likely in patients who had risk factors within the medical, exposure, and social history domains, with area under the receiver-operating characteristic curve 0.77 for the screening tool based on these 3 domains. The probability of HCV antibody positivity was higher with an increasing number of positive domains, and only 2% of patients with zero risk factors had HCV antibodies.

"A prediction tool can be used to accurately identify patients at high risk of HCV who may benefit from serologic screening," the study authors write. "Future studies should assess whether wider use of this tool may lead to improved outcomes."

Limitations of this study include population from an inner-city primary care practice, with lack of generalizability to other populations or settings; self-administered questionnaire presenting the possibility of recall bias; and significant differences between the subjects who chose to participate and those who refused.

"Widespread use of the tool may facilitate and increase overall screening and detection of HCV in diverse populations of primary care patients," the study authors write. "By targeting only patients at higher risk, it may lead to more cost-effective screening for a disease that is causing significant morbidity and mortality particularly in inner-city populations. An impact analysis or randomized control trial of this model is warranted to demonstrate both clinical value and cost-effectiveness."

The study authors have disclosed no relevant financial relationships.

Walter Reed Evaluation Concludes FirstVue(TM) HBSAG Test is Preferred over Other Rapid Tests

<http://www.marketwatch.com>

FirstVue(TM) HBSAG Test Found to Have Higher Sensitivity and Specificity than Other Rapid HBSAG Tests and FirstVue(TM) '...and was the preferred test in all phases of this evaluation'

CORAL SPRINGS, Fla., Oct 13, 2008 /PRNewswire via COMTEX/ -- AT First Diagnostic LLC an emerging worldwide marketing leader in rapid diagnostic test kits, today announced that a recent evaluation conducted by the Walter Reed Army Institute of Research of the FirstVue(TM) HBSAG Test, was released at the Advanced Technology Applications for Combat Casualty Care meeting, sponsored by the Department of Defense. The purpose of the evaluation, entitled "Laboratory Evaluation of Hepatitis B Rapid Test for Use in Screening Walking Blood Bank Donors," was to determine the best rapid HBSAG test to use for screening blood donors for Hepatitis B ("HBSAG") in the theater of war. The FirstVue(TM) HBSAG test was selected as the preferred test based on all facets of the study evaluation.

Out of all manufactures in the rapid diagnostic industry, six rapid tests were initially selected based on an evaluation of published claims and sensitivity testing using HBSAG positive samples. Those tests were then compared in a comprehensive evaluation of test performance using plasma and blood specimens. The study indicated that the FirstVue(TM) HBSAG test had the highest sensitivity (95.4%) and the highest specificity (99.7%) among all the tests evaluated. In addition, the evaluation indicated that the FirstVue(TM) HBSAG test detected HBSAG antibodies approximately three days sooner than available laboratory-based enzyme immunoassays. Early detection of seroconversion is an important measure of the sensitivity of a test and means that Hepatitis B infection can now be identified even with relatively recent exposure.

"We are very pleased with the results of the Walter Reed evaluation, it's just another confirmation of the quality of our product line and of the HBSAG rapid test we are providing the military," said Jonathan Barash President of AT First Diagnostic. "We are eager to complete our paperwork for the FirstVue(TM) HBSAG test and submit our findings and applications for both FDA and CE registrations on this product. Based on the performance data generated to date, we believe this test will play an important role in identifying HBSAG infections in the future and will enable infected individuals to receive the proper care and treatment they need."

This extensive study was conducted at The Walter Reed Army Institute of Research and involved investigators from the Walter Reed Army Institute of Research Division of Retrovirology, The U.S. Military HIV Research Program, Walter Reed Army Institute of Research Division of Military Casualty Research, the U.S. Army Blood Program, the Army Medical Department Center and School, the Robertson Blood Center and the American Red Cross.

Rapid Hepatitis "B" or "C" tests are not currently available for commercial sale in the United States by the U.S. Food and Drug Administration ("FDA"). AT First Diagnostic is in the process of collecting all the technical data together in order to obtain FDA guidance and approvals for

this HBSAG test utilizing multiple specimen types, whole blood, plasma and serum. The data stage is nearing completion and a pre-market application will be in progress for submission to the FDA soon.

Hepatitis B is a potentially life-threatening liver infection caused by the Hepatitis B virus. It is a major global health issue and the most serious type of viral hepatitis. It can cause chronic liver disease and puts people at high risk of death from cirrhosis of the liver and liver cancer.

Approximately 2 billion people worldwide have been infected with the virus and about 350 million live with chronic infection. About 25% of adults who become chronically infected during childhood later die from liver cancer or cirrhosis (scarring of the liver). Hepatitis B virus is 50 to 100 times more infectious than HIV. Most people who develop chronic Hepatitis B infection are not aware that they have the disease.

About AT First Diagnostic LLC

AT First Diagnostic LLC, Coral Springs, FL USA (Privately Held) markets, develops, and contract manufactures rapid medical devices using proprietary technologies under their brands FirstVue(TM) & inSTIcheck(TM); products include a wide range of various infectious disease tests for Chlamydia, Gonorrhea, Syphilis, etc... These tests are sold in the United States and internationally to clinical laboratories, hospitals, clinics, community organizations and other public health organizations, distributors, government agencies, physicians' offices, and commercial and industrial entities. For more information please go to <http://www.firstdiagnostic.com>.

About the Walter Reed Army Institute of Research

Walter Reed Army Institute of Research (WRAIR) is the largest, most diverse and oldest laboratory in the US Army Medical Research and Materiel Command. It conducts research on a range of military relevant issues, including naturally occurring infectious diseases, combat casualty care operational health hazards. WRAIR is the Department of Defense's lead agency for infectious disease research and a crucial source of research support for medical product development.

About the United States Military HIV Research Program

The U.S. Military HIV Research Program (USMHRP) is dedicated to, prevention, disease surveillance and care and treatment for HIV. USMHRP's extensive diagnostics expertise including familiarity with HIV rapid tests led the U.S. Army Blood Program to engage with USMHRP for this HBSAG rapid test evaluation.

SOURCE AT First Diagnostic LLC

<http://www.firstdiagnostic.com>

Oct 14, 2008

Aethlon Medical Announces Completion of Human Safety Study

<http://biz.yahoo.com/bw/081014/20081014005676.html?.v=1>

Reports Further Results of Hepatitis-C Patients Treated With the Aethlon Hemopurifier(R)

SAN DIEGO--(BUSINESS WIRE)--Aethlon Medical, Inc. (OTCBB:AEMD - News) today announced the completion of a human safety study conducted at the Fortis Hospital in Delhi, India. The primary objective of the study was to evaluate the safety of the Aethlon Hemopurifier® in health compromised end-stage renal disease (ESRD) patients that require kidney dialysis. The Hemopurifier® is a first-in-class medical device that assists the immune response in combating infectious disease through real-time therapeutic filtration of infectious viruses and immunosuppressive proteins. In addition to demonstrating safety, the study provided the opportunity to observe changes in viral load in ESRD patients infected with Hepatitis-C virus (HCV).

In the study, six ESRD patients received a series of three, 4-hour Hemopurifier® treatments every other day during the course of one week. The treatment regimen mirrored the patient's normal kidney dialysis schedule, which allowed for the inclusion of the Hemopurifier® without disrupting dialysis treatment. Blood chemistry and general health of the patients were monitored throughout the study, and at the conclusion of the study, the sole reported adverse event was hemolysis, which was observed in a total of four treatments, three of which occurred in the same patient. The physicians administering the study reported that the incidence of hemolysis did not cause any follow-on health concerns. No other adverse events have been reported in a total of 42 Hemopurifier® treatments administered in human studies. Aethlon previously completed a 24-treatment study at the Apollo Hospital, also located in Delhi.

Updated HCV Data

On September 17, 2008, Aethlon reported robust viral load reductions in tested HCV patients that completed the three Hemopurifier® treatment protocol. The outcomes were derived from consolidated viral load values of all three patients. The values resulted in an average viral load reduction of 60% when measured three days after final Hemopurifier® treatment, and an 82% reduction when measured seven days post treatment. Since this report, follow-on data provides for HCV viral load values to be calculated on an individual, patient by patient basis.

Patient #1 had a 95% reduction three days post treatment and 89% reduction seven days post treatment. The initial viral load for patient 1 was 5.3×10^5 viral units per ml of blood (IU/ml). Patient 1's viral load seven days post treatment was 5.7×10^4 IU/ml.

Patient #2 had a 85% reduction three days post treatment and 50% reduction seven days post treatment. The initial viral load for patient 2 was 9.2×10^6 IU/ml. Patient 2's viral load seven days post treatment was 4.6×10^6 IU/ml.

Patient #3 had a 60% reduction three days post treatment and 83% reduction seven days post treatment. The initial viral load for patient 3 was 3.0×10^8 IU/ml. Patient 3's viral load seven days post treatment was 5.1×10^7 IU/ml. All viral load measurements were performed with real-time quantitative polymerase chain reaction (RT-PCR). Control samples were measured in duplicate while treatment samples were generally measured in triplicate.

“With the Fortis study complete, we will update our investigational device exemption on file with the FDA and request permission to initiate human studies in the United States,” stated Aethlon Chairman and CEO, James A. Joyce. “Additionally, we are preparing to launch a four-week HCV treatment case study that could trigger early commercialization in India, and we have

initiated discussions with potential partners to evaluate the clinical opportunity for our Hemopurifier® in the European Union,” concluded Joyce.

The opportunity for new antiviral strategies to fight HCV is significant, as approximately 180 million people worldwide (3% of the world’s population) are HCV infected. According to the World Health Organization (WHO), only 30-50% of infected patients beneficially respond to the 48-week pegylated interferon-ribavirin treatment standard.

The Hemopurifier® is a first-in-class medical device designed to assist the immune response in combating infectious disease by rapidly clearing viruses and immunosuppressive proteins from circulation. The device provides a novel mechanism to complement antiviral therapies by suppressing the emergence of viral strains that cause drug resistance. The Hemopurifier® is also positioned to fill the unmet clinical need of treating patients resistant to drug therapy or infected by viral pathogens that are untreatable with drug and vaccine therapy. In HCV care, the device is positioned as an adjunct to improve clinical outcomes of the pegylated interferon-ribavirin treatment standard. Other opportunities in HCV care include the treatment of individuals who fail or are unable to endure standard of care therapy, end-stage renal patients infected with HCV, and HIV patients co-infected with HCV. On September 29th, Aethlon Medical announced that it has further expanded clinical programs by initiating enrollment of HIV-infected patients to be treated with the Hemopurifier® in a multi-site clinical program in India.

About Aethlon Medical

Aethlon Medical is the developer of the Hemopurifier®, a first-in-class medical device designed to treat infectious disease. The Hemopurifier® provides real-time therapeutic filtration of infectious viruses and immunosuppressive particles, and is positioned to address the treatment of drug and vaccine resistant viruses. Additionally, the device holds promise in cancer care, as research studies have verified the Hemopurifier® is able to capture immunosuppressive particles secreted by tumors. The Hemopurifier® is designed to act both as a stand-alone therapeutic, and as an adjunct treatment to enhance clinical benefit of established therapies. Pre-clinical studies conducted by researchers representing leading government and non-government health organizations both in the United States and abroad have documented the effectiveness of the Hemopurifier® in capturing from circulation the viruses that constitute pandemic threats, including H5N1 Avian Influenza (bird flu), and Dengue Hemorrhagic Fever (DHF) from circulation. The company is conducting studies to support the use of the Hemopurifier® as a broad-spectrum treatment countermeasure against bioterror threats, including Smallpox, and Ebola, Marburg, and Lassa hemorrhagic fever. Regulatory and commercialization initiatives in the United States are presently focused on bioterror threats, while international initiatives are directed toward naturally evolving pandemic threats, and chronic infectious disease conditions including the Human Immunodeficiency Virus (HIV) and Hepatitis-C (HCV). Aethlon has demonstrated safety of the Hemopurifier® in a 24-treatment human study at the Apollo Hospital in Delhi, India, and in an 18-treatment study at the Fortis Hospital, also located in Delhi. The company has submitted an investigational device exemption (IDE) to the U.S. Food and Drug Administration (FDA) to advance the Hemopurifier® as a broad-spectrum treatment countermeasure against category “A” bioterror threats. Additional information regarding Aethlon Medical and its Hemopurifier® technology is available online at www.aethlonmedical.com.

Source: Aethlon Medical, Inc.

Researchers Develop Blood Test For Liver Damage

<http://kdka.com>

Lorena Loarca will never forget hearing she was infected with hepatitis B.

"You may die of liver cancer or cirrhosis in 10, 15 years, and there's no cure for this disease. And this is the way that the doctor told me," she says.

Lorena's initial shock was replaced with a determination to hunt down answers.

"I started thinking, 'What if I become a scientist one day, and I found the cure for hepatitis B?!' I was, like, so naïve!"

Lorena did become a scientist. And though a cure has yet to be found, her colleagues at the Pennsylvania Biotechnology Center have found a way to keep tabs on the liver with a simple blood test.

"If you have significant scarring of the liver or significant fibrosis, that measurement is higher in the blood."

The blood test looks for an antibody that only shows up in people with liver damage.

"And it turns out that the more liver disease you have, the more of this antibody in you, that there is."

The theory is that the antibody is targeting a bacterial sugar that's not getting cleaned out of the already-scarred liver.

"Suddenly it becomes much harder to clear this sugar, and, and you'll see more and more and more of these sugars accumulating, aggravating the liver disease."

The test, which at this point is still in research, will not replace a liver biopsy entirely. If the test turns out to be reliable, it could encourage more frequent liver monitoring and give doctors a way to check on how well treatment is working.

Why are T cells tolerant to hepatitis B virus?

<http://www.eurekalert.org>

The level of PD-1 expression has been proved by recent studies to be positively correlated with the extent of HBV-specific T cell impairments. However, the degree of T cell exhaustion which affects the disease statuses of hepatitis B patients has so far been only evaluated in restricted and small groups of patients between those with established chronicity and subjects with acute HBV infection. Besides, whether levels of PD-1 expression on T cells differ between acute exacerbation of hepatitis B and chronic HBV infected patients is still unknown.

A research article to be published on July 28, 2008 in the *World Journal of Gastroenterology* addresses this question. The research team led by Shu-Ling Zhang from Tongji Medical College

of Huazhong University of Science and Technology in China examined the expression of PD-1 on antigen specific CD8+ T cells in peripheral blood of chronic hepatitis B (CHB) and acute exacerbation of hepatitis B (AEHB) patients.

They found that the levels of PD-1 on total CD8+ T cells in CHB patients were significantly higher than those in AEHB patients and healthy individuals. Conversely, lower frequencies of HBV-specific CD8+ T cells were detected in samples from chronic patients compared to AEHB patients. Our results confirmed reports that HBV specific CD8+ T-cell responses in peripheral blood were intensified in samples from AEHB patients than in those from patients with chronic hepatitis who remains viral persistence. Besides, there was a significant positive correlation between HBV viral load and percentage of PD-1 expression on CD8+ T cells in CHB and AEHB group of subjects. However, PD-1 expression was not in association with disease flare-ups indicator alanine aminotransferase (ALT). This study clarified the correlation between PD-1 expression and two different HBV infection statuses.

Reference:

Ye P, Weng ZH, Zhang SL, Zhang JA, Zhao L, Dong JH, Jie SH, Pang R, Wei RH. PD-1 expression is associated with the disease statuses of hepatitis B virus infection. *World J Gastroenterol* 2008; 14(28): 4551-4557 <http://www.wjgnet.com/1007-9327/14/4551.asp>

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Oct 15, 2008

Tibotec begins enrollment for Phase III study of telaprevir

<http://www.eurekalert.org>

An investigational agent, in HCV patients who failed prior treatment

- REALIZE is the first phase III study to evaluate a specifically targeted antiviral therapy for hepatitis C (STAT-C) across a full range of HCV-patients who failed prior treatment to current standard of care, including null responders -

MECHELEN, Belgium (October 15, 2008) – Tibotec BVBA announced today that it has begun enrolling patients in its phase III clinical trial evaluating telaprevir, an investigational hepatitis C virus protease inhibitor, in patients who failed prior therapy with peginterferon (Peg-IFN) plus ribavirin (RBV). The trial, known as REALIZE, will compare the efficacy, safety and tolerability of telaprevir combined with Peg-IFN plus RBV versus Peg-IFN and RBV alone, the current standard of care. Investigators at U.S. trial centers have begun screening patients for participation in the study, with global centers expected to begin screening in the coming weeks. Telaprevir is being co-developed by Vertex Pharmaceuticals Incorporated and Tibotec. Tibotec, the sponsor of the REALIZE trial, is managing the trial worldwide.

"We are excited about the ongoing development of telaprevir, potentially the first direct antiviral for the treatment of HCV, which may provide a new option for patients who have failed the

current standard of care," said Roger Pomerantz, MD, President, Tibotec Research and Development. "We are committed to examining the safety and efficacy of telaprevir through phase III trials and look forward to working with health authorities with the goal of making this therapy available to HCV infected patients."

The REALIZE trial (Re-treatment of Patients with Telaprevir-based Regimen to Optimize Outcomes) is a phase III, randomized, placebo-controlled double-blind study conducted over 72 weeks to examine two regimens of 750 mg telaprevir every eight hours (with and without a delayed start) combined with Peg-IFN and RBV versus Peg-IFN and RBV alone. To be eligible for the study, patients must belong to one of the following three groups:

- Null responders (defined as patients who achieved <2 log reduction in HCV RNA at week 12 of prior therapy);
- Partial responders (defined as patients who achieved at least a 2 log reduction at week 12, but never achieved undetectable HCV RNA during prior therapy); and
- Relapsers (defined as patients who had undetectable HCV RNA at the completion of at least 42 weeks of prior treatment, but relapsed during follow-up).

The trial will enroll approximately 650 HCV patients at more than 30 centers in the U.S., 50 centers in Europe and 20 centers in the rest of the world. The study will include 300 null- and partial-responder patients and 350 patients with viral relapse. REALIZE is the first phase III study to evaluate a direct antiviral (or STAT-C) treatment for HCV in null responder patients.

The primary endpoint of the REALIZE study is sustained virologic response (SVR), defined as undetectable HCV RNA (<10 IU/mL) 24 weeks after the completion of treatment. Patients enrolled in this study will be randomized to three treatment arms:

1. Telaprevir dosed at 750 mg every eight hours (q8h) for 12 weeks in combination with standard doses of Peg-IFN and RBV, followed by 36 weeks of treatment with Peg-IFN and RBV alone;
2. Delayed start arm, comprised of four weeks of treatment with Peg-IFN and RBV, followed by telaprevir dosed at 750 mg q8h for 12 weeks in combination with standard doses of Peg-IFN and RBV, followed by another 32 weeks of Peg-IFN and RBV alone; or
3. A control arm with standard doses of Peg-IFN and RBV dosed for 48 weeks.

Patients in all treatment arms will be followed for 24 weeks after completion of treatment to assess SVR.

For additional information on inclusion and exclusion criteria for this study, please see www.clinicaltrials.gov.

The REALIZE phase III study in treatment failure patients is part of a comprehensive clinical development program for telaprevir. Vertex is managing the ADVANCE phase III trial in treatment-naïve patients.

Tibotec has the right to develop and commercialize telaprevir in Europe, South America, the Middle East, Africa, India, Australia and New Zealand. Vertex will commercialize telaprevir in the U.S., Canada and Mexico.

As a global virology leader committed to patient care, Tibotec uses innovative science and expertise to research, develop, manufacture and market drugs of unmet need. Tibotec is dedicated to building a portfolio of novel antiviral therapies to address the significant unmet needs of patients with chronic hepatitis C. In addition to its partnership with Vertex to develop and commercialize telaprevir, Tibotec is currently developing with partner Medivir a second potential treatment for HCV which is in early stage trials. Through the application of its deep understanding of virology and viral resistance, Tibotec has become an established leader in HIV/AIDS, having developed and made available two antiretroviral agents for the treatment of HIV. Tibotec continues its commitment to developing novel therapies through a robust research and development program, which includes a third anti-HIV treatment as well as a potential treatment for tuberculosis.

About Tibotec BVBA

Tibotec BVBA is a global pharmaceutical and research development company. The Company's main research and development facilities are in Mechelen, Belgium with offices in Yardley, Pa. and Cork, Ireland. Tibotec is dedicated to the discovery and development of innovative HIV/AIDS and hepatitis C drugs, and anti-infectives for diseases of high unmet medical need.

NIH to hold press conference on October 22 following Consensus Development Conference on Management of Hepatitis B

<http://www.nih.gov>

Panel will weigh the benefits and harms of management strategies

Hepatitis B is a major cause of liver disease worldwide, ranking as a substantial cause of cirrhosis and liver cancer. Approximately 1.25 million people are chronically infected with the virus in the United States, resulting in 3,000 to 5,000 deaths each year. The incomplete understanding of the natural history of the disease, coupled with multiple conflicting guidelines, make the management of this complex disease challenging. These issues will be addressed at the upcoming NIH Consensus Development Conference: Management of Hepatitis B, October 20-22, 2008.

What:

Following two days of expert presentation, weighing of evidence, and audience commentary, the panel will present their statement at 9 a.m. on Wednesday, October 22. The statement will provide the panel's assessment of what we know and what we need to learn to effectively manage hepatitis B across diverse patient groups. A press conference will follow at 2 p.m.

Reporters registering for the conference as media will receive the conference panel's draft consensus statement and a press release highlighting their findings on Oct. 22 as soon as they are available. Register online by visiting <http://consensus.nih.gov>.

The conference presentations, open discussions, and the panel's statement will focus on these questions:

- What is the current burden of hepatitis B?
- What is the natural history of hepatitis B?

- What are the benefits and risks of the current therapeutic options for hepatitis B?
- Which persons with hepatitis B should be treated?
- What measures are appropriate to monitor therapy and assess outcomes?
- What are the greatest needs and opportunities for future research on hepatitis B?

When: Press conference | Wednesday, October 22 — 2 p.m.

- Monday, October 20, 2008 — 8:30 a.m. – 5:00 p.m.
- Tuesday, October 21, 2008 — 8:30 a.m. – 12:30 p.m.
- Wednesday, October 22, 2008 — 9:00 a.m. – 11:00 a.m.

All sessions are free and open to the public.

Where: NIH main campus or online (<http://videocast.nih.gov/>):

Attend the press conference in person at the Natcher Conference Center, NIH Main Campus - Building 45, 9000 Rockville Pike, Bethesda, Maryland 20892; or participate remotely via the webcast at <http://videocast.nih.gov>. Reporters will have the opportunity to submit questions via e-mail beginning at 1:30 p.m. on October 22.

Campus visitor information (<http://www.nih.gov/about/visitor/index.htm>)

Why:

Although an effective hepatitis B vaccine is available, it does not protect those who already have the infection. Chronic hepatitis B occurs more frequently in high-risk groups, including Asian-Americans, emigrants from areas of the world where hepatitis B is common (China, Korea, Southeast Asia, the Indian subcontinent, Africa and Micronesia), men who have sex with men, injection drug users, and recipients of blood and blood products before screening procedures were implemented in 1986. In non-protected individuals, transmission can result from exposure to infectious blood or body fluids containing blood. A major impediment to diagnosis is that many infected individuals are either asymptomatic or experience only non-specific symptoms of disease, such as fatigue or muscle ache.

For approximately 90 percent of adults, acute infection with the hepatitis B virus is resolved by the body's immune system, and does not cause long-term problems. The transition from acute to chronic infection appears to occur when the immune system does not effectively destroy and clear virus-infected cells. This leads to persistently detectable hepatitis B DNA and antigens in the blood, as well as antibodies produced by the body in an attempt to combat the infection.

Questions remain as to which groups of patients benefit from therapy and at which point in the course of their disease. Specific recommendations for hepatitis B therapy are limited by a lack of reliable long-term safety and efficacy information. This is a difficult decision for physicians and patients, as treatments are expensive and may have bothersome, if not harmful, effects on patients; left untreated, however, chronic hepatitis B can lead to liver failure and other serious liver problems.

Background:

The conference is presented through the NIH Consensus Development Program. A fact sheet describing the conference process and additional hepatitis B resources are available at <http://consensus.nih.gov/forthemedia.htm>.

A systematic literature review on the management of hepatitis B has been prepared under contract with the Agency for Healthcare Research and Quality (AHRQ). The executive summary will be released on October 22 at <http://www.ahrq.gov/clinic/tp/hepbtp.htm>; the full report will be available online shortly thereafter.

For More Information:

Conference agenda, speakers, logistics, and online registration are available at <http://consensus.nih.gov>.

The Office of the Director, the central office at NIH, is responsible for setting policy for NIH, which includes 27 Institutes and Centers. This involves planning, managing, and coordinating the programs and activities of all NIH components. The Office of the Director also includes program offices which are responsible for stimulating specific areas of research throughout NIH. Additional information is available at <http://www.nih.gov/icd/od/>.

The National Institutes of Health (NIH) — The Nation's Medical Research Agency — includes 27 Institutes and Centers and is a component of the U.S. Department of Health and Human Services. It is the primary federal agency for conducting and supporting basic, clinical and translational medical research, and it investigates the causes, treatments, and cures for both common and rare diseases. For more information about NIH and its programs, visit www.nih.gov.

Nearby tissue reveals liver cancer recurrence risk

www.reuters.com

By Gene Emery

BOSTON (Reuters) - The key to whether liver cancer is curable may lie not with the tumor, but in the apparently healthy liver cells surrounding it, scientists said on Wednesday.

An international research team reported that it has identified 186 bits of genetic material whose activity levels in surrounding tissue predict whether hepatocellular carcinoma, a form of liver cancer, is likely to reappear.

"What we found was that the information to predict future recurrence wasn't in the primary tumor itself, but was in the surrounding non-tumor liver tissue, which suggests that the so-called recurrences aren't really recurrences," Dr. Todd Golub, one of the researchers, said in a telephone interview.

"They're really new primary tumors that are arising in a liver that has been damaged, as opposed to the old tumor just coming back," added Golub, who heads the cancer program at the Broad Institute of the Massachusetts Institute of Technology and Harvard University.

The findings, published in the *New England Journal of Medicine*, could someday lead to a test that tells doctors which patients require aggressive treatment after surgery.

Liver cancer is the third-leading cause of cancer deaths worldwide.

The discovery grew out of an effort to find a way to look for genetic links to diseases using tissue preserved in a solution of formaldehyde. Until now, doctors had to use frozen tissue because formaldehyde chops up the genetic material needed for the analysis.

But a new technique, developed by Illumina Inc in San Diego, allows researchers to analyze the genetic material even though it has been broken up by the formaldehyde.

Because formaldehyde preservation has been around for decades, the new technique allows doctors to use tissue samples taken many years ago to look for genetic signatures in cases where they already know the outcome.

That could help speed the development of new drugs, Golub said.

"Rather than say we're going to treat all liver cancer patients with a new drug that holds promise to prevent future recurrences, let's focus on the subset of patients who are highest risk," he said. "If you're at low risk for recurrence it's probably not worth being exposed to the potential side effects of a new treatment."

In the new study, the researchers were able to look for gene patterns in liver cancer cases from New York, Tokyo, Milan and Barcelona going back as far as 24 years.

(Editing by Will Dunham and Eric Beech)

United States: Employment Advisory: Employers Are Required To Compensate Employees For Non-Working Hours And Travel Expenses For Medical Treatment Sought Under OSHA's Bloodborne Pathogens Standard

<http://www.mondaq.com>

Article by Mintz Levin

Employment, Labor and Benefits Group

Overview

The United States Third Circuit Court of Appeals ruled earlier this month that employers must compensate employees for the time they spend and the travel expenses they incur while seeking medical treatment for occupational exposures to bloodborne infectious diseases.¹

Facts and Procedural History

In separate incidents, two nurses employed by Beverly Healthcare-Hillview ("Beverly"), a nursing home in Pennsylvania, received "needlesticks" while at work, which potentially exposed them to a number of bloodborne infectious diseases, such as hepatitis and HIV. At the end of their shifts, both employees sought treatment at a medical clinic authorized by Beverly. Notably,

they scheduled these appointments during their non-working hours because the clinic was not open during their regular shifts. Beverly paid for both employees' medical treatments, but not for their time and travel expenses.

The Occupational Safety and Health Administration ("OSHA") cited Beverly for violating 29 C.F.R. § 1910.1030(f)(1)(ii)(A), a provision of the Bloodborne Pathogens Standard ("BPS"), for failing to compensate the nurses for their travel expenses and the hours of non-working time they spent receiving treatment for the needlesticks. The applicable provision of the BPS states: "(ii) The employer shall ensure that all medical evaluations and procedures including the hepatitis B vaccine and vaccination series and post-exposure evaluation and follow-up, including prophylaxis, are: (A) Made available at no cost to the employee." (emphasis added).

Beverly challenged the citations issued by OSHA before an administrative law judge ("ALJ"), arguing that the "at no cost" language was ambiguous. Beverly further argued that it fully complied with the plain language of the BPS because it paid for the cost of the medical tests and procedures and employees were not otherwise "charged" for seeking treatment. The ALJ upheld the citations, finding that the language of the BPS was not ambiguous. Beverly appealed the ALJ's decision before the Occupational Safety and Health Review Commission (the "Commission"), and again argued that the "at no cost" language was ambiguous. The Department of Labor ("DOL"), on behalf of OSHA, argued that its interpretation that the phrase "at no cost" includes an employee's time and travel expenses is reasonable. A two-member majority of the Commission decided that the "at no cost" language in the BPS was ambiguous, and reversed the ALJ's decision. The Commission also noted that Beverly lacked fair notice of the DOL's interpretation for due process purposes.

The Third Circuit's Decision

The DOL appealed the Commission's decision to the Third Circuit. The Court reversed the Commission, and held that the DOL's interpretation of the phrase "at no cost to the employee" not only conforms to the language and purpose of the BPS but also is consistent with the intent of the BPS as set out in its preamble. Moreover, the Court held that case law, compliance directives, and opinion letters regarding employers bearing costs under various OSHA standards provided adequate notice (for due process purposes) to employers that the BPS requires employers to compensate employees for travel time and non-working hours spent seeking medical treatment. As such, the Court ordered Beverly to reimburse its employees wages for time spent during non-working hours for treatment and for the costs of mileage driving to the clinic where they sought treatment.

Action Items for Employers

It is critical for employers subject to the BPS standard to understand the Third Circuit's decision whenever an employee receives a needlestick while at work. It is now clear that OSHA requires employers to compensate employees for non-working hours and travel expenses for medical treatment sought pursuant to the BPS. More specifically, if employers are not already following this practice, they now must ensure that employees are being adequately compensated for such costs.

Footnotes

¹ See *Sec'y of Labor v. Beverly Healthcare-Hillview*, No. 06-4810, 2008 WL 4107489 (3rd Cir. Sept. 4, 2008).

The content of this article is intended to provide a general guide to the subject matter. Specialist advice should be sought about your specific circumstances.

Oct 16, 2008

Boost for Youth Health in Hobart

<http://www.media.tas.gov.au>

Young people's health received a boost today with the opening of The Link's extended premises, enabling increased services to be offered from the Liverpool Street site.

While officially opening the upgraded service, Health Minister Lara Giddings also launched a new DVD designed to educate young people about one of the most important public health issues faced by them – Hepatitis C.

“Today's opening is a major step forward in health and counselling services for young Tasmanians,” Ms Giddings said.

“The extension to The Link's premises is the result of \$170,000 in funding through the Tasmanian Community Fund and the Department of Health and Human Services.

“New consulting rooms will provide young people with easier access to counselling and treatment by a range of health professionals.

“Three visiting counsellors and a clinical psychologist will offer general and specialised counselling for mental health problems and alcohol and drug use issues.

“There are also plans to expand the number of sessional service providers, including those from general practice, sexual health, alcohol and other drug services.”

Ms Giddings said the State and Federal Governments provided more than \$700,000 in funding to enable the service to deliver its vital youth health programs.

“Some of The Link's most important work concerns infectious diseases that are particularly relevant to young people, including Hepatitis C.

“The new DVD - ‘Hep C, The Movie’ - has been developed in partnership between The Link, the Department of Health's Hepatitis C Project Officer, and two young Tasmanian film makers, Harriet and Stella Macdonald of Tigermoth Productions.

“It provides teachers, school support staff, youth workers and community workers with good, clear information and preventative health messages for young people.

“Hep C is a blood borne virus and a significant public health issue affecting approximately 1% of the Australian community.

“Nationally, around 264,000 people have been exposed to the Hepatitis C virus, and in Tasmania it is estimated that between 3,400 and 6,000 people have been exposed.

“Almost 20% of all Hepatitis C notifications in Tasmania between 2002 and 2007 were in young people aged 15-24 years.

“Injecting drug users are at greatest risk of transmission, with the first year of injecting an especially high risk time.

“Unsafe tattooing and piercing practices also put young people at risk.

“Seventy-five percent of those infected with Hep C will have chronic symptoms such as fatigue, nausea and vomiting, muscular aches and pains, and other symptoms that have a significant impact on their quality of life.

“Only twenty-five percent of people infected with Hep C will clear the virus.

“Prevention is therefore the key to Hep C, and the new DVD should help to make a real difference,” Ms Giddings said.

Varying Combinations Of Antiviral Drugs May Effectively Treat Chronic Hepatitis Virus Infection In Woodchucks

<http://www.sciencedaily.com>

ScienceDaily (Oct. 16, 2008) — Oral administration of various combined and independent antiviral drug therapies may effectively treat chronic hepatitis B virus (HBV) infection in woodchucks, a well-characterized mammalian model for research with human implications, and provide an alternative strategy for managing drug resistance.

The researchers from Cornell University, Ithaca, New York; Gilead Sciences, Durham, North Carolina; and Georgetown University Medical Center, Washington, DC report their findings in the October 2008 issue of the journal *Antimicrobial Agents and Chemotherapy*.

Chronic infection with HBV is responsible for 1.2 million annual deaths worldwide. Statistics also show that 2 billion people currently or previously suffered from infection while 350 million people are chronic carriers of HBV and are at risk of developing chronic hepatitis, hepatic cirrhosis, and hepatocellular carcinoma. Preventative vaccines are currently offered, however, side effects and drug resistance are limiting the efficacy of available treatment therapies.

In the study researchers evaluated the antiviral effects of orally administered adefovir dipivoxil (ADV) or tenofovir disoproxil fumarate (TDF) alone or in combination with lamivudine (3TC) or emtricitabine (FTC) in woodchucks with chronic hepatitis virus infection. Initial results showed once daily treatment for 48 weeks with ADV plus 3TC or TDF plus FTC greatly reduced viral levels from those pretreatment. Additional treatment with TDF plus 3TC, ADV alone, ADV plus FTC, TDF alone, 3TC alone, and FTC alone showed pronounced declines in viral levels in all groups. Following drug withdrawal most woodchucks displayed renewed hepatitis virus replication, but some did experience sustained effects. Lastly, no toxicity was observed following administration of any of the drugs or drug combinations.

"In conclusion, the oral administration of 3TC, FTC, ADV, and TDF alone and in combination was safe and effective in the woodchuck model of HBV infection," say the researchers.

Journal reference:

S. Menne, S.D. Bulter, A.L. George, I.A. Tochkov, Y. Zhu, S. Xiong, J.L. Gerin, P.J. Cote, B.C. Tennant. Antiviral Effects of Lamivudine, Emtricitabine, Adefovir Dipivoxil, and Tenofovir Disoproxil Fumarate Administered Orally Alone and in Combination to Woodchucks with Chronic Woodchuck Hepatitis Virus Infection. *Antimicrobial Agents and Chemotherapy*, 2008; 52 (10): 3617 DOI: 10.1128/AAC.00654-08

Adapted from materials provided by American Society for Microbiology, via EurekAlert!, a service of AAAS.

Oct 17, 2008

Hepatitis C In Western New York

<http://www.wkbw.com>

By Sharon Osorio

[Watch the story](#)

The head of epidemiology at the Erie County Health Department will present a study about a cluster of Hepatitis C patients in Hamburg, how to treat Hepatitis, and how to keep people healthy, whether it's avoiding Hepatitis C or whether they have already contracted it.

Hepatitis C is often contracted by sharing needles during drug use. Last year, officials investigated a cluster of cases in Hamburg, studying 20 teens who had contracted the disease. 19 of the patients admitted to intravenous drug use, and they also reported other high-risk behaviors like having sex with up to 100 partners.

Still, the health commissioner says it's also a problem in Buffalo, and Hepatitis C cases are reported throughout Western New York.

Hepatitis C is a liver disease that can lead to liver cancer.

FSU researcher's discovery leads to \$1.5 million grant, potential new treatment of liver fibrosis

<http://www.eurekalert.org>

TALLAHASSEE, Fla. -- The discovery of a protein involved in the life-threatening mechanism of liver fibrosis has helped a researcher at the Florida State University College of Medicine attract a \$1.5 million grant from the National Institutes of Health.

Branko Stefanovic, associate professor in the department of biomedical sciences at the College of Medicine, hopes his discovery could lead to treatment methods that may stem the process of

liver fibrosis. Cirrhosis, the terminal phase of the disease, kills 26,000 Americans each year -- the ninth leading cause of death in the United States.

Liver fibrosis refers to the accumulation of excess scar tissue in the liver through excess deposits of collagen, a fibrous protein found in skin, bone, and other connective tissues. The formation of scar tissue is a normal bodily response to injury, but in fibrosis the scarring begins to accumulate to unacceptable levels. The process can result from one of multiple causes, the most frequent of which are alcohol abuse and hepatitis C infection.

Fibrosis is difficult to detect until collagen deposits reach a point where the scarring has severely impaired organ function, meaning individuals suffering from the disease typically do not receive any treatment until it's too late.

"The capacity of liver cells to regenerate is great, so therefore normally the primary diseases that can lead to fibrosis do not kill the patient," Stefanovic said. "What kills the patient is secondary scarring and the replacement of normal liver tissue with scar tissue. Once this happens a liver cannot regenerate anymore."

Stefanovic and his research team made the important discovery of a protein involved in the scar formation process while working on a previous NIH grant. The RNA-binding protein, which Stefanovic has successfully cloned in his lab at the College of Medicine, is found at the place and specific time when the body is making collagen as part of the normal wound healing resulting from the body's efforts to repair injured tissue.

"We had evidence of its existence, but we didn't have the protein," Stefanovic said. "We had been looking for this particular protein for several years until we used some very sophisticated methods of cloning. When I saw the results of the binding of the protein to our target I knew immediately we had found the right one."

Stefanovic said he doesn't believe there will ever be a cure for liver fibrosis but that research and development will one day lead physicians to be able to slow down the progress of the disease.

"At least if we slow down the chronic process, instead of dying in five years the patient will live 15 years or more," he said.

"The goal is to suppress excessive collagen synthesis. In order to do that we have to know the molecular mechanisms that regulate manufacture of the protein and then see what has gone wrong when the liver is creating excess collagen.

"Then we will be able to find specific points in this process where we can intervene, by designing either a drug of some kind or a therapeutic agent that will allow us to block these key points and slow down the scarring. Cloning of this protein is a major step toward this goal."

Report says Medicaid spending "unsustainable"

www.reuters.com

WASHINGTON (Reuters) - Spending on the Medicaid health program for the poor is on a path to grow at a much higher rate than the overall U.S. economy in the next 10 years, officials said on Friday.

Spending on Medicaid benefits will increase 7.3 percent from 2007 to 2008, reaching \$339 billion, and will expand at an annual average of 7.9 percent over the next decade, hitting \$674 billion by 2017, the U.S. Department of Health and Human Services said in a report.

Over that same time span, the projected rate of growth for the overall economy is 4.8 percent, the report stated.

The report's release comes at a time of growing worry over the fact that health spending has become an increasing burden on individual Americans, businesses and governments.

Medicaid is the joint state-federal health insurance program for low-income people.

Medicaid spending is projected to grow at a higher rate than spending on the Medicare federal health insurance program for the elderly and disabled, according to the report.

Spending on Medicaid over the next decade is forecast to amount to \$4.9 trillion, the report said. Average Medicaid enrollment is seen increasing 1.8 percent to 50 million people in 2008, and is projected to hit 55.1 million by 2017.

Medicaid is forecast to increase as a share of the federal budget from 7 percent in 2007 to 8.4 percent by 2013, according to the report.

"This report should serve as an urgent reminder that the current path of Medicaid spending is unsustainable for both federal and state governments," Health and Human Services Secretary Mike Leavitt said in a statement.

"If nothing is done to rein in these costs, access to health care for the nation's most vulnerable citizens could be threatened."

In 1970, the report said, combined federal and state expenditures for Medicaid represented 0.4 percent of the economy, but this percentage grew to 0.9 percent in 1980, 1.2 percent in 1990, 2.0 percent in 2000 and 2.3 percent in 2007.

(Reporting by Will Dunham)