

# HCV ADVOCATE WEEKLY NEWS REVIEW

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

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## In This Issue:

- [New Television Campaign In Mandarin To Educate Chinese Americans About Chronic Hepatitis B](#)
- [Ask the Mayo Clinic: Whatever happened to 'jet injectors?'](#)
- [EU looks at increasing supply of transplant organs](#)
- [Human Genome Sciences Announces Albuferon\(R\) Meets Primary Endpoint in Phase 3 Trial in Chronic Hepatitis C](#)
- [Nuts boost health benefit of Mediterranean diet](#)
- [Atazanavir-treated patients have increased risk of hyperbilirubinaemia after starting therapy for hepatitis C](#)
- [Leeds research points to new therapy for hepatitis C treatment](#)
- [Dementia risk not high in mild cognitive impairment](#)
- [Protecting Organ Recipients – From Donors](#)
- [Hepatitis C Deaths: Legacy Of Our Past Behaviour](#)
- [New pathway found for fatty liver disease](#)
- [30-Day Hepatitis C Treatment Study Announced by Aethlon Medical](#)
- [Employed women with fibromyalgia maintain health](#)
- [Schering-Plough Announces FDA Approval of PEGINTRON\(TM\) and REBETOL\(R\) Combination Therapy for Treating Pediatric Hepatitis C](#)
- [Sixth Annual Hepatitis C Summit](#)

## ***New Television Campaign In Mandarin To Educate Chinese Americans About Chronic Hepatitis B***

<http://www.medicalnewstoday.com>

Today, Bristol-Myers Squibb Company (NYSE: BMY) announced the launch of its first-ever, non-English-language television campaign in the United States. The campaign, exclusively in Mandarin, seeks to raise awareness of chronic hepatitis B and encourages people to talk with their doctors about managing the disease - one that is disproportionately affecting the Chinese community.

The campaign features two chronic hepatitis B patients in 60-second television segments with an educational message about the importance of seeking appropriate care. The segments encourage people to start a dialogue with their healthcare provider about the disease. In addition, the campaign will be extended to reach additional Asian American audiences in 2009.

"We commend Bristol-Myers Squibb for this new initiative and believe it will have a positive impact among those most at-risk for this serious disease," said Jeff Caballero, Executive Director of The Association of Asian Pacific Community Health Organizations (AAPCHO). "We've found that people are most receptive and more likely to speak with their doctor when information is given to them in a culturally-relevant format and in their primary language. It is especially important in the Asian community, where there is still a lot of stigma associated with this disease, deterring patients from seeking proper care."

Chronic hepatitis B is a serious disease. In the United States, it is estimated that Asians and Pacific Islanders account for more than half of the chronic hepatitis B infections. A recent survey of perceptions of hepatitis B in the Asian American community showed that while most are aware of the disease, many cited general lack of information and uncertainty about disease symptoms, transmittability, treatment options and vaccination.

"Bristol-Myers Squibb is committed to helping patients prevail against serious diseases," said Robert Zito, Bristol-Myers Squibb's Chief Communications Officer. "Reaching non-English speaking communities in their native languages about diseases is consistent with our promise to patients."

### **About Chronic Hepatitis B and Asian Americans**

An estimated 1.25 million Americans are chronically infected with hepatitis B,<sup>3</sup> and over half are of Asian and Pacific Island descent.<sup>4</sup> Each year, more than 5,000 Americans die from liver complications related to hepatitis B. More specifically:

- Chinese Americans have a five to six times higher risk for liver cancer caused by hepatitis B than Caucasian Americans.
- Korean Americans have an eight times higher risk for liver cancer caused by hepatitis B than Caucasian Americans.
- Vietnamese Americans have a 13 times higher risk for liver cancer caused by hepatitis B than Caucasian Americans.

## ***Ask the Mayo Clinic: Whatever happened to 'jet injectors?'***

<http://seattlepi.nwsourc.com>

Dear Mayo Clinic: I remember we used to get vaccines and other shots using an air gun, and lots of people could get shots quickly. I haven't seen this done for a long time. Why? Were problems discovered with that method? It seems that it would be an efficient way to give flu shots, for instance, in a really short time.

A: Using an air gun -- also called a jet injector -- is a fast way to deliver vaccines. But jet injectors were discontinued for mass vaccinations about five years ago because of possible health risks.

A jet injector uses high pressure to force a vaccine or other medication through a person's skin. Their speed made jet injectors very efficient, so many people could be vaccinated quickly. They were often used in the military. Although they weren't pain-free, jet injectors didn't involve needles. The result was less discomfort than a needle injection, and they caused less anxiety in people who were afraid of needles.

In some cases, however, jet injectors could bring blood or other body fluids to the surface of the skin while the vaccine was being administered. Those fluids could contaminate the injector, creating the possibility that viruses could be transmitted to another person being vaccinated with the same device.

Of particular concern were viruses transmitted by blood, such as human immunodeficiency virus (HIV), hepatitis B and hepatitis C. HIV can lead to acquired immunodeficiency syndrome (AIDS) -- a chronic, life-threatening condition caused by damage to the immune system. Hepatitis can cause chronic inflammation of the liver and lead to serious liver damage.

Greater awareness of these diseases and other blood-borne illnesses led to increased scrutiny of ways they might be spread. Although no widespread outbreaks of these diseases were caused by jet injectors, the risk of blood and body fluid contamination of the equipment made jet injectors no longer acceptable for vaccinations. Instead, most vaccines now are administered by needle injection, typically in the arm for adults and in the thigh for children.

In the case of the flu vaccine, another option that became available about three years ago is a nasal mist. All it takes is one spray in each nostril. It's easy, quick and painless. No needles are involved.

This method has limitations, though. The nasal spray vaccine contains a low dose of weakened live virus. If a person's immune system is severely suppressed due to illness or medical treatment, the live virus could, theoretically, cause the flu in that person. Also, the flu vaccine nasal spray appears to be less effective than needle injection (flu shot) in people 50 and older. For these reasons, the nasal spray is only approved for healthy people ages 2 to 49.

The flu shot is approved for people 6 months and older. Because the viruses in the flu shot aren't live, it can't cause you to get the flu but it will enable your body to develop the antibodies necessary to ward off influenza viruses.

Mayo Clinic recommends that everyone get the flu vaccine. Although people tend to think of influenza as a minor illness, it can cause pneumonia and lead to hospitalization, particularly in high-risk groups. At particularly high risk for influenza are all children 6 months to 18 years and everyone older than 50. Others at increased risk of flu-related complications are pregnant women, people who have a chronic medical condition such as heart disease, diabetes or asthma, and anybody whose immune system is compromised.

Unfortunately, about 36,000 Americans die each year as a result of influenza. So, it's important to get a flu vaccine every year to protect yourself.

The current methods of delivering the vaccine are safe and effective and, although they aren't as fast as the jet injectors, getting a flu vaccine doesn't take much time.

Flu season lasts from fall through early spring. The earliest Mayo Clinic usually sees a flu outbreak is September or October. But about 60 percent of influenza outbreaks in the U.S. occur after January.

Contrary to popular belief, even if you don't get your flu vaccine by the end of November, it's not too late. The majority of outbreaks occur after that time, and you can still receive the vaccine as late as March or April.

-- *Gregory Poland, M.D.,  
Vaccine Research Group, Mayo  
Clinic, Rochester, Minn.*

**Dec 8, 2008**

## ***EU looks at increasing supply of transplant organs***

[www.reuters.com](http://www.reuters.com)

BRUSSELS (Reuters) - Europe's health chief proposed ways Monday to improve availability of transplant organs across frontiers and reduce the number of people who can die while awaiting an operation.

Organ shortage is a common problem in all European Union countries, with some 56,000 patients waiting for a suitable organ donor across the EU's 27 member countries and 12 people dying every day while waiting for organ transplantation.

Now, the European Commission wants to see every EU country set up a national authority to ensure compliance with EU quality and safety standards -- including a traceability system for human organs and checks on serious adverse events and reactions.

Data collection on specific organ characteristics would be standardized to ease exchange of human organs, under proposals presented by EU Health Commissioner Androulla Vassiliou. They will now be discussed by EU ministers.

"These measures are all about saving lives," Vassiliou said.

"We want to reassure citizens and patients across Europe that the EU and member states are working together to maximize efforts to provide high quality and safe transplantation systems," she said in a statement.

Under an accompanying but non-binding six-year plan to run from 2009, EU countries would be encouraged to create transplant donor coordinators in every hospital and take steps to improve donor identification to increase cross-border organ donation.

Vassiliou aims to improve the quality and safety of organs across Europe, while raising organ availability and minimizing risks for the recipients as well as providing the transplant surgeon with the necessary information to make the best choice.

For many patients, transplantation is the only life-saving treatment available. But there are wide variations across the EU in yearly donation rates, ranging from 34.6 donations per million people in Spain to 0.5 per million in Romania.

There are also big differences in people's willingness to donate organs. According to a 2007 poll carried out at the request of the Commission, for example, 40 percent of families in Britain said they would refuse to donate an organ from a deceased family member. The EU average was about 50 percent.

(Reporting by Jeremy Smith)

## ***Human Genome Sciences Announces Albuferon(R) Meets Primary Endpoint in Phase 3 Trial in Chronic Hepatitis C***

<http://br.sys-con.com>

By: PR Newswire

*- Albuferon (albinterferon alfa-2b) met its primary endpoint of non-inferiority to Pegasys (peginterferon alfa-2a) in the ACHIEVE 2/3 trial in patients with genotypes 2 and 3 chronic hepatitis C -*

*- Patients receiving 900-mcg Albuferon had comparable rates of serious adverse events, severe adverse events and discontinuations due to adverse events, vs. peginterferon alfa-2a -*

ROCKVILLE, Md., Dec. 8 /PRNewswire-FirstCall/ -- Human Genome Sciences, Inc. (Nasdaq: HGSI) today announced that Albuferon(R) (albinterferon alfa-2b) met its primary endpoint of non-inferiority to peginterferon alfa-2a (Pegasys) in ACHIEVE 2/3, a Phase 3 clinical trial of Albuferon in combination with ribavirin in treatment-naive patients with genotypes 2 and 3 chronic hepatitis C (p=0.0086). Albinterferon alfa-2b is being developed by HGS and Novartis under an exclusive worldwide co-development and commercialization agreement entered into in June 2006.

"We are pleased that Albuferon met its primary endpoint in the ACHIEVE 2/3 trial. These Phase 3 data show that the efficacy of Albuferon was comparable to Pegasys, with half the injections," said H. Thomas Watkins, President and Chief Executive Officer, HGS. "We look forward to

having the results of ACHIEVE 1, our other Phase 3 trial of Albuferon, in March 2009. If ACHIEVE 1 is successful, we believe Albuferon could become the market-leading interferon for the treatment of chronic hepatitis C, and we expect that global marketing applications will be filed by fall 2009."

David Nelson, M.D., Professor of Medicine, Medical Director of Liver Transplantation, and Chief of the Hepatobiliary Disease Section, University of Florida, said, "Chronic hepatitis C represents a significant unmet medical need. These Phase 3 results suggest that albinterferon alfa-2b has the potential to become an important new treatment option for patients with chronic hepatitis C. Albuferon requires half as many injections as the pegylated interferons, and clinical results to date suggest that it may offer comparable efficacy, with no difference in clinically significant adverse events. The observed variation in response by geography is an unexpected finding and requires further analysis. We look forward to results from the ACHIEVE 1 trial, which is evaluating albinterferon alfa-2b in the treatment of patients with genotype 1 hepatitis C."

In the randomized, multi-center, active-controlled non-inferiority Phase 3 trial, 933 treatment-naive patients with genotypes 2 and 3 chronic hepatitis C were initially assigned to one of three treatment groups, including two groups that received albinterferon alfa-2b once every two weeks at doses of 900-mcg or 1200-mcg, and an active control group that received peginterferon alfa-2a once weekly at a dose of 180-mcg - with all patients receiving oral ribavirin daily at 800-mg in two divided doses. In January 2008, a dose modification was made and patients originally assigned to receive the 1200-mcg dose of albinterferon alfa-2b had their dose reduced to 900-mcg albinterferon alfa-2b every two weeks. The dose modification was recommended by the independent Data Monitoring Committee (DMC) for the Albuferon Phase 3 trials, following their observation during a routine review of unblinded data from both trials that serious pulmonary adverse events were higher in the 1200-mcg Albuferon treatment group. Following the dose modification, the study continued to follow all patients randomized into the trial on an intention-to-treat (ITT) basis according to their original dose assignment. The primary data analysis compares the 900-mcg albinterferon alfa-2b treatment group to the peginterferon alfa-2a treatment group. The trial included 24 weeks of treatment, and the primary efficacy endpoint was non-inferiority to peginterferon alfa-2a, based on a comparison of the rate of SVR, defined as undetectable viral load (HCV RNA < 10 IU/mL) at Week 48 (24 weeks following completion of treatment).

"We are encouraged that albinterferon alfa-2b met the primary efficacy endpoint of non-inferiority to peginterferon alfa-2a in the ACHIEVE 2/3 study," said David C. Stump, M.D., Executive Vice President, Research and Development, HGS. "These data show that the rate of sustained virologic response was comparable for the treatment group receiving the 900-mcg dose of albinterferon alfa-2b every two weeks, versus the treatment group receiving the standard dose of peginterferon alfa-2a once weekly. Importantly, the number of serious and severe adverse events, including pulmonary adverse events, was also comparable. When we have ACHIEVE 1 results in March, we will be in a position to assess the full therapeutic potential of albinterferon alfa-2b."

### **Key Findings from ACHIEVE 2/3**

The topline ACHIEVE 2/3 results include the following key findings:

Treatment Group Receiving Albinterferon Alfa-2b 900-mcg Every Two Weeks, vs. Treatment Group Receiving Peginterferon Alfa-2a 180-mcg Every Week

- Based on an ITT analysis of the treatment group assigned to receive 900-mcg albinterferon alfa-2b every two weeks, the topline results demonstrate that albinterferon alfa-2b met its primary efficacy endpoint of non-inferiority to peginterferon alfa-2a, with 79.8% (249/312) of patients achieving SVR in the 900-mcg albinterferon alfa-2b treatment group, vs. 84.8% (263/310) in the peginterferon alfa-2a treatment group (p=0.0086 for non-inferiority).
- By region, SVR rates were
- North America: 82.5% (85/103) for 900-mcg albinterferon alfa-2b, vs. 81.5% (88/108) for peginterferon alfa-2a;
- Asia: 79.8% (75/94) for 900-mcg albinterferon alfa-2b, vs. 95.5% (85/89) for peginterferon alfa-2a;
- Europe: 78.1% (64/82) for 900-mcg albinterferon alfa-2b, vs. 81.7% (67/82) for peginterferon alfa-2a;
- Other regions: 75.8% (25/33) for 900-mcg albinterferon alfa-2b, vs. 74.2% (23/31) for peginterferon alfa-2a.
- Patients receiving 900-mcg albinterferon alfa-2b had comparable rates of serious adverse events, severe adverse events, and discontinuations due to adverse events, vs. peginterferon alfa-2a.
- The incidence of severe and/or serious adverse events was comparable between the two groups, with 17.3% (54/313) in the albinterferon alfa-2b 900-mcg treatment group, vs. 17.5% (54/309) in the peginterferon alfa-2a treatment group.
- The incidence of severe and/or serious pulmonary adverse events was also comparable between these groups: severe and/or serious pulmonary infections were 0.6% (2/313) for 900-mcg albinterferon alfa-2b, vs. 0.6% (2/309) for peginterferon alfa-2a; and severe and/or serious respiratory, thoracic or mediastinal disorders were 1.0% (3/313) for 900-mcg albinterferon alfa-2b, vs. 1.3% (4/309) for peginterferon alfa-2a.
- Overall, adverse events observed were those typically associated with interferon therapy, and the rate of discontinuations due to adverse events was comparable: 4.8% (15/313) for 900-mcg albinterferon alfa-2b, vs. 3.6% (11/309) for peginterferon alfa-2a.

Treatment Group Originally Randomized to Receive Albinterferon Alfa-2b 1200-mcg Every Two Weeks and Reduced to 900-mcg Following January 2008 Dose Modification, vs. Treatment Group Receiving Peginterferon Alfa-2a 180-mcg Every Week

Due to the dose modification announced in January 2008, patients in the treatment group originally randomized to receive albinterferon alfa-2b 1200-mcg every two weeks had their dose modified to 900-mcg albinterferon alfa-2b every two weeks. All patients had completed at least 12 weeks of treatment at the time of the dose modification. Data from all three treatment groups in the ACHIEVE 2/3 study were analyzed according to the original dose assignment. The following topline results for the treatment group originally randomized to receive 1200-mcg albinterferon alfa-2b every two weeks did not impact the primary analysis comparing the 900-mcg albinterferon alfa-2b treatment group to the peginterferon alfa-2a treatment group.

- Based on an ITT analysis of results for the treatment group originally randomized to receive 1200-mcg albinterferon alfa-2b every two weeks, 80.0% (248/310) of patients in this

treatment group achieved SVR, vs. 84.8% (263/310) in the peginterferon alfa-2a treatment group, which statistically demonstrated non-inferiority (p=0.0059).

- The incidence of severe and/or serious adverse events was comparable between the two groups, with 16.8% (52/310) in the treatment group originally randomized to receive 1200-mcg albinterferon alfa-2b every two weeks, vs. 17.5% (54/309) in the peginterferon alfa-2a treatment group.
- The incidence of severe and/or serious pulmonary adverse events was also comparable between these groups: severe and/or serious pulmonary infections were 1.3% (4/310) in the treatment group originally randomized to receive 1200-mcg albinterferon alfa-2b, vs. 0.6% (2/309) in the peginterferon alfa-2a treatment group; severe and/or serious respiratory, thoracic or mediastinal disorders were 1.6% (5/310) in the treatment group originally randomized to receive 1200-mcg albinterferon alfa-2b, vs. 1.3% (4/309) in the peginterferon alfa-2a treatment group.
- Overall, adverse events observed were those typically expected with interferon therapy. The incidence of discontinuations due to adverse events was 5.5% (17/310) in the treatment group originally randomized to receive 1200-mcg albinterferon alfa-2b every two weeks, vs. 3.6% (11/309) in the peginterferon alfa-2a treatment group.

### **About Albinterferon Alfa-2b (Albuferon)**

Albinterferon alfa-2b is a novel, longer-acting form of interferon alfa that was created using the proprietary HGS albumin-fusion technology. Human albumin is the most prevalent naturally occurring blood protein in the human circulatory system, persisting in circulation in the body for approximately 19 days. Research has shown that genetic fusion of therapeutic proteins to human albumin decreases clearance and prolongs the half-life of the therapeutic proteins. Albuferon results from the genetic fusion of human albumin and interferon alfa.

Albuferon is being developed by HGS and Novartis for the treatment of chronic hepatitis C under an exclusive worldwide co-development and commercialization agreement entered into in June 2006. HGS and Novartis will co-commercialize Albuferon in the United States and will share clinical development costs, U.S. commercialization costs and U.S. profits equally. Novartis will be responsible for commercialization in the rest of the world and will pay HGS a royalty on those sales. Clinical development, commercial milestone and other payments to HGS could total as much as \$507.5 million, including \$132.5 million received to date.

### **Conference Call**

HGS management will hold a conference call to discuss this announcement today at 8:15 AM Eastern. Investors may listen to the call by dialing 888-215-6982 or 913-312-0389, passcode 7154642, five to 10 minutes before the start of the call. A replay of the conference call will be available within a few hours after the call ends. Investors may listen to the replay by dialing 888-203-1112 or 719- 457-0820, confirmation code 7154642. Today's conference call also will be webcast and can be accessed at [www.hgsi.com](http://www.hgsi.com). Investors interested in listening to the live webcast should log on before the conference call begins to download any software required. Both the audio replay and the archive of the conference call webcast will remain available for several days.

*SOURCE Human Genome Sciences, Inc.*

## **Nuts boost health benefit of Mediterranean diet**

[www.reuters.com](http://www.reuters.com)

LONDON (Reuters) - Adding nuts to a traditional Mediterranean diet rich in fruit and vegetables appears to provide extra health benefits, Spanish researchers said on Monday.

A daily serving of mixed nuts helped a group of older people manage their metabolic syndrome, a group of related disorders such as obesity, high cholesterol, high blood pressure and abnormal blood sugar, Jordi Salas-Salvado of the University of Rovira i Virgili in Spain and colleagues said.

"The results of the present study show that a non-energy-restricted traditional Mediterranean diet enriched with nuts, which is high in fat, high in unsaturated fat and palatable, is a useful tool in managing the metabolic syndrome," they wrote in the *Archives of Internal Medicine*.

The findings add to existing evidence of the health benefits of a Mediterranean diet that emphasizes vegetables, fish and healthy fats such as olive oil over red meat and alcohol. Studies have linked the diet to reduced risk of diabetes, asthma and a range of other conditions.

The researchers looked at 1,224 people in Spain aged 55 to 80 at high risk of heart disease. One group received advice on a low-fat diet while two others followed a Mediterranean diet, one getting an extra liter of olive oil per week and the other receiving an additional 30 grams of mixed nuts daily.

At the start of the study nearly two thirds of the men and women met the criteria for metabolic syndrome, but after one year the condition decreased by about 14 percent among those who ate nuts compared with 7 percent in the olive oil group and 2 percent in the control group on a low-fat diet.

Nuts contain beneficial nutrients such as fiber, arginine, potassium, calcium and magnesium, as well as a high level of unsaturated fats similar to olive oil, the researchers noted.

(Reporting by Michael Kahn; editing by Will Dunham and Tim Pearce)

## **Atazanavir-treated patients have increased risk of hyperbilirubinaemia after starting therapy for hepatitis C**

[www.aidsmap.com](http://www.aidsmap.com)

Michael Carter

Treatment for hepatitis C increases the risk of hyperbilirubinaemia for HIV-positive patients taking atazanavir (Reyataz), investigators report in the November 30th edition of *AIDS*. The proportion of atazanavir-treated patients with hyperbilirubinaemia increased from 9% to 45% after hepatitis C therapy consisting of pegylated interferon and ribavirin was started.

Atazanavir is a protease inhibitor with a number of attractive features. It can be taken once daily and does not cause the lipid increases associated with many other protease inhibitors. The main

side-effect of atazanavir is hyperbilirubinaemia, a built of bilirubin, a waste product produced by the liver during the breakdown of old red blood cells. It is not dangerous but can cause jaundice that persists unless treatment with atazanavir is discontinued.

A significant proportion of HIV-positive individuals are also infected with hepatitis C. Current treatment for hepatitis C consists of pegylated interferon with ribavirin. Interactions between ribavirin and anti-HIV drugs from the NRTI class have been reported, but there are no known interactions between ribavirin and atazanavir.

However, both drugs can increase bilirubin levels and this could mean that patients treated with atazanavir could have an increased risk of developing hyperbilirubinaemia and jaundice after starting hepatitis C treatment.

Investigators therefore designed a study to monitor changes in bilirubin in 72 HIV and hepatitis C coinfecting patients who were taking antiretroviral therapy. Half of these patients were taking atazanavir and the investigators compared changes in serum bilirubin in the atazanavir-treated patients and those taking other antiretroviral drugs after the initiation of treatment for hepatitis C. Tests were also conducted to see if the gene \*28 effected bilirubin levels.

At baseline, median bilirubin level was 1.25 mg/dl. There was a significant increase in both arms of the study four weeks after starting treatment with ribavirin ( $p = 0.014$ ). This increase was significantly more marked in the atazanavir-treated patients than in the patients taking other antiretroviral drugs (0.80 vs. 0.15 mg/dl,  $p = 0.003$ ). The researchers calculated that bilirubin increases following the initiation of hepatitis C treatment including ribavirin were 1.9 fold higher in the patients taking atazanavir compared to individuals taking HIV treatment based on an alternative drug.

Furthermore, the investigators found that 45% of patients taking atazanavir experienced an increase in their bilirubin of more than 1 mg/dl compared to only 3% of individuals taking another drug ( $p = 0.001$ ).

The proportion of atazanavir-treated patients with moderate-to-severe hyperbilirubinaemia increased from 9% at baseline to 45% after the initiation of ribavirin therapy ( $p = 0.021$ ). None of the patients in the control arm developed hyperbilirubinaemia.

Equal proportions of the patients in the two study arms had the \*28 gene. However, there was no evidence that this gene increased the risk of developing increased bilirubin.

In statistical analysis, the only factors that were significantly associated with increases in bilirubin following initiation of hepatitis C therapy including ribavirin were current treatment with atazanavir and ( $p = 0.005$ ) and falls in haemoglobin (per 1 g/dl,  $p = 0.008$ ).

“The present study shows that a large number of HIV-infected patients on stable atazanavir therapy may experience an increase in total serum bilirubin levels following the initiation of hepatitis C therapy”, write the investigators.

They conclude, "the normal clearance of bilirubin might be compromised due to inhibitory competition of atazanavir, causing jaundice in HIV patients following initiation of hepatitis C therapy."

### **Reference**

Rodriguez-Novoa, S. et al. Increase in serum bilirubin in HIV/hepatitis C virus-coinfected patients on atazanavir therapy following initiation of pegylated-interferon and ribavirin. *AIDS* 22: 2535-37, 2008.

**Dec 9, 2008**

### ***Leeds research points to new therapy for hepatitis C treatment***

<http://www.eurekalert.org>

Combination therapies similar to those used for HIV patients may be the best way of treating hepatitis C virus (HCV), say researchers from the University of Leeds.

A study of a protein called p7, has revealed that differences in the genetic coding of the protein between virus strains - known as genotypes - alter the sensitivity of the virus to drugs that block its function.

The p7 protein assists the spread of HCV around the body and is a promising target for new drug treatments for the virus. Its role was discovered in 2003 by Dr Steve Griffin with Professors Mark Harris and Dave Rowlands of the University's Faculty of Biological Sciences. In laboratory tests their latest research shows that inhibiting p7 with drugs can prevent the spread of HCV..

"One of the challenges in finding treatments for viruses is their ability to constantly change their genetic makeup," says Professor Harris. "Our research shows there can't be a one-size-fits-all approach to treating HCV with p7 inhibitors in the future. We believe combination treatments will work much more efficiently, as they take into account the variability of the p7 protein."

Approximately 180 million people worldwide are infected by HCV, which causes inflammation of the liver and can lead to liver failure or liver cancer. Spread by contact with infected blood or other bodily fluids, there is no vaccine against the disease which is largely asymptomatic in its early stages. The disease is currently treated with broad spectrum, non-specific anti-viral drugs.

Dr Griffin and Prof. Harris examined the response of HCV to a panel of compounds including the well known anti-viral drug, rimantadine, which targets a similar protein in the flu virus. They found that the drug's effectiveness was altered depending on the genetic makeup of the p7 protein.

"We 'borrowed' rimantadine to test its effects because p7 behaves similarly to a protein found in the flu virus," says Dr Griffin. " Although rimantadine works well in the laboratory, we now need to develop new drugs specifically targeted against p7 that we can take forward for future therapies."

**Dec 10, 2008**

## ***Dementia risk not high in mild cognitive impairment***

[www.reuters.com](http://www.reuters.com)

By David Douglas

NEW YORK (Reuters Health) - People with mild cognitive impairment appear to have a lower risk of future dementia than previously believed, according to UK researchers reporting in the *Journal of Neurology, Neurosurgery and Psychiatry*.

Lead investigator Dr. Alex J. Mitchell from the University of Leicester told Reuters Health that mild cognitive impairment is a condition often seen in both primary and secondary care. "Although mild cognitive impairment is a high-risk condition, some people remain stable and some actually improve."

Mitchell, along with Dr. M. Shiri-Feshki of Nottinghamshire Healthcare NHS Trust in Nottingham, analyzed data combined from 15 studies that lasted at least 5 years.

The two researchers determined that the yearly progression rate from mild impairment to dementia was 4.2 percent, much lower than "the widely cited 10 to 15 percent conversion rate."

Among explanations for their long-term results, the investigators point out that populations studied at specialist centers, such as memory clinics, might have high rates of early progression. "In the first few years of follow-up, many of those with the most adverse risk profile will tend to progress, dropout or die, leaving a (group) of less vulnerable sufferers," they write.

Altogether, continued Mitchell, "we found the rate of deterioration was about one third of that expected." The team also found "that over 10 years, most people with the condition do not appear to develop dementia, although the risk is still substantial."

Because of the possibility of improvement, Mitchell concluded that "health professionals should look for potentially treatable causes of cognitive impairment at the earliest opportunity."

*SOURCE: Journal of Neurology, Neurosurgery and Psychiatry, November 2008.*

## ***Protecting Organ Recipients -- From Donors***

<http://online.wsj.com>

By Laura Landro

For the sickest patients, donated blood, organs and human tissue can be the gift of life. But they can also bring life-threatening risks, from deadly infections contracted through a donated liver, to fatal lung injuries and allergic reactions in blood-transfusion recipients.

Despite rapid growth in blood transfusions and transplants, the U.S. lags behind other countries in creating a system to monitor threats of disease transmission and complications, according to the Centers for Disease Control and Prevention. As a result, the CDC is teaming up with a coalition of private blood banks, tissue banks and organ-donation groups to develop a national "biovigilance" network. The network will use Web-based reporting systems to collect data on

complications and deaths; identify emerging disease threats; and rapidly notify hospitals about infected donors whose organs and tissues may be earmarked for multiple recipients.

### **'We Are Behind'**

"The medical field is racing forward in finding ways to save and improve lives," with new types of transplants, such as limbs and faces, says Matthew Kuehnert, director of the CDC Office of Blood, Organ and other Tissue Safety. "But the technology has leapt ahead of public-health surveillance efforts, and we are behind in detecting the risks of transmitting diseases through biologic products."

The CDC has added a new electronic reporting system -- to flag adverse events linked to blood transfusions -- to its existing National Healthcare Safety Network. The network currently is used by hospitals on a voluntary basis to report data confidentially about hospital infections. The federal government has provided \$1 million in funding for the blood reporting system, and the AABB (formerly the American Association of Blood Banks) is raising funds from its members and other donors to support initial costs. The system will be piloted in nine facilities starting next month and then expanded nationally, though AABB officials say more federal funding will be necessary to operate the program over the long term.

At the same time, the United Network for Organ Sharing, or Unos, a nonprofit group that contracts with the federal government to allocate organs from deceased donors, is working with the CDC and other groups, including the American Association of Tissue Banks and eye banks, on a prototype of a Transplantation Transmission Sentinel Network. This network would allow organ-procurement groups and transplant centers to search a database prior to a transplant to find any reports of disease in recipients of other organs or tissues. Because tissues such as skin, bone and tendons are often stored longer than organs, the network could be effective if a problem emerges long after an organ transplant.

More than 150 people could be recipients of organs and tissues from one person, "so it is all the more important to have some kind of tracking system," says Gloria Taylor, Unos standards and process improvement administrator and staff ethicist. Unos conducted a pilot program from April 12 to Aug. 12 to test electronic reporting of adverse events. While no adverse events were reported during the pilot at that time, she says, it demonstrated that information could be immediately shared.

Jay Fishman, associate director of the transplantation center at Massachusetts General Hospital in Boston, says that while hospitals are required to report donor infections to organ banks and notify other hospitals who may have organs and tissues from the same donor, "it's just not a rapid system and it could take days." Moreover, he adds, "you can't query the system and say I have a patient with an unusual syndrome, what's happened with other patients?"

The U.S. is behind because it has no single national authority for collecting and distributing blood, Dr. Kuehnert says. The FDA regulates blood and tissue products and requires that adverse events and deaths be reported by hospitals, but organ donation is regulated by another agency -- and a patchwork of groups procure donors and manage organ and tissue banks.

There is little reliable national data about the rates of complications from organ and tissue donors, and even the data collected on blood issues underestimates the problems, according to

the AABB. In a survey, the group found 72,000 transfusion-related adverse reactions in 2006. But D. Michael Strong, AABB's president, says that may reflect only half the problems that occur, such as lung injury and transfusion of the wrong blood into a patient.

### **Creating Standards**

The AABB has already had success with a West Nile virus reporting network, introduced in 2006, which helped identify where the virus was turning up so that blood banks could change testing procedures and pick up more cases, Mr. Strong says. For the biovigilance network, it is creating standard definitions for a range of adverse events and near-misses so hospitals can report nearly anything that happens during blood donation and transfusion -- including labeling errors, injuries and allergic reactions.

The blood reporting system is intended to identify trends, design patient-safety programs and measure their effectiveness. For example, if patients began developing fatal reactions to a certain kind of blood product, the network could identify trends and enable the CDC to start analyzing other factors, including whether all the fatalities were linked to the same reaction -- such as bacterial sepsis -- and whether all the blood components were processed in the same way. Local hospitals could use the data to respond to problems in their own facilities, and compare their safety results to other hospitals.

Generally, blood transfusions and organ and tissue transplants are safe. There are new tests to screen donors for diseases and new drugs to treat complications. But screening tests can't catch all diseases, especially as new infectious threats emerge. In one case, three recipients of organs from a deceased donor in Rhode Island died after contracting a rare virus known as LCMV. It was later determined that the donor had contact with a pet hamster that carried the virus, but the donor never tested positive for it.

Francis Delmonico, a transplant surgeon who was involved in removing some of the donor's organs, and helped write a New England Journal of Medicine paper about the deaths, says that he and other surgeons had never encountered such a situation before, and that there was no way of knowing the donor had been exposed. But the incidents highlight the need for a national system for tracking and disseminating patient data and putting multiple transplantation centers, organ procurement agencies and public-health authorities on alert to monitor other patients with organs or tissues from a donor with a suspected infection, Dr. Delmonico says.

### **Legal Liability**

Hospitals and organ procurement organizations also face growing legal liability from complications related to blood and organs. The University of Chicago Medical Center is facing a lawsuit from a patient, identified only as Jane Doe, who contracted HIV and hepatitis C after receiving a kidney from an infected donor. Thomas Demetrio, the attorney representing the patient, says the hospital didn't inform her that the donor was from a high-risk group, among other things, and that the donor was apparently infected too close to his death to register on hospital screening tests.

While the hospital declines to comment on the case, it now uses nucleic-acid testing that can identify an HIV infection if a donor was exposed within about a week prior to death, according to Michael Millis, chief of transplantation surgery.

Dr. Millis supports the idea of sharing information about donor disease transmission risks through the biovigilance network, but notes that a recipient who turns up with hepatitis C six months after a transplant may have contracted it from IV drug use after his transplant instead of from his liver donor, a possibility doctors should explore before rejecting other tissues from the same donor as too risky. "One of the problems of rapid fire communications is that you have to have certainty before you start disseminating information," Dr. Millis says.

Email [informedpatient@wsj.com](mailto:informedpatient@wsj.com)

## ***Hepatitis C Deaths: Legacy Of Our Past Behaviour***

<http://www.emaxhealth.com>

Many hepatitis C infections in the UK stem from recreational injecting drug use that began in the 1960s according to a new report released today by the Health Protection Agency.

Hepatitis C in the UK, an annual report for 2008, profiles the burden of hepatitis C and highlights that many people remain unaware of their infections. Decades on from the 60s, evidence is continuing to emerge of hepatitis C related liver disease, a worrying trend that, according to the Agency, will continue unless more people are tested, diagnosed and given access to effective treatment.

Hepatitis C is a chronic blood borne viral infection that affects the liver. The infection is usually silent for many years, but long-term inflammation of the liver can lead to liver damage. By the time illness becomes apparent, it may have caused serious liver disease and this can result in liver failure and death.

It is thought that around 250,000 people in the UK have ever been infected with the virus, with only one quarter of these expected to have cleared the infection. It is estimated that around a half of people living with hepatitis C have not been tested for the infection and are unaware they have contracted it. Without treatment, these individuals will be living with the virus and are at risk of developing serious liver disease.

Dr Helen Harris, a hepatitis C expert from the Health Protection Agency, said: "Hepatitis C is a disease many people associate with current drug use, but we should not forget people who could have been infected many years ago and are unaware of their infection. For example, people may have been infected by sharing needles once or twice when they were younger, and are now living stable everyday lives."

In England, the Agency has estimated that the number of people becoming infected increased dramatically after 1960, reaching almost 15,000 new infections in 1988. This increase is now being reflected in deaths from liver disease more than two decades later.

People who feel that they may have unknowingly put themselves at risk are being urged to come forward and get tested. The number of laboratory confirmed diagnoses of hepatitis C infection in England reported to the HPA in 2007 was 7540; a 12 per cent increase on the previous year. This increase suggests that more people are coming forward to be tested. Much of the increase this

year is thought to be due to increased awareness about hepatitis C amongst both health care workers and the public.

The main risks in the UK are injecting drug use and the sharing of contaminated needles or equipment, and receiving a blood transfusion before screening began in 1991. People born and raised in high prevalence countries (many countries in Africa, Latin America and central and South-Eastern Asia) could have also been infected through other forms of blood exposure such as unsterile medical equipment.

Dr Mary Ramsay, Consultant in Public Health at the Health Protection Agency, said: "The Health Protection Agency monitors trends in hepatitis C at a national level and works with other agencies through our network of local leads to improve services for the prevention, diagnosis and treatment of hepatitis."

### ***New pathway found for fatty liver disease***

<http://www2.med.umich.edu>

by Kim Roth

*U-M investigators uncover clues about how cells under stress may lead to disease*

ANN ARBOR, Mich. — Fatty liver disease is the most common liver pathology in the western world, affecting up to 25 percent of adults in the United States and setting some of them up for future liver failure. Now, University of Michigan researchers describe their new understanding of how metabolic diseases such as fatty liver disease may develop.

The research was published online yesterday in the journal *Developmental Cell*, and recent papers in the journals *Proceedings of the National Academy of Sciences* and *Journal of Clinical Investigation*.

The work focuses on the stress-sensing pathways of cells and what might happen when they are disrupted by environmental factors, such as heavy alcohol use or high-fat diets.

Eventually, the findings may allow doctors to help patients stave off complications of fatty liver disease, diabetes and even neurodegenerative diseases such as Parkinson's.

“What we've come across is a new cellular pathway that might contribute to fatty liver disease and the complications associated with it,” says Thomas Rutkowski, Ph.D., the study's first author, who conducted the research while completing his postdoctoral work at the Howard Hughes Medical Institute (HHMI) at the University of Michigan, under the direction of Randal J. Kaufman, Ph.D.

Kaufman is a professor in the Department of Biological Chemistry at the U-M Medical School and an investigator with HHMI. Rutkowski is currently assistant professor of anatomy and cell biology at the University of Iowa Carver College of Medicine.

Chronic alcoholism and hepatitis C infection can cause fatty liver disease; it is also associated with diabetes and obesity. People with accumulated fat in the liver may not show symptoms at

first, but over time it can lead to liver inflammation and injury, a condition called steatohepatitis. Complications of steatohepatitis include cirrhosis and liver failure, and they can shorten a person's quality and length of life.

The research involved studying how three separate pathways in the unfolded protein response (UPR) protect cellular function in the endoplasmic reticulum (ER), the area of the cell where proteins begin their journey to the world outside.

Secreting proteins or inserting them into the cell membrane is how the cell communicates with the environment. These proteins are first synthesized in the ER, a network of tubes and sacs where these proteins "fold" into their correct three-dimensional shapes before they reach the cell's surface.

If proteins fail to fold properly, they won't be able to carry out their functions. Worse yet, they can form damaging protein aggregates such as the amyloid plaques that characterize the brains of Alzheimer's disease patients. Changes or stresses outside the cell can result in abnormal folding inside the ER. If this happens, the cell adapts by initiating the unfolded protein response.

The UPR is a cell's way to ensure its ability to secrete proteins is working properly. Its role is to turn on genes that help the ER properly fold proteins, akin to adding quality control inspectors in a factory. With these genes turned on, the cell is better equipped to handle the stress of protein folding problems in the ER. However, sometimes the stress can be too severe, overwhelming the UPR and leading to abnormal cellular function.

The finding of the link between fatty liver disease and ER stress was "a bit of serendipity," Rutkowski says.

Initially, Kaufman and his researchers set out to understand the basic mechanism by which cells sense that there is ER stress and respond and adapt to it.

"Any time the cell senses any stress, there are three proteins -- ATF-6, IRE-1 and PERK -- whose job is to sense disruption in ER function," Rutkowski says. "We wanted to understand what role they played in keeping the ER healthy."

### **Research details**

Using mice that had ATF-6, IRE-1 and PERK deleted from their cellular makeup, researchers discovered that animals lacking any of these components of the UPR were more sensitive to ER stress. Over time these animals developed fatty liver, as the authors describe in the *Developmental Cell* paper.

"What we realized is that maybe the unfolded protein response protects against ER stress, and unresolved ER stress can cause fatty liver. That's how we got to the actual mechanism -- that the UPR protects against fatty liver," Rutkowski says.

The *Developmental Cell* paper builds off of research recently published in the *Journal of Clinical Investigation*, which examined cells' reaction in the ER when researchers deleted a gene called CHOP, or C/EBP homologous protein. CHOP signals unfolded protein and stress, and its presence leads to cell death.

CHOP can act as a “bad guy” that appears any time stress is severe or persistent enough. Previous research, and the work conducted in the Developmental Cell study, suggests that CHOP inhibits the action of other members of the gene family that would normally regulate fat metabolism, Rutkowski says.

In the JCI study, also led by Kaufman, researchers learned that they could prevent beta cells in the pancreas from shutting down insulin production by deleting the CHOP gene that caused ER stress.

This finding has potential therapeutic implications primarily for diabetes, but patients with other diseases involving inflammation, such as atherosclerosis, may also eventually benefit from scientists' understanding of CHOP, says Donalyn Scheuner, Ph.D., a research investigator in U-M's Department of Biological Chemistry.

Also playing a role in the authors' understanding of ER stress is their recent paper published in the Proceedings of the National Academy of Sciences. Their work found that treatment with antioxidants reduced UPR response and cell death – while also improving secretion of a clotting factor, FVIII, that is missing in people with hemophilia A, a rare inherited bleeding disorder.

Antioxidants improve ER stress caused by misfolding of the FVIII protein, says Jyoti Malhotra, Ph.D., research investigator also in the Department of Biological Chemistry. Antioxidant treatment reduced ER stress, oxidative stress, cell death and increased FVIII protein secretion in mice and cells grown in the laboratory. Antioxidants also could have far-reaching benefit for other diseases that involve protein misfolding, such as Parkinson's and other neurodegenerative diseases, Malhotra says.

### **Implications**

“Our study and the others that come before it start to put together a picture of lipid metabolism and what is important in terms of physiology and pathology,” Rutkowski says.

“A next step might involve asking whether there is evidence that these pathways contribute to pathological fatty liver disease, which we are now pursuing at Iowa, and to diabetes, metabolic syndrome and coagulation diseases, which Dr. Kaufman is pursuing,” he continues.

“I would call it opening a new door. We've demonstrated that if you disrupt the ER, you can get fatty liver,” says Rutkowski. “What we don't know is that any or all instances are caused or exacerbated by ER stress, but it gives us another avenue to pursue. The more weapons you have against complex metabolic diseases, the better off you are.”

Additional U-M authors are first author Jun Wu, Sung-Hoon Back, Michael U. Callaghan, Sean P. Ferris, Robert Clark, Hongzhi Miao, Justin R. Hassler, Benbo Song, Jayanth Swathirajan, Junying Wang, Grace D.-Y. Yau, and Randal J. Kaufman.

Funding for the research came from the National Institutes of Health, the Howard Hughes Medical Institute and University of Iowa.

### **Citations:**

DevCell, <http://www.cell.com/developmental-cell/home> ; JCI, <http://www.jci.org/articles/view/34587> ; PNAS, <http://www.pnas.org/content/105/47/18525.abstract?sid=702ab0e4-3564-4765-8956-1913fbfcaace>

Dec 11, 2008

### **30-Day Hepatitis C Treatment Study Announced by Aethlon Medical**

<http://www.marketwatch.com>

SAN DIEGO, Dec 11, 2008 (BUSINESS WIRE) -- Aethlon Medical, Inc. (AEMD:aethlon med inc com) announced today that it has accepted enrollment of a Hepatitis C (HCV) infected patient who will initiate a 30-day treatment case study of the Aethlon Hemopurifier(R) in the coming week. The Hemopurifier(R) 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 being HCV infected, the enrolled patient suffers from end-stage renal disease (ESRD) requiring regular kidney dialysis treatment. The study goal is to demonstrate the Aethlon Hemopurifier(R) is able to inhibit HCV proliferation in an infected ESRD patient. The study design calls for 12 Hemopurifier(R) treatments to be administered during normally scheduled dialysis. As a result, four-hour Hemopurifier(R) treatments will be administered thrice weekly over a period of 30 days. The study is being conducted at the Fortis Hospital in Delhi, India.

"In addition to reinforcing the clinical value of our Hemopurifier(R), the ability to manage HCV infection during ESRD patient dialysis would introduce a significant untapped profit opportunity to the dialysis industry," stated Aethlon Chairman and CEO, James A. Joyce.

It is estimated that up to 20% of the 1.6 million global ESRD population is infected with HCV. Beyond the treatment of infected ESRD patients, the overall opportunity for the Hemopurifier(R) is HCV care 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 will beneficially respond to the 48-week pegylated interferon-ribavirin treatment standard.

In a previous study conducted at the Fortis Hospital, six ESRD patients received a series of three, 4-hour Hemopurifier(R) treatments every other day during the course of one week. The treatment regimen also mirrored the patient's normal kidney dialysis schedule, allowing for the inclusion of the Hemopurifier(R) without disrupting dialysis treatment. Robust viral load reductions were observed in three HCV patients that completed the three treatment protocol.

- 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  $5.3 \times 10^5$  viral units per ml of blood (IU/ml). Patient 1's viral load seven days post treatment was  $5.7 \times 10^4$  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  $9.2 \times 10^6$  IU/ml. Patient 2's viral load seven days post treatment was  $4.6 \times 10^6$  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  $3.0 \times 10^8$  IU/ml. Patient 3's viral load seven days post treatment was  $5.1 \times 10^7$  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.

The Hemopurifier(R) 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(R) 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, and ESRD patients infected with HCV.

### **About Aethlon Medical**

Aethlon Medical is the developer of the Hemopurifier(R), a first-in-class medical device designed to treat infectious disease. The Hemopurifier(R) 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(R) is able to capture immunosuppressive particles secreted by tumors. The Hemopurifier(R) 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(R) 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(R) 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 have been 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(R) 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 also submitted an investigational device exemption (IDE) to the U.S. Food and Drug Administration (FDA) to advance the Hemopurifier(R) as a broad-spectrum treatment countermeasure against category "A" bioterror threats. Additional information regarding Aethlon Medical and its Hemopurifier(R) technology is available online at [www.aethlonmedical.com](http://www.aethlonmedical.com).

*SOURCE: Aethlon Medical, Inc.*

### ***Employed women with fibromyalgia maintain health***

[www.reuters.com](http://www.reuters.com)

NEW YORK (Reuters Health) - Women with fibromyalgia seem to benefit from being employed, maintaining their health status over time, study findings suggest.

However, employment did not appear to protect women from developing the condition, report Dr. Susan Reisine and colleagues at the University of Connecticut, School of Dental Medicine in Farmington.

Reisine's group reports their findings in the medical journal *Arthritis and Rheumatism*.

Fibromyalgia, which mostly affects women, is characterized by pain, fatigue, sleeplessness and body stiffness. The cause of this condition is not known and the few studies that have been done report mixed results on the prognosis.

Reisine and colleagues point out that previous research findings have suggest an association between employment and the health status of women with fibromyalgia. To further investigate, they followed 241 mostly white women who had fibromyalgia for an average of 4.9 years. About half of the women were employed.

The women were 47 years old at the start of the study and reported high levels of functional disability, similar to women with rheumatoid arthritis. The women also reported high levels of fatigue and depression, as well as average pain scores of 57 on a low-to-high scale of 1 to 100.

Over 5 years of observation, all health measures, except pain, declined significantly in the group, overall. However, women employed at the start of this observation period reported greater improvements in fatigue, functional status, and depression compared with unemployed women.

"This finding suggests that women with fibromyalgia can remain employed with no negative consequences to their condition," note Reisine and colleagues. They further propose women should attempt to remain employed "as a strategy to maintain better health."

The investigators suggest additional research assess whether race and ethnicity alter the associations reported in this study.

*SOURCE: Arthritis and Rheumatism, December 2008.*

**Dec 12, 2008**

## **Schering-Plough Announces FDA Approval of PEGINTRON(TM) and REBETOL(R) Combination Therapy for Treating Pediatric Hepatitis C**

[www.marketwatch.com](http://www.marketwatch.com)

KENILWORTH, N.J., Dec 12, 2008 /PRNewswire-FirstCall via COMTEX/ -- First and only approved peginterferon in combination with ribavirin for previously untreated children with chronic hepatitis C addresses unmet medical need

Schering-Plough Corporation (SGP:Schering-Plough Corporation) today announced that the U.S. Food and Drug Administration (FDA) has granted marketing approval to PEGINTRON(TM)

(peginterferon alfa-2b) and REBETOL(R) (ribavirin, USP) combination therapy for use in previously untreated patients 3 years of age and older with chronic hepatitis C. This represents the first and only approved peginterferon in combination with ribavirin for treating pediatric hepatitis C. It is estimated that approximately 130,000 children in the United States are infected with the hepatitis C virus (HCV). The most common mode of HCV infection for pediatric patients today is maternal-infant transmission.

The only previously approved therapy in the United States for treating pediatric hepatitis C is Schering-Plough's conventional interferon INTRON(R) A (Interferon alfa-2b, recombinant) in combination with REBETOL. REBETOL is available both as capsules and in an oral solution formulation specifically available for pediatric use.

"With the FDA approval of PEGINTRON combination therapy for this new indication, U.S. physicians now have access to the current standard of care for hepatitis C for use in treating their pediatric patients. Thankfully, the number of children with hepatitis C is small, although this chronic infection over time can lead to serious liver disease," said Robert J. Spiegel, M.D., chief medical officer and senior vice president, Schering-Plough Research Institute. "This approval further underscores Schering-Plough's leadership and long-term commitment to developing new treatment options and innovative therapies to meet the needs of patients with hepatitis C."

The approval of PEGINTRON for the pediatric indication is based on the results of a clinical trial in 107 previously untreated patients 3 to 17 years of age with chronic hepatitis C and compensated liver disease. In the study, patients infected with HCV genotype 1 or 4 and those with HCV genotype 3 with HCV RNA greater than 600,000 IU/mL (high viral load [HVL]) were assigned 48 weeks of therapy, while those infected with HCV genotype 2 or 3 with HCV RNA less than 600,000 IU/mL (low viral load [LVL]) received 24 weeks of therapy. Of the patients with HCV genotype 1, 4 or 3 HVL who were assigned to 48 weeks of treatment, 55 percent achieved SVR. As with adult patients, SVR in pediatric patients with HCV genotype 2 or 3 LVL was much higher than in those with genotype 1; the SVR rate was 96 percent in children with HCV genotype 2 or 3 LVL.

In the pediatric population, the recommended dose of PEGINTRON, based on body surface area, is 60 mcg/m<sup>2</sup>/week subcutaneously in combination with 15 mg/kg/day of REBETOL, based on body weight, orally in two divided doses. The treatment duration for patients with HCV genotype 1 is 48 weeks and for patients with HCV genotype 2 or 3 it is 24 weeks. Patients receiving PEGINTRON combination therapy (excluding those with HCV genotype 2 or 3) should be discontinued from therapy at week 12 if their HCV RNA dropped less than 2 log<sub>10</sub> compared to pretreatment or at 24 weeks if they have detectable HCV RNA at treatment week 24.

During the course of therapy lasting up to 48 weeks in patients 3 to 17 years of age, weight loss and growth inhibition were common. Some children who experienced growth inhibition during therapy still had inhibited growth velocity 6 months following the end of treatment. Most common adverse reactions (more than 25 percent) observed in these studies were pyrexia, headache, neutropenia, fatigue, anorexia, injection site erythema and vomiting. Three percent were treated for clinical hypothyroidism.

Dose modifications were required in 25 percent of patients, most commonly for anemia, neutropenia and weight loss. Therapy was discontinued prematurely in two percent of the patients.

*SOURCE Schering-Plough Corporation*

## **Sixth Annual Hepatitis C Summit**

<http://www.drugpolicy.org>

The Hepatitis C Task Force of Los Angeles brought the medical and prevention community together on November 21 to discuss the state of the hepatitis C epidemic in Los Angeles County. Drug Policy Alliance (DPA) Southern California led the charge in prevention strategies for reducing the further outbreak of the disease at this Sixth Annual Hepatitis C Summit held at the California Endowment.

Meghan Ralston, DPA's Harm Reduction Coordinator, gave a highly energetic presentation about how pharmacies in the Los Angeles County are able to sell syringes without a prescription to those who need them. The Disease Prevention Demonstration Project (DPDP) is a pilot program put together by Senate Bill 1159, the Drug Policy Alliance, California Endowment and the LA Department of Public Health to stop the ever increasing rates and spread of HIV and Hepatitis C. DPDP has signed up over 300 pharmacies in the county and the number is still increasing, with new ground being broken for those in the Antelope Valley area.

Besides preventing the spread of these serious diseases, Meghan Ralston has built relationships with organizations, the health and treatment community as well as city departments that we might not see as an ally in the harm reduction community such as the city Department of Waste Management. Meghan has been working closely with them to implement a proper removal of syringes by dispensing sharps containers throughout the county. It is these "outside the box" strategies that help create stronger relationships with the city of Los Angeles.

The Hepatitis C Summit had a turnout of 250-300 people from all parts of California. Their keynote speaker was Christopher Kennedy Lawford, an actor, who spoke of how he first contracted Hepatitis C and his journey to fight the disease. He spoke about the importance of not only the drugs to treat the disease but the prevention efforts, by expanding treatment for addiction and using harm reduction policies to stop the spread.

The conference ended with a remembrance to keep programs like DPDP up and running, and to continue the fight for treatment instead of incarceration strategies in public health policies. SB 1159 will sunset in 2010, making it a vital piece of legislation DPA will be watching in the new legislative cycle. We encourage all DPA members to remind your legislators how important this bill is to saving lives in California.