

# 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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Week Ending: June 14, 2008

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June 9, 2008

### ***Vertex Unveils More Upbeat Hep C Drug Data***

<http://www.thestreet.com>

Adam Feuerstein

An experimental hepatitis C drug from Vertex Pharmaceuticals VRTX can knock back the virus even in the most difficult-to-treat patients, according to results from a clinical trial announced Monday.

The news sent Vertex shares up 63 cents, or 2%, to \$32.87 in recent trading Monday morning.

The Vertex drug, telaprevir, was able to reduce levels of the hepatitis C virus down to undetectable levels in 52% of so called non-responder or relapse patients. These are patients considered the hardest to treat because they either did not respond to current drugs like interferon and ribavirin, or their virus returned after treatment.

Based on previous studies, roughly 10% of treatment-resistant hepatitis C patients who are then retreated with interferon and ribavirin are successfully cured of their disease.

The new data on telaprevir come from the PROVE 3 study, a phase II clinical trial that enrolled 453 hepatitis C patients who failed to respond to prior treatment. This is an interim analysis, which means that, to date, telaprevir patients have only been followed for 12 weeks post-treatment. A hepatitis C patient is not considered "cured" of the disease until they have undetectable viral levels 24 weeks, or six months, after treatment.

### **A Race for Market Share**

Based on these results, Vertex and partner Johnson & Johnson JNJ said Monday that they will start a pivotal phase III study in treatment-failure patients during the third quarter. There has been great market speculation whether Vertex might be able to seek regulatory approval for telaprevir based on PROVE 3 data alone, however.

John Alam, Vertex's chief medical officer, says it is still too early to comment on the company's ultimate plans for telaprevir in treatment-failure patients. The company intends on sharing final data from PROVE 3 with the U.S. Food and Drug Administration by the end of the year or early 2009. In the meantime, Vertex and Johnson & Johnson are moving ahead on finalizing the design for the phase III study of telaprevir in treatment-failure patients, Alam said.

If telaprevir is found to be effective for these hardest-to-treat hepatitis C patients, the commercial potential for Vertex is significant. There are an estimated 250,000 to 300,000 hepatitis C patients in the U.S. who have failed current interferon-ribavirin therapy and are waiting for something new and more effective to be approved so they can be retreated, and hopefully cured.

This is one of the major reasons why the race to develop and market a new hepatitis C drug is so frenzied. Vertex and J&J are facing off with companies like Schering-Plough SGP, InterMune ITMN, Roche and Pharmasset VRUS -- all of which are hoping that their respective hepatitis C drugs are superior or can be approved first to be the go-to drug for treatment-resistant patients.

A phase III study of telaprevir in hepatitis C patients not previously treated is underway, with data expected in the first half of 2010. If positive, Vertex plans to seek regulatory approval in the second half of 2010.

### **PROVE 3 Data Breakdown**

Breaking down the PROVE 3 interim results further, 41% of telaprevir-treated patients who had previously not responded at all to standard treatment (non-responders) reached undetectable levels of viral load at 12 weeks post treatment. For those patients who did respond to standard treatment but then relapsed during follow-up, treatment with telaprevir led to an undetectable

viral load rate of 73% after 12 weeks of follow-up.

Patients were treated with 12 weeks of telaprevir plus interferon and ribavirin, followed by another 12 weeks of interferon and ribavirin alone.

There is a control arm in the PROVE 3 study, but these patients are still being followed. At this point, 8% of these patients retreated with standard therapy (interferon and ribavirin) had undetectable levels of virus after 12 weeks of treatment. After 36 weeks of treatment, the undetectable level rose to 30%.

While the control arm patients appear to be doing better with longer re-treatment, Vertex's Alam says most of these difficult-to-treat patients must reach undetectable levels by week 12 if they have any real chance for a long-term cure. Most of the patients who reach undetectable levels after 12 weeks of treatment ultimately relapse again, he says.

### ***Greater hepatitis testing needed***

<http://www.independent.ie/>

*Selective: hepatitis C screening for pregnant women isn't working*

Pregnant women should be routinely tested for hepatitis C during their clinic visits, according to a study carried out in Dublin's Rotunda, Mater and Temple Street hospitals.

Currently, only women with risk factors, such as a history of injecting drugs, are tested.

However, over the final six months of last year doctors in the Rotunda asked all women booking their antenatal visits to be tested for hepatitis C.

Hepatitis C can seriously damage the liver over many years causing cirrhosis, cancer or even liver failure.

Mothers can pass on the virus to their unborn child although the risk is low -- about five-10pc of babies become infected.

The doctors said the vast majority of the 4,118 mothers attending the clinics agreed to the tests.

The tests showed that 34 of the women were positive for the virus and six in 10 of these were Irish. Three quarters reported one or more risk factor which could have exposed them to the virus -- mostly sharing needles while injecting drugs.

But the rest had no risk factors, which meant the virus would not otherwise have been picked up.

The findings of the study carried out by doctors in the three hospitals were recently presented at the Royal College Of Physicians spring meeting.

They pointed out the selective screening for hepatitis C that currently exists is not identifying all cases.

"This provides persuasive evidence for the inclusion of hepatitis C virus testing during routine ante-natal screening," they added.

Most people do not experience any symptoms when they first become infected with hepatitis C.

They may have vague flu-like symptoms including fatigue, loss of appetite, joint pain and nausea some weeks after being infected.

In around 20pc of people, the virus is cleared from the body by the immune system within six months.

For others, the virus remains active but may not cause any symptoms throughout their life or for many years.

There is currently no vaccine to protect against the hepatitis C virus.

However, there are increasingly effective treatments available that can clear the virus in approximately half those treated.

The treatment is usually with a combination of two drugs, Interferon and Ribavirin.

Even if the treatment does not clear the virus, it may still slow down the progression of inflammation and liver damage.

**June 10, 2008**

## ***Act now if you're at risk for hepatitis C***

<http://www.heraldnet.com>

By Dr. Elizabeth Smoots

*Herald* Columnist

Dixie contracted hepatitis C from a blood transfusion during surgery years ago. She had no symptoms and, if it weren't for a routine blood test, Dixie wouldn't have known she had the disorder.

She certainly wouldn't have known she had chronic liver disease that is treatable. The test made Dixie aware that she had a condition contagious to others and that could potentially shorten her life. So she decided to act.

### **Course of natural disease**

Hepatitis C virus is the most common blood-borne infection in the U.S. The virus currently infects an estimated 4 million Americans, most of whom are between the ages of 30 and 59.

The majority of people who come down with the illness either have no signs or experience a mild flulike illness. About a third develop specific symptoms such as abdominal pain, loss of appetite, fatigue, achy joints, yellow skin or eyes or a rash for several weeks.

A few people are able to overcome the virus permanently. But up to 85 percent of infected people go on to develop chronic hepatitis C. The vast majority of these people have chronic liver disease.

Elevated blood tests for liver function are one sign. This can occur as chronic liver disease slowly prevents the liver from removing toxins in the blood.

Over about 20 to 30 years, ongoing damage can result in severe complications such as cirrhosis (scarring of the liver), liver failure or cancer. Hepatitis C is the most frequent reason for needing a liver transplant in the U.S. Still, more people die of the disease every year.

### **Effective treatment available**

Luckily, treatment may lessen some of these risks. The combination of interferon and ribavirin can bring sustained resolution of infection in many people with chronic hepatitis C. This is the treatment that Dixie received and she enjoys good health to this day.

She also learned how to avoid spreading the disease to others. Steps include not donating blood or organs and not sharing personal-care items that might have blood on them, such as toothbrushes, dental appliances, razors, nail clippers or home therapy equipment. Using a condom can help reduce the risk of spreading the virus to a sexual partner.

### **Important screening guidelines**

It wasn't until after Dixie discovered she had hepatitis that she was able to get appropriate advice and treatment.

Ask your doctor if you may be at risk.

*Common reasons for getting a screening blood test include:*

- Persistently abnormal liver function tests or undiagnosed liver disease
- Any history of illegal injection drug use or sharing straws for snorting cocaine
- Receiving a blood transfusion, other blood product or organ transplantation before July 1992.  
Note: Screening for hepatitis C after this date has dramatically reduced the risk.
- Needle-stick injuries in health care workers
- Tattoos or body piercings using unsterilized equipment
- Kidney dialysis
- Sharing personal items like razors, nail clippers or toothbrushes with a hepatitis-infected person
- Child born to a mother who has hepatitis C

Studies indicate the virus is not passed from sharing food, water or utensils, kissing or other casual contact.

For more information: American Liver Foundation, [www.liverfoundation.org](http://www.liverfoundation.org) .

Contact Dr. Elizabeth Smoots at [doctor@practicalprevention.com](mailto:doctor@practicalprevention.com)

## ***Love in sickness and in health***

<http://www.venturacountystar.com>

By Tom Kiskan

### *Fight against disease strengthens bond*

It was worse than his cancer, chemotherapy and chance of dying.

As Steve Maheux struggled over two years of treatment and side effects, his wife faced her own battle over hepatitis C. She endured medicine injected into her body every seven days, trips to the hospital for emergency transfusions and the possibility of not surviving.

"It was OK when I was going through it," Steve Maheux said, sitting next to his wife. "Then I'd sit and watch her go through it. It was heartbreaking every week."

As nightmares go, the Maheuxs were hit with a double feature. He was diagnosed with cancer of the lymph nodes on Super Bowl Sunday 2006. Several months later, Diane Maheux began receiving injections for a hepatitis virus contracted through a blood transfusion in 1983.

She took care of him when he struggled with allergic reactions to medicine, lost 50 pounds in a few weeks and worried that if he fell asleep he might not wake up. He administered her weekly shots, alternating between her legs and stomach.

When the treatments drained her body of blood and forced her into the hospital, he kept her going.

"If he wasn't there by her bedside pushing and encouraging her, I think she would have given up," said Dr. Tesu Lin, the Ventura specialist who treats Diane Maheux.

Husband and wife are now in remission, though they struggle with emotional and financial trauma brought on by their illnesses.

He's 47 and she's 51. They met at work and, about 23 years ago, were married in Canoga Park. They raised a daughter in Ventura and share their home with a cockatiel named Whistles who sings from Diane Maheux's shoulder, six other birds and a boxer named Buddy.

Steve Maheux, a mechanical design drafter, made news about 12 years ago as part of a volunteer search party looking for the remains of Sherri Dally. He found the body in a ravine and testified in murder trials that rank among the most sensational in Ventura history. Michael Dally, the victim's husband, and his mistress, Diana Haun, were convicted of murder.

About the same time as the Dally investigation, Diane Maheux was diagnosed with hepatitis C, a blood virus that can cause liver failure and cirrhosis.

Maheux said she contracted the virus from contaminated blood given when she started hemorrhaging three weeks after the birth of her daughter.

Faced with a stigmatized disease often mistakenly linked only to drug use and sexual activity,

she put off treatment. She spent much of the next decade trying to block the diagnosis out of her mind.

"I was afraid of it and I didn't want to deal with it," she said.

About three years ago, doctors told her she needed to start treatment. She postponed it, this time because of her husband.

His legs had grown swollen. His lungs filled with so much fluid he had to prop his head up when he slept.

He was diagnosed with non-Hodgkin's lymphoma, a cancer that starts in lymph nodes and can spread to the rest of the body.

He started intense chemotherapy that included traditional cancer drugs and a newer medication called Rituxan designed to attack lymphomas like a missile.

The treatment lasted eight hours every three weeks and brought nausea, allergies and steroids that made him look like a different man.

"I'd find myself sitting here in the middle of the night looking at my insurance policy," he said. "I didn't know what was going to happen. I prayed a lot."

Diane Maheux said the cancer made her feel guilty about starting treatment for her own illness. But when the Rituxan and other drugs brought Steve Maheux into remission, allowing a milder form of chemotherapy, doctors told her she was running out of choices. The virus was attacking her body. Waiting increased the chance of liver failure.

Her treatment involved biological drugs that create proteins to attack the virus. But the drugs tricked her body into attacking its own blood cells.

She needed transfusions that were complicated by her rare blood subtypes, meaning she had to wait dangerously long for the blood.

After receiving one transfusion, the whole cycle was repeated.

"I think she had to be admitted three times for this," Lin said. "Basically she could barely move. She was debilitated to a point she had to be fed and encouraged to eat."

It was her husband who did much of the encouraging.

"He was the guy who was always there by her bedside," Lin said. "He slept in the room."

Diane Maheux said she also leaned heavily on support of other relatives and friends. Because of the damage to her blood supply, doctors stopped the treatment early. But it still appears to have worked. Lin said there are no signs of hepatitis.

Tests also show that Steve Maheux is in remission, though he continues to receive

chemotherapy. His oncologist cautions him about the chances of relapse and tells him to live day by day.

"He tells me to enjoy life," Steve Maheux said.

He has returned to work full time but the family is far from recovered. Though insurance covered much of the cost, they're paying about \$14,000 a year for healthcare and face a growing mass of bills including foreclosure warnings.

"I think right now we're just keeping our heads above water," Steve Maheux said of the family's finances. "I go to bed thinking about it and I wake up thinking about it."

Tara Hester, their 25-year-old daughter, has moved with her husband into her parents' home to help share the burden of the mortgage payments. As she pays bills and worries about relapses, she's noticed something different about her parents.

"I think they've never been closer than they are now," she said.

"I think when you come within inches of losing someone you count on to be there, your outlook changes."

## ***Hepatitis A Mortality Rates Down Sharply Since Advent of Vaccine***

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

By Martha Kerr

NEW YORK (Reuters Health) Jun 10 - Since the introduction of the hepatitis A vaccine in the mid-1990s, deaths due to hepatitis A are down 32% overall, researchers report in the May 1 issue of the Journal of Infectious Diseases.

Dr. Tara M. Vogt of the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia, and colleagues analyzed US death certificates from 1990 through 2004 on which the underlying cause of death was listed as hepatitis A. Deaths that occurred between 1990 and 1995 in the pre-vaccine era were compared with those occurring between 2000 and 2004. Hepatitis A-related deaths in which chronic liver disease (CLD) was a contributing factor were also identified.

There were 1,476 deaths due to hepatitis A, or an average of 96 deaths per year. The peak was in 1995 with 142 deaths, and the low point was in 2003 with 54 deaths. States that established vaccine recommendations had a 45% decline in deaths, while states that did not institute recommendations only had a decline of 23%.

These reductions "parallel documented decreases in the incidence of hepatitis A," Dr. Vogt and colleagues point out.

The investigators also found that "the proportion of hepatitis A deaths that were CLD-related rose during the study period and...declined less dramatically in the age group/birth cohort with the highest prevalence of CLD." This is consistent with "low vaccination coverage and a modest impact of herd immunity in this group."

In an accompanying editorial, Dr. Jules L. Dienstag of Massachusetts General Hospital and Harvard Medical School in Boston comments: "Vaccines should prevent disease and disease consequences. For hepatitis A, the time from virus discovery to vaccine availability was two decades, and the time from vaccine availability to fulfillment of the vaccine's promise may be even quicker -- the vaccine dividend has been dramatic."

*J Infect Dis* 2008;197:1220-1222,1282-1288.

**June 11, 2008**

## ***Silent no more: viral hepatitis B and C***

<http://thechronicleherald.ca>

By KEVORK PELTEKIAN

There are many diseases in Canada that generate the awareness, funding, advocacy and research that they deserve. As terrible and serious as these diseases are, they are not silent.

Viral hepatitis B and C are not among them.

As a practising liver specialist and chairman of the Canadian Liver Foundation, I often ask myself: What is it about viral hepatitis that makes it almost invisible? Why is no one talking about it?

One of the reasons is the stigma that the more than 600,000 Canadians who suffer from hepatitis B and C live with. Indeed, hepatitis B and C affect one in 12 people worldwide – a phenomenally huge number. It can affect anybody at any time, but is often viewed to be only a problem for the more marginalized populations. Not only can it be deemed socially unacceptable to talk about it, but it can be difficult to diagnose because there may be few, if any, symptoms. If left untreated, however, hepatitis B and C can lead to scarring (cirrhosis), severe chronic illness, cancer and death.

Liver cancer is most frequently a result of hepatitis B and C and its incidence is increasing more rapidly than almost any other cancer. Proper care can prevent this cancer, but due to gaps in the health care system, the majority of patients who develop liver cancer will die from their disease.

Almost half a billion people worldwide have either hepatitis B or C and while this is far higher than the prevalence of HIV or any cancer, awareness is inexplicably low and the majority of those infected are unaware until it is too late.

A colleague of mine compares this disease to an iceberg – one that the health care system is steaming directly toward. The need is immense. And that is why patients, physicians and others who care about this disease have come together to call on the federal government to do more than just piecemeal funding and stopgap measures. In Canada, with no national strategy to deal with this disease, limited funding for research and a shortage of physicians and nurses, the result is a sub-standard level of care. In a country that prides itself on its publicly funded health care system, this is unacceptable.

My physician colleagues, nurses and other health care professionals are pressed to manage the demand now, never mind when these huge numbers of Canadians with hepatitis B and C start getting sicker. These folks will start to suffer complications, develop liver cancer or require liver transplants.

What frustrates us most is the knowledge that there are safe and more effective medications available and approved, but not funded. In this region, the Atlantic provincial governments' attention has been sporadic. I think sometimes these governments feel that if they give minimal attention to those affected by hepatitis B or C, the problem may just go away

But it won't. The situation will only get worse. In Canada, there is no national strategy or comprehensive system for care, treatment and prevention of hepatitis B and C. As health care professionals, we see the looming crisis ahead and are trying to sound the alarm before it is too late.

More Canadians will be affected by this inaction and ignorance. The misconception and stigma that surround hepatitis continue to prevent people who have it from speaking out, and people who don't have it from caring about it.

What do we need? We have to counter the stigma with a national will to manage this disease. We need people to get tested for hepatitis B and C early, so that we can treat them and help prevent the further spread. Once diagnosed, we need patients to have access to the best therapies as they become available, regardless of where they live and their ability to pay. We need ongoing research to better understand hepatitis and to develop more effective drugs with fewer serious side effects. We need to increase the number of people who register as potential organ donors and we need more trained and qualified health professionals to care for patients. In short, to be most effective, we need an organized strategy to tackle the looming crisis of hepatitis B and C.

The Canadian World Hepatitis Alliance, made up of medical specialists, patient groups and people with hepatitis, speaks with one voice on this issue. Its message – the time for action is now.

The Canadian World Hepatitis Alliance unveiled six national "asks" of government that address these hepatitis priorities. These are part of a global campaign to bring much-needed attention to these deadly diseases.

We are calling on the government of Canada to take a leadership role in creating a national strategy that, by 2012, will address the issues that are contributing to the suffering and death of so many Canadians.

We are lending a voice to those who have lived with this in silence, both to help them and to protect those who should never have to suffer this fate.

*Dr. Kevork Peltekian, a leading Canadian hepatologist from QEII and Dalhousie University, is chairman of the Canadian Liver Foundation and member of the Canadian World Hepatitis Alliance. For more information, go to [www.liver.ca](http://www.liver.ca).*

## **Untreated Celiac Disease May Impede Immune Response to Hepatitis B Vaccine**

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

NEW YORK (Reuters Health) Jun 03 - An inadequate antibody response to hepatitis B (HBV) vaccination may be a sign of undiagnosed celiac disease, according to a Hungarian study. However, immune response to the vaccine is near normal in patients compliant with a gluten-free diet, the research team reports in the June issue of *Pediatrics*.

Dr. Eva Nemes, at the University of Debrecen, and colleagues compared immune response among 128 patients with celiac disease and 113 age-matched controls who were given 2 or 3 doses of recombinant HBV vaccine within a 6-month period.

Twenty-two of the patients with celiac disease were prospectively vaccinated after diagnosis while they were on a gluten-free diet. Blood samples collected 4 weeks after the third HBV vaccination to check for anti-HBV antibodies showed a seroconversion rate of 95.5%.

The other 106 patients with celiac disease, as well as the control group, were vaccinated at age 14 years, and anti-HBV titers were measured roughly 2 years later. Seventy of the celiac patients were diagnosed and following a strict gluten-free diet at the time of vaccination, 27 were undiagnosed and untreated, and nine were diagnosed but not compliant with the diet.

The seroconversion rate was 61.4% among celiac patients who were diagnosed and treated, the authors report, not a significant difference from the 75.2% rate in the control group.

In the undiagnosed patients, the response rate of 25.9% was significantly lower than among controls ( $p < 0.001$ ). The nine noncompliant patients with diagnosed, active celiac disease had a response rate of 44.4%.

Thirty-seven nonresponders in the celiac disease group received a booster dose during a gluten-free diet, and 36 (97.3%) had seroconverted 4 weeks later.

"Success with repeated vaccinations after controlled diet and correlation of nonresponse with celiac autoantibody positivity and diet transgressions suggest that disease activity may play a primary role in vaccination failure," Dr. Nemes and her associates conclude.

They recommend that antibody response to HBV vaccination be determined in newly diagnosed patients with celiac disease, and that nonresponders be revaccinated after treatment with a gluten-free diet.

*Pediatrics* 2008;121:e1570-e1576.

## **Liver Disease Score Predicts Outcome of Variceal Hemorrhage**

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

By David Douglas

NEW YORK (Reuters Health) Jun 02 - In patients with cirrhosis and acute variceal hemorrhage, the MELD (Model for End-stage Liver Disease) score and the need for packed red blood cells (PRBCs) are indicative of early re-bleeding and death, researchers report in the June issue of *Gut*.

Dr. Patrick S. Kamath and colleagues at the Mayo Clinic, Rochester, Minnesota note that there is no well-established model for accurate prediction of survival after variceal bleeding in patients with cirrhosis.

However, they point out, the MELD score for classifying liver transplant candidates was originally developed from a cohort of patients with cirrhosis undergoing intrahepatic portosystemic shunting.

The researchers investigated the prognostic utility of the MELD score in 256 cirrhotic patients with acute variceal hemorrhage who had taken part in a subsequently abandoned randomized clinical trial of lanreotide, an agent that proved to have no influence on the condition.

Thirty-five patients (14%) died within 6 weeks of hemorrhage and 14 (40%) of these deaths took place within 5 days.

Univariate analysis showed that only the MELD score and the number of units of PRBCs needed during the first 24 hours were predictive of death. For every 1 point increase in the MELD score there was an 8% increase in the risk of death at 5 days and an 11% increase at 6 weeks.

In total, 37 patients (15%) experienced re-bleeding within 5 days. For every 1 point increase in the MELD score, there was a 5% increase in the risk of re-bleeding within 5 days. In addition, patients with a MELD score of 18 or more were at significantly greater risk than those with lower scores.

Dr. Kamath told Reuters Health that, because patients with a MELD score of more than 18 who require more than 4 units of red-cell transfusion are at greater risk for 6-week mortality, "these patients should preferably be treated at or referred promptly to centers that carry out liver transplantation."

In addition, because patients with a MELD score of greater than 18 have a higher risk of re-bleeding within days, he concluded, such patients with "active esophageal variceal bleeding should be hospitalized for at least 5 days."

*Gut* 2008;57:814-820.

## ***Liver Transplant Outcomes Similar in Obese and Nonobese Patients***

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

Louise Gagnon

June 3, 2008 (Toronto) — Morbidly obese patients should not be excluded as candidates for liver transplantation because outcomes with these patients are no worse than in nonobese patients undergoing liver transplantation, according to retrospective research presented here.

Speaking at the American Transplant Congress, the joint annual meeting of the American Society of Transplant Surgeons and the American Society of Transplantation, Federico Aucejo, MD, a staff transplant surgeon at the Cleveland Clinic in Ohio, indicated that there had been inconsistent data on the outcomes with obese and morbidly obese patients undergoing liver transplantation and that some transplant centers in the United States are choosing not to perform these procedures in these patients.

"Some centers are reluctant to transplant these patients because of some data showing higher complications following transplantation," Dr. Aucejo told Medscape Transplantation after presenting his team's data in an oral session.

### **Retrospective Study**

The investigators compared perioperative and clinical outcomes after orthotopic liver transplantation in 25 obese patients, defined as having a body mass index (BMI) of 38 kg/m<sup>2</sup> or more, and 50 nonobese subjects, defined as having a BMI of 26 kg/m<sup>2</sup> or less. The procedures had been performed between June 2005 and October 2007.

Dr. Aucejo noted that a BMI of 40 kg/m<sup>2</sup> is often used a criterion for morbid obesity, but investigators reduced the threshold to a BMI of 38 kg/m<sup>2</sup> to provide adequate power to the study.

Researchers matched the patients for various characteristics, such as age, race, sex, and donor height. There were no statistically significant differences in any patient characteristics for obese vs nonobese patients other than nonalcoholic steatohepatitis (42% vs 10%;  $P = .002$ ) and presence of type 2 diabetes mellitus (50% vs 20%;  $P = .01$ ).

They looked at various measurements including hospital length of stay, case duration, death or retransplant within 6 months, red blood cell count, days in the intensive care unit (ICU) on mechanical ventilation, length of stay in the ICU, and episodes of ICU infection. They found a statistically significant difference only in case duration between the nonobese patients and the obese patients: 526 min vs 631 min;  $P < .003$ . Median follow-up time was 23.1 months, with a range of 6 to 45 months.

"We start counting the minutes from the time the induction of anesthesia starts, which is before actual surgery," Dr. Aucejo told Medscape Transplantation. "It is harder to find intravenous access [in obese patients] than in patients that are not obese."

Employing statistical analysis (log rank tests), researchers found no statistically significant differences in either patient survival (0.93) or graft survival (0.44) for obese vs nonobese patients.

### **Significant Difference in BMI After Transplant**

However, there was a statistically significant difference ( $P = .001$ ) reported in BMI among obese patients 3 months after surgery. The results suggest that patients with a BMI that categorizes them as obese may in fact not have real obesity; those who experience substantive weight loss after transplantation may simply have substantial fluid retention, according to Dr. Aucejo.

"We wanted to show that a significant number of patients that might not be transplanted at some centers actually have a high BMI due to total fluid retention," Dr. Aucejo told Medscape Transplantation. "That fluid retention is due to kidney function. The pretransplant patients with cirrhosis sometimes have hepatorenal syndrome, where kidney function is not normal and they tend to retain fluid. Immediately after transplantation, both the kidney and the liver get better and they get rid of the excess fluid."

Dr. Aucejo said the data support that more centers in the United States consider liver transplantation in morbidly obese patients.

Adrian Reuben, MBBS, FRCP, FACP, professor of medicine and director of liver service in the Division of Gastroenterology and Hepatology at the Medical University of South Carolina in Charleston, said the investigators did not consider that obese patients might be ruled out as candidates for transplantation for other reasons, such as associated illnesses.

### **Comorbidities May Rule Out Transplant**

"There are a lot of patients who are excluded with that BMI [around 40 kg/m<sup>2</sup>] because of comorbidities that go along with morbid obesity, such as...diabetes, infections, and coronary artery disease," Dr. Reuben told Medscape Transplantation.

Dr. Reuben indicated that physicians should be taking fluid excess into account when screening patients for transplantation. "If the BMIs were artificially inflated because of fluid excess, you can make an estimate of what their BMI would be without the fluid," he said. "It's wrong to include fluid retention as part of their weight."

Dr. Reuben added the distribution of weight, and not the BMI alone, in morbidly obese patients is a factor to consider when deciding whether to perform liver transplantation, noting those patients with predominantly abdominal obesity would be regarded as higher risk for complications.

The study was independently conducted. Dr. Aucejo and Dr. Reuben have disclosed no relevant financial relationships.

*American Transplant Congress 2008: Abstract 309. Presented June 2, 2008.*

**June 12, 2008**

### ***Valeant says hepatitis C drug causes less anemia***

<http://biz.yahoo.com>

*Valeant says hepatitis C candidate could replace drug that can cause anemia*

DANA POINT, Calif. (AP) -- Valeant Pharmaceuticals International said Thursday that its mid-stage hepatitis C candidate **taribavirin** could replace a drug used in a common treatment regimen.

Ribavirin and peginterferon are considered the standard of care regimen for hepatitis C. Speaking

at the Goldman Sachs Global Healthcare Conference, Valeant Senior Vice President of Drug Development Harry Mansbach said that many patients, however, develop anemia upon taking ribavirin.

Mansbach said that because fewer cases of anemia have been associated with Valeant's taribavirin drug, it could be prescribed instead of ribavirin for hepatitis C patients at risk for anemia, such as those who also are HIV-positive.

Chief Executive J. Michael Pearson said, though, that the company won't move taribavirin into late-stage trials until a partner for the drug is found.

Vertex Pharmaceuticals Inc. and Schering-Plough Corp. also have hepatitis C drugs in mid-stage development. Both Vertex's telaprevir and Schering-Plough's boceprevir would be added to standard therapy.

Separately, Pearson said Valeant is eyeing an application for its late-stage epilepsy drug retigabine in the third quarter. He noted that following the release of positive late-stage data in May, partnership interest in the drug has accelerated.

Over the past six months, Valeant has been undergoing a strategic restructuring, which has included selling off some of its drugs, reducing staff and divesting some of its operations around the world.

On Tuesday, Valeant divested its Argentina commercial operations for an undisclosed sum. In January, it sold its hepatitis C drug Infigen to Three Rivers Pharmaceuticals LLC for about \$91.3 million.

Valeant shares rose 69 cents, or 4.3 percent, to \$16.66 in midday trading.

## ***Endoscopy Center of Southern Nevada: More Revelations***

<http://www.lawyersandsettlements.com>

By Gordon Gibb

Las Vegas, NV: As lawsuits continue to mount with respect to the Endoscopy Center of Southern Nevada and the Hepatitis C outbreak linked to the facility, new questions are surfacing as to just how much malpractice insurance Dr. Dipak Desai, the majority owner of the clinic, carried for the Center.

It has been reported that inquiries up to this point have revealed a mere \$3 million in coverage which, averaged out over the 40,000 patients of the Center thought to be at risk for Hepatitis C, would amount to \$75 per patient. True, it would be somewhat beyond the realm of possibility that all 40,000 patients with a link to the Center would sue for damages, especially those who test negative for the blood-borne virus. Still, there would be those so emotionally traumatized by the mere possibility that infection might have occurred, together with the estimated \$275 cost of the test, that a lawsuit would be considered.

One might conclude, therefore, that those litigants first out of the gate would stand the best

chance of realizing actual dollars at the end of the day, beyond any other assets the principles of the Endoscopy Center of Southern Nevada might have at their disposal, to liquidate for payment of debts, pending conviction.

The Endoscopy Center of Southern Nevada was implicated earlier this year in a Hepatitis C outbreak. Workers at the Center were accused of re-using syringes, and single-dose vials of anesthesia, together with other practices capable of spreading infection from unhealthy patients, to healthy individuals. The two principals of the Center, one of whom is Dr. Dipak Desai, were fined and the business license for the Center revoked by the State of Nevada.

Some have suggested that corners were cut at the Center in an effort to reduce costs. Thus it would come as no surprise to those same critics that Dr. Desai carried a mere \$3 million dollars worth of malpractice insurance on behalf of the Center—which might be sufficient, one would think, to cover damages sought by one, or a handful of patients. But not hundreds, or even thousands.

As the investigation continues into the alleged lapses in sound medical protocol and judgment, and other failings of the Endoscopy Center of Southern Nevada, other curious issues are coming to light.

For example, it has been learned that the insurance company, which provided coverage for the Endoscopy Center, is doctor-owned. What's more, it has been reported that Desai served on the Board of Directors of the company that provided coverage for his facility. That smacks of a conflict.

One legal official close to the issue has said that it proves interesting that Desai is on both sides of the controversy. On one hand, the facility that he controls is at the center of a major health-related investigation. And yet, as a sitting Board member of the entity providing insurance to his Center, Desai could quite possibly have a say in who gets paid, within the context of any pending settlement.

The company, Nevada Mutual Insurance Co., was named in a class-action lawsuit filed in March. The allegation is that Desai, as a Board member, was effectively regulating himself, as well as other defendants, in the Endoscopy Center case.

As more details emerge from the investigation, it will be interesting to see what comes out in the wash—and whether these latest revelations will serve to deter, or motivate victims, or potential victims of the Endoscopy Center, to get in the queue for damages, whatever they may be...

**June 13, 2008**

## ***Central Asia: World Bank Warns Of Tainted Blood Transfusions Across Region***

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

*Children were infected at hospitals in Kazakhstan and Kyrgyzstan*

In a new study, the World Bank has raised the alarm over tainted blood transfusions across

Central Asia, saying people face significant risk of contracting HIV, hepatitis, and other deadly diseases.

In the report, released to mark World Blood Donor Day on June 14, the World Bank says, "The health systems in Central Asian countries have an urgent need to improve their screening efforts in order to prevent the use of infected blood in transfusions."

Since 2006, hundreds of people, including many children, have been infected with HIV/AIDS through tainted blood transfusions in Central Asian hospitals. That includes 149 children in Kazakhstan (10 of whom have already died), 69 children in Kyrgyzstan, and several more in Tajikistan. Some 30 mothers in Kazakhstan and Kyrgyzstan were also infected with HIV/AIDS.

The World Bank-sponsored a study is titled "Blood Services in Central Asian Health Systems -- A Clear and Present Danger of Spreading HIV/AIDS and Other Infectious Diseases." The study, in which blood given by some 7,500 donors was retested, said such "retesting identified cases of HIV that had been undetected by the blood center laboratories that originally tested the samples."

The incidence of HIV/AIDS-infected blood was rather low. The study put it at 0.2 percent. But it said 2.7 percent of the samples tested positive for hepatitis B, 3 percent for hepatitis C, and 3.6 percent for syphilis.

Based on these results, the World Bank said Central Asia needs to "strengthen screening of blood donors on the occasion of each blood donation."

### **Dysfunctional Health-Care Systems**

In Kazakhstan, HIV-infected blood was discovered in 2006 after the outbreak of infections among children was made public. However, the record-keeping system had not accurately catalogued donors, making it difficult to track the sources of the tainted blood.

The children, all under the age of 5, received the blood when they were admitted to children's hospitals in the Shymkent area.

"In one of the children's hospitals there are 150 beds and only 13 catheter [tubes]. They are using these catheters without any disinfection," Yerbolat Dosaev, the Kazakh health minister at the time, told RFE/RL in September 2006.

"It is the responsibility of local officials, not mine," Dosaev said. "If it were [my hospital], I would have sacked the local administration as of July 20," when the first hospital officials were dismissed.

Dosaev was eventually dismissed along with several health-care officials, while some hospital workers and local officials were charged with criminal negligence. The Kazakh government -- and more importantly, President Nursultan Nazarbaev -- vowed there would be no repeat of the tragedy and ordered a complete overhaul of the blood-donor system.

There are now 14 health-care workers on trial in neighboring Kyrgyzstan for the infection of children in 2007.

Kyrgyzstan is trying to improve its blood-screening system after the accidental infections in hospitals in the Osh area. The head of the country's blood-donor center, Sagynbek Abazov, tells RFE/RL's Kyrgyz Service that the chances of receiving tainted blood are low, but they do still exist.

"During blood transfusions, there can be accidents," Abazov says. "There is a danger because the effectiveness of the [screening] system is estimated to be 99.9 percent. That means the danger [of infection] is about 0.1 percent."

But one of the local Kyrgyz health officials facing charges of negligence for the infection of children in Osh said during his trial last month that as many as 69 children and several of their mothers may have been infected from blood transfusions.

Figures for Turkmenistan and Uzbekistan are difficult to come by, so the situation with their blood-donor banks is not clear.

The World Bank notes that "until recently, little was known about blood-transfusion systems in Central Asia and their contribution to disease transmission." With more data now emerging, the hope is that Central Asian patients will eventually be able to concentrate on getting better -- and not have to worry about the tainted transfusions.

*Tynchtykbek Tchoroev, Eleonora Mambetshakirova, and Torokul Doorov of RFE/RL's Kyrgyz Service and Merhat Sharipzhan of RFE/RL's Kazakh Service contributed to this report*

## ***Father died from cancer, not from taking the wrong drug***

<http://icwales.icnetwork.co.uk>

Our Correspondent, *Western Mail*

A FATHER-of-three suffering from terminal liver cancer died from natural causes, despite being prescribed the wrong drug.

An inquest yesterday heard that plasterer Alan Clark from Prestatyn was mistakenly given the antidepressant drug Sertraline by a pharmacist last September instead of Spironolactone, which is used to treat water retention.

The 59-year-old took the wrong drug for 22 days before he fell ill, the inquest heard.

He was admitted to Ysbyty Glan Clwyd in October 2007 with shortness of breath, and swelling in his stomach and legs. He died in the hospital 12 days later.

During the initial post-mortem examination, pathologist Andrew Dalton discovered that Mr Clark was suffering end-stage liver sclerosis, which had been complicated by liver cancer.

His examinations suggested that he had died after suffering liver failure.

But when the coroner was informed about the prescription error a second post-mortem examination, which was carried out by Home Office pathologist Bryan Rogers, was ordered.

A series of toxicology tests was carried out, which revealed that the amount of the drug Sertraline in Mr Clark's blood was at a low level.

Dr Rogers told the inquest yesterday: "This test was taken 10 days after the last dose of Sertraline. The level would have been higher but unlikely it would have been toxic. You never get fatal toxic levels from the build up of Sertraline."

He added: "It could be argued that he could have been affected by not taking the other drug, but I do not believe this had a great bearing because of the stage of liver disease. He was in the terminal stages of liver disease. He was fortunate that he died rather than linger with advanced cancer."

Dr Rogers said that he believed Mr Clark had developed sclerosis of the liver as a result of contracting Hepatitis C – not from alcohol abuse.

When asked by North-East Wales coroner John Hughes if the mistake in prescribing had played a part in Mr Clark's death, Dr Rogers replied "No".

Sertraline belongs to the class of anti-depressant drugs known as selective serotonin re-uptake inhibitors and is used in the treatment of depression, obsessive- compulsive disorder – an urge to continually repeat the same action – and post-traumatic stress disorder in women.

It works by helping to regulate the levels of serotonin in the body – low levels of the chemical are thought to cause depression and other conditions.

Spironolactone belongs to the group of medicines known as diuretics, which are also known as water tablets.

The medicine is known as a potassium-sparing diuretic because, unlike some other diuretics, it does not cause the body to lose potassium.

It is used to treat oedema – water retention – which is often caused by liver disease, kidney problems or heart failure.

Spironolactone prevents the build up of fluid by increasing the amount of urine produced by the kidneys.

Mr Hughes said: "He was effectively a dying man. If it is any consolation he died quickly and cleanly rather than the appalling way he may have died."

He recorded a verdict of death by natural causes.