

# The Future Burden of HCV: Part 3



Alan Franciscus, Editor-in-Chief

In the previous two articles about the future disease burden of hepatitis C I wrote about the projected costs and deaths that will be attributed to hepatitis C. The third and final installment in this series is a review of a recent study that analyzes the costs for HCV-related hospitalizations, hospital days, charges and physician visits from 1992 to 2001 and validates the future HCV disease burden projections reported in previous studies.

“Trends in Health Care Resource Use for Hepatitis C Infection in the United States,” by W.C. Grant and colleagues (2005), analyzed inpatient data from Healthcare Cost and Utilization Project (HCUP), outpatient data from the National Ambulatory Medical Care Survey (NAMCS), and drug data from the Verispan Source Prescription Audit (VSPA).

The authors examined the recent growth in the use of health care resources among hepatitis C patients by age for increased hospitalizations, outpatient, and prescription data over an 8 year period (1994 -2001).

## HOSPITAL TRENDS

The criteria for hospital trends identified as liver-related hos-

pitalizations using HCUP data included:

- The principal diagnosis was HCV- or alcohol-related liver disease
- Any diagnosis of cirrhosis, portal hypertension, any consequence (sequelae) of liver disease, hepatitis encephalopathy (brain disease), ascites (accumulation of fluid in the abdominal area), hepatorenal syndrome (kidney failure with liver disease), hepatocellular carcinoma (liver cancer), or combined hepatocellular carcinoma and cholangiocarcinoma (bile duct tumors) or,
- The patient underwent liver transplantation.

*Note: It was assumed that there was an underreporting or miscoding of hepatitis C so some of the above criteria were used, but the data was adjusted and verified using the Kim et al. criteria.*

## OUTPATIENT TRENDS

The criteria for HCV outpatient trends included any office visit related to the three diagnostic criteria listed above using NAMCS data from 1996-2002.



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## DRUG OR PRESCRIPTION TRENDS

Total spending on prescriptions for interferon plus ribavirin therapy from 1998 – 2000 was taken from the Verispan Source Prescription Audit, which provides total national prescription payments collected from more than 35,000 retail pharmacies in the United States. The prescription information only lists the drug name and not what the prescription was prescribed to treat. Only prescription costs for interferon plus ribavirin combination therapy were used in this analysis. Interferon plus ribavirin therapy is only used to treat hepatitis C, whereas interferon monotherapy is used to treat a variety of other illnesses. So theoretically, the prescription costs in this review could be lower than the actual costs incurred.

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## BURDEN

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### RESULTS

Hospitalizations (hospital days, total charges, and deaths) increased at average annual rates exceeding 20%. It was found that the highest percentage increases occurred in the patients in their 40s and 50 who spent more time in the hospital, incurred greater costs, and died more frequently than patients in other age groups. In the period from 1994 to 2001, the share of HCV patient liver-related hospital days increased:

- Aged 40 to 49 from 32.3% to 37.6%.
- Aged 50 to 59 from 17% to 30.1%

When compared to hospital stays for any reason, HCV liver causes for all age groups accounted for almost 4 times as many hospital days in 2001 as in 1994 (371 vs. 98 per 100,000). In 2001 HCV-related hospitalizations resulted in \$427 for every \$100,000 in nationwide charges for all hospitalizations – up from \$145 in 1994. The large majority of the increase was attributed to patients in the 40s and 50s age group.

In a subgroup analysis of patients with HIV and HCV coinfection, it was found that there were nearly 3 times as many HIV patients hospitalized for liver-related reasons in 2001 than in 1994. In addition coinfecting patients comprised 44.9% of HIV liver-related hospitalizations in 2001, up from 9.1% in 1994.

Relative to all HIV hospitalizations and charges, people with HIV and hepatitis C represented 7.5 times as many hospitaliza-

tions and incurred 2.9 times the charges in 2001 than in 1994. The burden of HIV still remains larger than that of HCV – from the period 1994 to 2001 HIV hospitalizations occurred at 3.4 times the number of HCV liver-related hospitalizations. Total inpatient charges for HIV hospitalizations were 2.9 times higher than for HCV liver-related hospitalizations.

### PHYSICIAN VISITS

The number of office visits also increased by an average annual rate of 36% according to 9 year data from NAMCS. In the period between 1996 and 2002, the 3-year moving average increased by about 1 million annual office visits, from 449,800 in 1996 to 1.49 million in 2002. The largest increase was in the age group 40-59.

### PRESCRIPTION DRUGS

According to the VSPA data \$352.5 million was spent on 372,000 prescriptions of combination interferon plus ribavirin therapy between 1998 and 2001. For every \$100,000 spent in new prescriptions, spending for combination therapy rose from \$78 in 1998 to \$259 in 2000.

Data from this study confirms that the future disease burden will likely match or even exceed the projections made by the studies in part 1 and part 2 of this series. In previous studies the number of people who will progress to severe liver disease is estimated to at least quadruple from 1990 to 2015. The authors in this study found a 3-fold to 4-fold increase from 1994-2001 and stated that “[b]y 2015, longstanding infections may lead to even greater numbers of complications than have been pre-

dicted.”


The authors concluded by stating that “[a]cross the United States, Health care providers are using tremendous amounts of resources for HCV care.”

We hope that this series of articles has clearly shown that the effects of the hepatitis C disease burden is escalating and that the projected future disease burden and the associated costs and deaths will continue to grow as projected. What is worrisome is the possibility that the increase may come a lot sooner than expected.

### Reference

“Trends in Health Care Resource Use for Hepatitis C Infection in the United States,” by W.C. Grant and colleagues. *Hepatology* 2005; vol 42 no 6:1406-1413





**Chronic Hepatitis C in the Hispanic Population**

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# HealthWise:

## *April Fool: A Smart Way to Live*



Lucinda K. Porter, RN

When I was a child, I loved April Fool's Day. I schemed for weeks, hoping to trap my parents in one of my pranks. Of course, they were way ahead of me and by day's end, I was always the April fool. Fortunately, I enjoyed being the brunt of a good joke.

The average child laughs around 400 times every day. Contrast this with the average adult who laughs approximately 25 times a day. This fact makes me want to either cry, read Dave Barry or watch Carol Burnett reruns. For me, laughter is the backbone of physical, emotional and spiritual health. Humor is the thread that keeps me from unraveling. I find ways to inject appropriate humor into nearly everything.

The potential health benefits of laughter are well-researched. This is my 9<sup>th</sup> April Fool's column and I would rather provide a few laughs than the data promoting it. If we need data to tell us to laugh more, we are in deep trouble. However, for you die-hard data devourers, at the end of this column there are some web addresses so you may dig for details.

For those of you who appreciate laughter, you may be delighted to learn that there is a practice called Laughter Yoga. Originating in India, Laughter Yoga is the practice of laughing as a discipline rather than merely for pleasure. Dr. Madan and Madhuri Kataria developed Laughter Yoga about ten years ago and now there are laughter clubs worldwide. Training is available for anyone interested in becoming a certified Laughter Yoga instructor.

The Laughter Yoga website takes laughter very seriously. So much so, that the following warning is given: "*Too much of a good thing can become a bad thing. You cannot laugh too little, but you can laugh too much and put your body into distress* (sic)." I assume that this is a typo or translation error and the author meant *distress* rather than *destress*. Heck, to de-stress is the main reason why I laugh. Also, I have a hard time believing the statement that one can laugh too much.

The Laughter Yoga caution goes on to say that too much laughter can actually be dangerous, especially for older people (geezers like me). Well, this may seem closed-minded, but I cannot imagine getting through the geezer years without laughing a lot. Between the loss of eyesight, hearing, brain, keys, stamina, waistline, and sex, I am hanging onto laughter as if it is a life preserver. Besides, death by laughter sounds like a great way to go.

I think that humor helps me cope with all of life's challenges, particularly hepatitis C (HCV). HCV was not a laughing matter when I was first diagnosed, but over time, it has provided some amusing moments. This is particularly true when I am in an HCV group with others who live with this virus. Laughing with others is a communal act. It is like sharing an intimate moment or a fine meal. Laughter lifts the spirits and for a brief time suspends the hard edge of reality. It reminds us that we are all in the same boat.

I end with a joke. If you think it is funny, pass it along. Telling jokes is as much fun as hearing them. Q: What was written on the hypochondriac's gravestone? A. "See, I told you I was sick."

### Resources

- <http://science.howstuffworks.com/laughter6.htm>
- [www.helpguide.org/life/humor\\_laughter\\_health.htm](http://www.helpguide.org/life/humor_laughter_health.htm)
- [www.laughteryoga.org](http://www.laughteryoga.org)

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# Stress and the Liver



Alan Franciscus, Editor-in-Chief

It is an established fact that stress can have a negative impact on both mind and body. People with hepatitis C often comment that a period of stress usually leads to a ‘flare-up’ of symptoms, especially fatigue. Surprisingly, there is a wealth of information about how stress can affect liver disease. This article will cover some of the data from a recent review article titled “Does Stress Exacerbate Liver Disease?,” by Y. Chida and colleagues, and sheds some light on the effects of stress on liver disease and raises some interesting questions.

In the review article, previously known or hypothetical reasons for the effect of stress on liver disease were discussed, including:

- ‘Fear’ and ‘anxiety’ induced by hypnotic suggestion significantly decreased hepatic (liver) blood flow (Hirose et al.)
- In people with chronic hepatitis B, a significant positive correlation between the degree of depression and alanine aminotransferase or ALT levels was established (Fukudo et al.)
- In people with chronic hepatitis

C, type I personality scales (Grossarth-Maticek) have been associated with severity of liver disease even after adjusting for age, sex, education level, smoking, drinking, and duration of illness (Nagano et al.)

- Patients who had personality traits of ‘submissive,’ ‘relatively controlled,’ and ‘of indifferent mood’ before liver transplantation were more likely to have acute transplant rejection (Hildebrandt et al.)

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# HCV Sexual Transmission Revisited: A Look at the Latest Research



Liz Highleyman

Sexual activity has traditionally been regarded as a rare route of hepatitis C virus (HCV) transmission. In the past few years, however, clusters of apparently sexually transmitted HCV – mostly among HIV positive gay men – have cast doubt on this assumption.

## TRANSMISSION AMONG MONOGAMOUS COUPLES

Most studies indicate that sexual transmission of HCV is very uncommon among long-term, monogamous, HIV negative heterosexual couples, with rates in the range of 0%-3%. As reported in the May 2004 *American Journal of Gastroenterology*, for example, Carmen Vandelli and colleagues followed 895 HCV negative individuals who had monogamous sexual relationships with HCV positive partners. Over 10 years of follow-up, just three new HCV infections occurred, for an incidence rate of 0.37 per 1,000 person-years (PY). The authors concluded that “the risk of sexual transmission of HCV within heterosexual monogamous couples is extremely low or even null.” Likewise, V. Tahan and colleagues reported in the April 2005 *American Journal of Gastroenterology* that none of 216 HCV negative individuals with opposite-sex HCV positive spouses seroconverted during an average follow-up period of about three years.

## TRANSMISSION AMONG HIV POSITIVE GAY MEN

But the picture is different for HIV positive individuals. At the 13<sup>th</sup> Conference on Retroviruses and Opportunistic Infections (CROI) this past February, two research teams presented the latest data on clusters of acute hepatitis among gay men in England and the Netherlands, while a French team reported on apparent sexually transmitted HCV in heterosexual women.

Since 2002, more than 200 cases of acute hepatitis C have been reported among men who have sex with men (MSM) in London and Brighton in the UK. Mark Danta from London’s Royal Free Hospital gave an update on a cohort of 111 HIV positive men diagnosed with HCV between October 2002 and August 2005 (CROI abstract 86). The men who contracted HCV had three times more sex partners (30 vs 10) in the past year than men who remained HCV negative. Other significant risk factors included unprotected receptive and insertive anal intercourse, fisting, use of sex toys, group sex, and sexual activity under the influence of recreational drugs (92% vs 62%). What’s more, these factors appeared to interact: individuals who engaged in three or four of these practices in group sex settings had 23 times the risk of HCV infection. In addition, the men who contracted HCV

were more likely to meet partners in sex clubs or bathhouses or over the Internet, and most (92%) had concurrent sexually transmitted diseases (STDs). “High-risk and mucosally traumatic sexual factors are significantly associated with the recent transmission of HCV,” Danta concluded.

Roel Coutinho and Thijs van de Laar reported on a retrospective study of sexual transmission of HCV among 1,836 HIV positive and HIV negative gay men in the Amsterdam Cohort Study (CROI abstract 87). A total of 29 cases of acute HCV have been detected in Amsterdam since 2000, all but one in HIV positive men. The post-2000 HCV incidence rate among men with HIV was 0.87 per 100 PY – a 10-fold increase over the pre-2000 rate. The largest cluster of cases had HCV genotype 4, which is uncommon in Europe. Like Danta, the Dutch researchers found that among the 20 men interviewed about sex and drug use, HCV infection was associated with fisting (practiced by 50%) and STDs that cause genital ulcers (e.g., syphilis, genital herpes simplex, lymphogranuloma venereum) (reported by 65%). The researchers concluded that “HIV infection and/or mucosal trauma caused by extreme sexual techniques and concurrent STD might facilitate sexual transmission of HCV.”

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## SEX

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### EVIDENCE FROM NORTH AMERICA

Clusters of apparently sexually transmitted HCV among MSM have also been seen in France, but, interestingly, not in North America. In the March 2005 *American Journal of Public Health*, M. Alary and colleagues reported that in a cohort of 1,085 MSM in Montreal, only one new HCV infection was detected during eight months of follow-up (in a man who shared needles), despite the fact that 63% reported unprotected anal sex. After controlling for injection drug use, the researchers concluded that sexual behavior was not significantly linked to HCV infection (although this was not an HIV positive cohort). In the U.S., Sriganayatri Bollepalli and colleagues found that injection drug use was the only risk factor significantly associated with HCV infection among HIV positive MSM in Arizona, concluding that “[s]exual transmission of HCV among HIV [positive] patients is extremely rare” (56<sup>th</sup> AASLD, 2005; abstract 65573).

But such cases aren’t unknown. In the January 1, 2006 *Journal of AIDS*, Annie Luetkemeyer and colleagues reported on a series of nine cases of acute HCV infection in HIV positive men seen at the University of California in San Francisco. Sex with men was the only risk factor reported by six of these individuals, while two reported unprotected sex with women, and three had concurrent STDs. The authors suggested that “MSM sexual activity as well as sexually transmitted infections may play an important

role in HCV transmission in HIV-infected patients.”

### WHAT ABOUT WOMEN WITH HIV?

A new development at this year’s Retrovirus conference was a report of acute HCV infections in HIV positive heterosexual women. J. Ghosn and colleagues analyzed data from 402 patients recently infected with HIV in the French PRIMO Cohort (abstract 843). They detected acute hepatitis C in two women and three men, for an incidence rate of 3.56 per 1000 PY (7.81 per 1000 PY for the women; 2.61 per 1000 PY for the men). As in Amsterdam, the incidence of acute hepatitis C increased in the early 2000s, from 1.81 per 1000 PY before January 2002 to 4.69 per 1000 PY after that date (all but one of the five new HCV infections were detected since 2002). Because none of the five reported “classical risk factors,” such as injection drug use or blood transfusions, the researchers concluded that “[t]he only identified risk factor for HCV acquisition was unsafe sex,” and suggested that “women are also at risk of acquiring HCV via the sexual route.”

Ghosn’s results conflict with a study from the U.S. Women’s Interagency HIV Study (WIHS), reported in the November 15, 2003 issue of *Clinical Infectious Diseases*, showing no evidence of sexual HCV transmission in this cohort of 2,059 HIV positive and 569 HIV negative women. On the other hand, as reported in the May 1, 2003 *Journal of Infectious Diseases*, data from the HIV Epidemiology Research Study (HERS), looking at 871 HIV positive and 439 HIV negative women, suggested that 10.5% of the

women coinfecting with HCV had sex as their only risk factor (some also had genital herpes simplex).

### BETTER SAFE THAN SORRY

Two other recent studies indicate that sexual HCV transmission is biologically plausible, since HCV is present in semen and female genital fluid. As reported in the November 4, 2005 issue of *AIDS*, Aureliea Briat and colleagues from Paris analyzed HCV RNA levels in the semen of 82 HIV/HCV coinfecting and 38 HCV mono-infected men. They detected HCV genetic material more often in the seminal fluid of coinfecting men than men with HCV alone (38% vs 18%). Similarly, as reported in the November 1, 2005 *Journal of Infectious Diseases*, M.J. Nowicki and colleagues measured HCV RNA levels in the cervicovaginal lavage fluid from 58 HIV/HCV coinfecting and 13 HCV mono-infected women enrolled in WIHS. HCV RNA was detected in the genital fluid of 29% of the coinfecting women, but none of the HCV mono-infected women.

While studies have yielded conflicting data, there is increasing evidence that sexual transmission of HCV may be more common than previously thought – and that it appears to be occurring more frequently in recent years. Until more is known, it is prudent for people with any of the risk factors seen in these studies (e.g., HIV positive, multiple sexual partners, fisting, STDs) to practice safer sex, including the use of latex condoms and gloves.



## STRESS

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- Research on healthy animal (rodent) models found that restraint and electric foot-shock stress triggered slightly elevated ALT levels (Fernandez et al, Chida et al.)

The authors went on to describe the possible links between stress and liver disease which may influence liver injury:

- The release of glucocorticoids (cortisol in humans, corticosterone in rodents) controls the homeostasis (steady or healthy state) of each organ. In corticosterone pretreated mice, it was found that “a remarkable exacerbation of liver injury” occurred.

- During stress natural killer cells (NKT) are expanded in the liver and, in some of these cases, contributed to liver cell death and worsening of liver disease.

- In the part of the brain that controls the liver, stress was found to impair blood flow and may lead to or trigger liver damage

- Stress can exert a dual effect (enhancement or reduction) of the inflammatory process that takes place in the liver

- A certain nerve (vagus) from the brain to the liver when stimulated with anti-stress therapy (hypnosis, meditation, acupuncture) may actually improve or reduce the negative effect of stress on the liver

The authors concluded that even though all of the interactions between stress and the liver are not completely understood there appears to be a negative impact of stress on liver disease progression. The authors noted that the link between liver disease and stress needs to be identified so that “physicians and other healthcare


practitioners would be better able to treat liver disease by helping their patients learn coping and relaxation skills.”

This is another important piece of information for people living with hepatitis C to know in order to help keep the mind, body and liver healthy. Of interest, the emotion that is attached to the liver in Traditional Chinese Medicine is anger. Stress, depression and anger can go hand in hand. There are many strategies that can help with dealing with stress, such as meditation, yoga, prayer and acupuncture, to name a few. Hepatitis C support groups can also help by talking about the complex issues of dealing with a chronic illness such as hepatitis C. The bottom line is that learning to control stress should be a high priority for anyone living with hepatitis C.

### Reference

“Does Stress Exacerbate Liver Disease?,” Yoichi Chida, Nobuyuki Sudo and Chiharu Kubo. *Journal of Gastroenterology and Hepatology* 20 (2006) 202-208





**Hepatitis C in  
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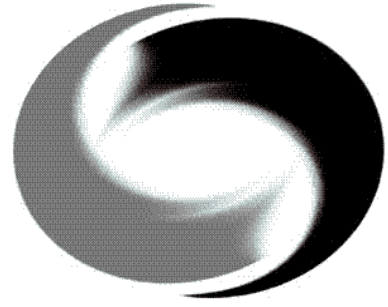
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