

April
2003

Volume 6
Issue 4

HCV Advocate

A monthly newsletter of the Hepatitis C Support Project
www.hcvadvocate.org

HCV Reports from the Retrovirus Conference

Liz Highleyman
Contributing Editor

The 10th Conference on Retroviruses and Opportunistic Infections took place February 10-14 in Boston. Although this conference primarily focuses on HIV, there were several presentations related to viral hepatitis, reflecting the growing importance of HCV and HBV coinfection in people with HIV. But the major hepatitis-related news this year concerned the hepatitis G virus (now more often called GBV-C), which appears to slow HIV disease progression. (See GBV-C article on page 8 of this month's issue.)

HIV/HCV Coinfection

HIV/HCV coinfection continues to draw increasing attention as the magnitude of the "twin epidemics" becomes ever more apparent. HCV-related liver failure is now one of the major causes of death among people with HIV (abstract 827).

Dr. Mark Sulkowski of Johns Hopkins and colleagues presented final results of a multi-site trial showing that daily standard interferon plus ribavirin is more effective than thrice-weekly standard interferon in coinfecting patients (abstract 841). Using an intent-to-treat analysis, sustained virological response (SVR) rates were 9% for daily administration and 4% for thrice-weekly administration. These numbers are far from promising, but many experts feel that standard interferon is already obsolete: the new standard of care—pegylated interferon plus ribavirin—can produce response rates of 50-60% in people with HCV alone and about 44% in HIV/HCV-coinfecting patients.

Past research indicates that few people who do not show a substantial HCV viral load reduction at week 12 (so-called early virological response, or EVR) rarely go on

to achieve a sustained virological response. Spanish researchers at the retrovirus conference reported results from 89 HIV/HCV-coinfecting patients receiving either standard or pegylated interferon plus ribavirin (abstract 842). Of these, 29 had a sustained virological response, 15 initially responded but then relapsed, and 45 were non-responders. No patients who did not achieve at least a 2-log drop in viral load by week 12 had a sustained virological response. Given the difficult side effects of interferon therapy, many doctors recommend that people stop treatment after 12 weeks if little response is seen. This study appears to confirm that the 12-week cutoff applies for coinfecting people as well as those with HCV alone. However, some studies indicate—and the researchers acknowledge—that HIV/HCV-coinfecting people may take longer to respond to interferon therapy, and therefore should perhaps stay on treatment longer before concluding that it is not working.

HIV/HBV Coinfection

Two research teams reported on the presence of "occult" (hidden) HBV infection in people with HIV (abstracts 820 and 821). In one study, out of 240 participants randomly selected from nationwide ACTG HIV treatment studies, 156 (65%) showed evidence of either past HBV exposure or current HBV

See Retrovirus Conference on page 9

In This Issue:

Diet and Hepatitis C.....page 2
Alcohol and HCV.....page 3
Sexual Activity.....page 5

Diet and Hepatitis C

Alan Franciscus

Editor-in-Chief, HCV Advocate

Hepatitis C (HCV) is a virus that infects the liver. The data has shown that between 55% and 85% of people exposed to the hepatitis C virus will develop chronic liver disease. In general, chronic HCV appears to be a slowly progressive disease that may gradually advance over 10-40 years and varies considerably from one chronically infected individual to another. Although it is not totally understood, many factors influence the rate of disease progression. Diet may play an important role in this process, since all food and drink that we ingest must pass through the liver to be metabolized. The Centers for Disease Control guidelines for individuals infected with hepatitis C include maintaining a healthy lifestyle, eating a well-balanced, low-fat diet, and avoiding alcohol. Eating a healthy diet can help your immune system fight HCV as well as keep your energy level up to help fight off fatigue. A diet high in complex carbohydrates may be helpful in providing calories and maintaining weight. Since hepatitis C infection may lead to loss of appetite, those individuals whose appetite is lessened may find frequent, small meals much easier to tolerate. Adequate rest and moderate exercise can also contribute to a feeling of well being and really help overcome feelings of “lowness” and depression which are frequently experienced in people with HCV.

The right diet for those with hepatitis C is very important as it will help to maintain normal weight and provide the nutrients that the body needs to keep the immune system operating at its maximum capacity. When talking about the importance of diet and hepatitis C it is important to remember what functions the liver actually has. The liver stores vitamins, iron and other minerals that the body needs. The liver makes new proteins needed for all bodily functions. The liver makes bile to aid in the digestion of food. The liver rids the body of the toxins that we take in including alcohol, drugs, smoke, exhaust fumes, etc. Additionally, the liver stores energy in the form of complex sugars, makes clotting factors to help stop the bleeding from injuries, and helps the body fight off bacterial and viral infections.

Alcohol can lead to serious liver damage in people with hepatitis. Alcohol is a direct toxin (*poison*) to your liver. Excessive intake can lead to cirrhosis and its complications, including liver cancer. It prevents your body from

absorbing certain vitamins that it needs to work properly. Alcohol can also make your hepatitis C medicines less effective. Heavy drinkers are not the only individuals at risk for liver diseases, as damage can occur in even some moderate “social drinkers.” HCV has commonly been isolated from patients with alcoholic liver disease. In fact, these patients have been found to have a higher occurrence of severe liver damage, cirrhosis, and a decreased lifespan, when compared to individuals without the virus. It is suggested that the combination of alcohol and HCV accelerates the progression of liver disease. Therefore, patients with HCV would be unwise to drink alcohol in excess, and total avoidance of all alcohol is often recommended.

What are some recommendations regarding fat and hepatitis C? In general, fats are neutral lipids (triglycerides), acidic lipids (fatty acids), and sterols (cholesterol, plant sterols). Triglycerides (dairy products, meats, oils, butter, and margarine) are the most common type of dietary fat and represent a major source of energy. The liver is uniquely proficient in regulating and processing triglycerides. Dietary triglyceride is digested in the intestine by lipase, an enzyme secreted by the pancreas in response to meals. Bile, which is a clear yellow to golden-brown substance containing water, electrolytes (salts), cholesterol, bile salts (detergents), phospholipids, and proteins, is secreted by the liver to aid in the digestion of fat as well as promote its absorption. Absorbed fat is then repackaged and transported into the blood, where the liver ultimately removes it from the circulation. Fat that reaches the liver is processed in three ways: (1) stored as fat droplets in liver cells, (2) metabolized as a source of energy, and (3) repackaged, secreted back into blood, and delivered to other cells in the body. Ultimately, all fats and oils find their way to the liver where they are sorted and processed. Because of the alteration in bile production in liver disease and its necessity for the metabolism of fats, patients with chronic hepatitis C should monitor their fat intake. Both the types and quantities of fats in our diets need to be considered when the liver is compromised in any way. The most important issue with regards to type has to do with “trans-fatty acids” which are produced by “hydrogenation” and are found in large amounts in altered vegetable oils; oils like margarine and vegetable shortenings. High levels of trans-fatty acids found in our modern diets are unnatural and very difficult for even a healthy liver to metabolize.

Alcohol and HCV: A Dangerous Brew

Ian Campsall, MA

Until recently, medical science understood the relationship between alcohol and cirrhosis of the liver to be so direct that alcohol was considered to be the central, if not the only factor in the progression of liver disease. However, in 1967 the discovery of the hepatitis B virus (HBV) contradicted this belief and led medical science to reconsider the role of alcohol in cirrhosis of the liver. When hepatitis C (HCV) was discovered in 1989, all patients with idiopathic liver cirrhosis were reevaluated, and the presence of HCV in the majority of such cases was revealed.

In fact, in the fourteen years since the identification of HCV the number of persons worldwide diagnosed with cirrhosis due purely to alcoholism has decreased significantly. In Italy the liver cirrhosis of 51% of patients was thought to be purely the result of alcoholism in 1982. By 1991 that figure had dropped to 22%, and by 1997 it had fallen to 8%, while in the USA the number of alcoholics diagnosed as being HCV positive increased from 18% in 1993 to 35% in 1996, and in Japan from 65% in 1991 to 84% in 1996. This dramatic shift represents a complete reversal in medical science's understanding of liver disease.

Subsequently, many scientific studies have been conducted in order to clarify the true role of alcohol in cirrhosis of the liver, and to develop effective treatment strategies. However, most studies have focused on the progression of liver disease in chronic alcoholics, or people who drink 50g of alcohol per day or more. Many patients who are not alcoholics stop drinking when they are diagnosed with HCV, and then request information about what constitutes a safe daily intake of alcohol. Unfortunately, while it has been proven that more than 50g of alcohol per day increases the rate of progression of fibrosis by as much as 34%, no safe level below 50g has been established.

Chronic alcoholism in combination with HCV is a significant factor in the progression of chronic liver disease. More than ten studies conducted in the United States, Japan, Italy, and Great Britain have shown that alcohol aggravates HCV by escalating the rate of fibrosis progression and cirrhosis, pre-disposing the development of liver cancer, and enhancing fibrogenesis through stimulation of stellate cells by hypoxia (inadequate oxygen supply). Moreover, it generates lipid peroxides from damaged hepatocytes, alters cytokin-endotoxin and reactive oxygen species (ROS) patterns, and produces acetaldehyde, which has a direct fibrogenic effect on the liver.

Alcohol is metabolized by the liver. When the liver metabolizes large quantities of alcohol over a period of time the cells of the liver become damaged. This causes problems, including an enlarged and fatty liver, cirrhosis, and, potentially, liver failure. The degree of damage correlates to the quantity and duration of alcohol consumption. Eventually the liver may have difficulty producing materials that the body needs to be healthy, such as blood clotting factors, and this makes an individual more susceptible to infections and diseases.

Furthermore, alcohol interferes with the antiviral processes of interferon-based therapy, which operates both as an antiviral agent, and as an immune modulator (enhancer). It is known that alcohol blunts immune response, but its effect on interferon therapy is not fully understood. Recent studies in Japan, Italy, and the United States have shown that a sustained period of abstinence from alcohol for a period of three or more months before commencing interferon therapy significantly improves the patient's response to therapy.

However, most studies designed to measure the effectiveness of interferon treatment have excluded people with a recent history of alcoholism, and, as part of their controls, have required all of the participants to give up alcohol for a period of one to two years before the beginning of the study. Furthermore, the studies that have been conducted to examine the results of drinking alcohol while undergoing treatment have concentrated solely on alcoholics.

As a result, a significant portion of the hepatitis C community has found itself without solid data as to how much liquor they can safely consume without risking unnecessary liver damage, or potentially impeding interferon treatment. Unfortunately, most studies have concentrated on extreme levels of alcohol consumption, and have placed little emphasis on an intake of one to two drinks per day—less than 20g/day. The two studies that did analyze lower amounts of alcohol intake—less than 30g/day—found that, while a lower level of alcohol intake increased the rate of development of fibrosis in hepatitis C, it was not statistically significant.

Patients without a history of alcoholism should consider that being over 40 and being male are the two major independent risk factors other than alcohol that are associated with an increased progression of liver cirrhosis.

HealthWise: April Fool

Lucinda K. Porter, RN, BA, CCRC

It is April and time for the annual April Fool's column. This year I attempt to make light of some aspects of treatment for chronic hepatitis C virus (HCV) infection. Many of us have heard about the side effects of interferon and ribavirin. This month I hope to inject a little humor into the process.

HealthWise

Tips for managing HCV treatment:

- 1) Do not attempt more than one task at a time. For instance, do not drive while talking on a mobile phone, walk and chew gum, or carry on a conversation while dicing vegetables.
- 2) Practice saying, "I meant to do that." This offsets embarrassment when performing mindless acts, such as getting into a strange car in a parking lot.
- 3) Avoid reality T.V. and the news. Some patients report feeling irritable during treatment. The news and prime time television can be especially irritating. Confine television to classic comedy shows, such as Bill Cosby, Lucille Ball, Mary Tyler Moore, and Dick Van Dyke.
- 4) Do not store tubes of ointments in the vicinity of toothpaste. It only takes a minor lapse in concentration before you might find yourself brushing your teeth with anti-itch ointment. Additionally, toothpaste does not relieve skin rash.
- 5) If you drink the recommended amount of water, always know where the closest restroom is at all times.

6) Establish priorities. If beauty is more important than treatment, then interferon and ribavirin may not be for you. Dry skin, injection site redness, and a little hair loss are not very attractive. However, neither is liver disease.

7) Do not expect to lose weight while on treatment. Combination treatment with interferon and ribavirin is not a reliable diet plan. For those who want to lose weight, if you are lucky enough to shed some pounds, it will very likely return quickly when you are celebrating your completion of therapy.

8) Do not plan on using your accumulated sick leave for catching up on your television shows. Many patients report that the new pegylated interferons are easier to tolerate. Some patients never miss a day of work.

9) When all else fails, laugh.

10) Do not publish anything while receiving treatment for chronic hepatitis C. Inevitably, someone will take you seriously or worse, not think you are very funny. Now that can be irritating.

Copyright, April 2003 Lucinda Porter, RN, and Hepatitis C Support Project / HCV Advocate www.hcvadvocate.org – All Rights Reserved.

Lucinda K. Porter, RN is a research nurse and patient educator at Stanford in the area of hepatology. She co-facilitates a support group and is active in many aspects of hepatitis C education. In addition to being HCV positive, she has a life which includes her husband and daughter.

HCV Advocate

Alan Franciscus.....Founder/Editor-in-Chief
e-mail: sfhepcat@msn.com
C.D. Mazoff, PhD...Webmaster/Managing Editor
e-mail: cdmazoff@hcvadvocate.org
Liz Highleyman.....Contributing Editor

Back To Life A group dedicated to providing patient education and support.
Orange County.....Carol Craig 949-654-4250

You may contact us at:

P.O. Box 427037
San Francisco, CA 94142-7037

The HCV Advocate offers information about various forms of intervention in order to serve our community. By providing information about any form of medication, treatment, therapy or diet we are neither promoting nor recommending use, but simply offering information in the belief that the best decision is an educated one.

Permission to reprint is granted and encouraged with credit to the Hepatitis C Support Project.

Hepatitis C Support Project - A Tides Center Project

Sexual Activity as a Risk Factor for HCV

Alan Franciscus
Editor-in-Chief, HCV Advocate

Percutaneous exposures, such as injection drug use or a blood transfusion prior to effective screening are well-documented risk factors for HCV, hepatitis B and HIV transmission. There are, however, clear differences between these viruses when it comes to their ability to be transmitted through sexual activity. There is an adequate amount of evidence indicating that HCV can be sexually transmitted but with much less efficiency than both hepatitis B and HIV.

To date the epidemiological studies evaluating the degree of risk of HCV transmission by sexual contact have had quite a few methodological limitations that are inclined to overestimate the amount of HCV infections associated with sexual contact. Early studies used first-generation anti-HCV assays, which have a higher false positive rate than second and third-generation assays. Studies vary in the completeness of risk ascertainment and many fail to carefully exclude HCV acquirement from non-sexual sources. Non-disclosure of injection drug use (IDU) as a risk factor is particularly important since assessing the contribution of sexual activity to HCV transmission is difficult in the presence of injection drug use. Finally, only a limited number of studies perform virological analyses to confirm that sexual partners are infected with the same virus thereby excluding acquirement from outside sources.

Sexual transmission of virus occurs when infected body secretions or infected blood are exchanged across mucosal surfaces. The presence of virus in body secretions is necessary but may not be sufficient for transmission to occur. Other factors that may influence transmission include the titer or amount of virus in body secretions (body secretion viral load), the integrity of the mucosal surfaces (some sexual practices may traumatize the mucosa, e.g., anal receptive sex and fisting), and the presence of other genital infections, both viral or bacterial including herpes simplex virus, trichomonas and gonorrhea.

Studies to detect HCV RNA in semen (seminal fluid and cells), vaginal secretions, cervical smears, and saliva have produced mixed results. Inability to detect HCV RNA in body secretions may be caused by technical aspects, including specimen collection and storage, and the ability to exclude cellular components and surmount the presence of polymerase chain reaction inhibitors. Even in studies using the most favorable methods for isolating HCV RNA, the majority of samples were negative for HCV RNA and those that were positive were of low titer (equal to 1000 copies/mL). A low titer of virus in genital secretions could explain why HCV is transmitted less efficiently than hepatitis B virus or HIV. Furthermore, there may be a lack of suitable target cells in the genital tract to allow infection to occur or infection may require the presence of abnormal mucosa (ruptured or damaged mucosa which would result from sexual

See Sexual Risk on page 7

Help Us Reach More People with Hepatitis C! Support us through either a paid subscription or donation.

Yes, I'd like to subscribe.

- \$18 one year—12 issues
 \$9 one year—12 issues
 (for those with fixed incomes)
 Renewal

Yes, I'd like to donate.

- \$10 \$25 \$100 other

Please make checks payable to:
HCSP/The Tides Center

The Hepatitis C Support Project does not share its mailing list with any individual or organization. All subscribers names and addresses are strictly confidential

Name _____

Address _____

City _____

Please mail form to: HCV ADVOCATE
P.O. Box 427037
San Francisco, CA
94142-7037

Alcohol *Continued from page 3*

While no safe intake of alcohol below 50g/day has been established, individual responses to any amount of alcohol cannot be calculated. This does not mean that everyone with HCV should become a teetotaler, but rather that individuals should empower themselves through education and awareness.

A good starting point in this process is talking openly and honestly with your doctor about your medical history, and your lifestyle—past and present. Remember it is not your doctor's job to judge you, but to provide you with relevant information and assist you in making informed choices. Being HCV+ does not confiscate your power of choice, but, like any other set of circumstances, it presents certain factors that must be taken into consideration when making decisions.

Alcohol is a contentious issue between doctors and patients because it often represents a link to the patient's pre-infection lifestyle. While the doctor may see it as an unnecessary risk that can easily be avoided, the patient may see occasional alcohol consumption as a harmless indulgence that improves his or her quality of life. Be honest with yourself and your doctor. What is the condition of your liver? Have you had a biopsy recently? Have you ever had to deal with a previous addiction? It is certainly not necessary to drink in every social situation in which others are also drinking—try substituting fruit juice or mineral water. However, the most important consideration is to work towards developing and maintaining a health-positive lifestyle that is rewarding and fulfilling.

For patients for whom alcoholism is an issue, tell your physician that you need help to stop drinking. You may be advised to enter a detoxification treatment program to evaluate your physical and mental health, as well as any psychosocial, occupational and family stresses, as well as to monitor and assist your withdrawal from alcohol. For example, if you are diagnosed with depression, an alcohol-free treatment plan can be created to help you manage that condition. Furthermore, many social support programs such as Alcoholics Anonymous and other national programs are available to provide social support for people who want to stop drinking.

Sources:

www.alcoholics-anonymous.org

www.hcvanonymous.com

www.liverfoundation.org

www.liver.ca

Diet *Continued from page 2*

Trans-fatty acids suppress a cholesterol regulating enzyme and also lead to raised triglyceride levels. Read the labels and avoid fats that are hydrogenated. A hepatitis-damaged liver uses and metabolizes the essential fatty acids very easily and this places very little strain on the liver, so look for natural fats (flaxseed, canola oils, nuts, fish oils, etc.) and try to reduce your dietary fats to around 15%-20% of your total caloric intake. The liver is also intimately involved with the processing of dietary cholesterol and is the main source of newly synthesized cholesterol in the body. Liver disease may be associated with both high and low blood cholesterol levels. In general, as liver disease progresses in patients with hepatitis C, the blood level of cholesterol drops.

Overweight individuals are often found to have abnormalities related to the liver, ranging from steatosis (fatty deposits in the liver) to steatohepatitis (fatty deposits in the liver accompanied by inflammation). In overweight patients with a fatty liver who subsequently lose weight, liver related abnormalities improve. In a study published in the *American Journal of Clinical Nutrition* in 2002 researchers put 19 overweight people with hepatitis C on a 12 week diet and exercise program with a goal of losing 1 pound per week. At the conclusion of the study, average weight loss was approximately 13 pounds. In addition, several markers of liver health improved, including a decrease in liver enzymes and a reduction in the amount of scar tissue and fat in the liver. These changes indicated a decrease in the severity of the liver disease. Those who continued on the weight loss program for another 12 months had sustained improvement in the health of their liver. A surprising finding was that these improvements occurred even though the virus was not eradicated from the body. This study therefore suggests that overweight individuals may be able to improve liver health by losing weight. Therefore, patients with chronic HCV are advised to maintain normal weight. For those who are overweight, it is vital to start a sensible exercise routine and a low fat, well-balanced, weight reducing diet. It is essential that patients consult with their physicians before beginning any diet or exercise program.

Future parts will include information on protein, carbohydrates, iron, sodium, caffeine, vitamins plus healthy tips on eating right!

Sexual Risk *Continued from page 5*

injury or a bacterial or viral infection). Finally, while the presence of HCV RNA in semen, vaginal or cervical secretions supports the argument that HCV is sexually transmissible, a cell culture system or animal model is still needed to prove that HCV RNA detected in genital secretions represents infectious virus.

Sexual transmission has been assessed in varying populations of HCV infected individuals, and two main risk groups have been identified. The first risk group comprises those who have more sexual encounters and who are more likely to have multiple sexual partners, including men who have sex with men, female sex workers, attendees of sexually transmitted disease clinics, and those in HIV surveillance studies. The second risk group comprises persons who are in a long-term monogamous sexual relationship with someone who is chronically infected with HCV. There are differences in the rates of anti-HCV positivity by risk group with higher rates reported for the first risk group. These differences in rates of HCV infection may correlate with differences in sexual risk behaviors including and not limited to frequency or type of sexual activities. On the other hand, differences between risk groups may indicate inconsistent rates of exposure to non-sexual sources of HCV including injection drug use, intranasal cocaine use, tattooing, body piercing, dental exposure, toothbrushes, razors, etc. For this reason, sexual transmission findings from one risk group cannot be considered as widespread fact.

With that said, it has been found consistently in both prospective and retrospective studies that the risk of HCV transmission via sexual contact differs by the type of sexual relationship. Among individuals with multiple partners or those at risk for sexually transmitted diseases (STDs), the median seroprevalence of antibody to HCV is 4% (range, 1.6% to 25.5%) with the median rates being 6% (range, 1% to 19%) among female sex workers, 4% among men who have sex with men (range, 2.9% to 13%), and 4% among attendees of STD clinics as well as individuals participating in HIV surveillance studies (range, 1.6% to 26%, which dropped to a range of 1.6% to 7% when limited to individuals without a history of IDU). HIV coinfection increases the rate of HCV transmission by sexual contact even though the precise mechanism is unknown.

Persons in long-term monogamous partnerships, on the other hand, are at lower risk of acquiring HCV (0% to 0.6% per year) than persons with multiple partners or those at risk for sexually transmitted diseases (0.4% to 1.8% per year). This difference may reflect differences in sexual risk behaviors or differences in rates of exposure to nonsexual sources of HCV. Early studies found that the rate of HCV positivity in partners increased with the longer duration of marriage, suggesting that the risk of sexual transmission correlated with frequency of contact. However subsequent studies adjusting for age did not find a consistent relationship between the duration of the sexual relationship and the HCV positivity of the partners. Overestimation of the rate of sexual transmission of HCV occurs when antibody testing alone is used to make the assessment. So, based on only those seroprevalence studies that used genotyping or sequence analysis of the hypervariable region of E2 (the envelope region of the HCV genome), in monogamous, heterosexual partners of hepatitis C-infected, HIV-negative persons, the frequency of antibody-positive and genotype-concordant couples is 2.8% to 11% in Southeast Asia, 0% to 6.3% in Northern Europe, and 2.7% in the United States.

The mounting evidence indicates that HCV virus can be transmitted by sexual contact but much less efficiently than other sexually transmitted viruses, including both the hepatitis B and the HIV viruses. However, because sex is such a common behavior and the numbers of HCV-infected individuals in the United States is substantial, sexual transmission of HCV likely contributes to the total burden of infection in the United States. Current recommendations about sexual practices are different for persons with chronic HCV infection who are in steady monogamous partnerships versus those with multiple partners or who are in short-term sexual relationships. HCV positive individuals in longer-term monogamous relationships need not change their sexual practices although they should discuss safer sex options if either partner is concerned about sexual transmission. If couples wish to reduce the already low risk of HCV transmission by sexual contact, barrier precautions may be used. Partners of HCV-positive persons should be considered for anti-HCV testing. For HCV-infected individuals with multiple or short-term sexual partners, barrier methods or abstinence are recommended.

GBV-C and HIV

Liz Highleyman

Can a common and apparently harmless relative of the hepatitis C virus (HCV) help slow the progression of HIV disease? This intriguing possibility was big news at the recent Conference on Retroviruses and Opportunistic Infections, held February 10-14 in Boston.

GB virus type C, or GBV-C (also known as hepatitis G virus, or HGV), is structurally related to HCV, but does not appear to cause disease. Some 1-2% of healthy blood donors have detectable GBV-C, but the virus is much more common in HIV positive people.

Data presented at the conference confirm previous research showing that GBV-C can help slow HIV disease progression. Dr. Carolyn Williams and colleagues looked at the effect of GBV-C coinfection in 271 men in the Multicenter AIDS Cohort Study, all of whom had recently been infected with HIV (abstract 159LB). Analysis of samples from an early clinic visit (1-1.5 years after HIV infection) showed that 39% of the men had detectable GBV-C viral load and 46% showed evidence of past infection and clearance of the virus. Looking at samples from a second visit 4-5 years later, men who cleared GBV-C between the two visits were nearly six times more likely to die, and men who were never infected with GBV-C were over two times more likely to die, compared with men who remained GBV-C positive. After 11 years, about 75% of the men who remained GBV-C positive were still alive, compared with 39% of the persistently GBV-C negative men and 16% of those who cleared the virus. In addition, men who cleared GBV-C experienced a steeper CD4 cell decline than either persistently positive or persistently negative men. "GBV-C viremia assessed 5-6 years after HIV seroconversion was a strong predictor of survival, and loss of GBV-C predicted a higher risk of death," the researchers concluded.

A Swedish team reported similar results (abstract 157). In their study, 27% of 230 HIV positive patients had detectable GBV-C viral load and 30% showed evidence of past infection. GBV-C was less common in people with AIDS (about 6%) than in those with asymptomatic HIV infection (about

30%). As in the previous study, patients who cleared GBV-C over the course of their illness (25%) had more rapid CD4 cell declines, a greater incidence of AIDS, and a higher risk of death.

While most GBV-C research has been done in people not receiving anti-HIV therapy, another study presented at the conference looked at GBV-C/HIV coinfection in patients taking AZT, alone or in combination with ddI or ddC (abstract 849). In this study, GBV-C positive people had higher CD4 cell counts and lower HIV viral loads. They also had better CD4 responses to anti-HIV therapy, which may help explain their slower progression to AIDS or death.

It is not clear how GBV-C exerts its protective effect, but it seems to help prevent HIV from entering cells. In laboratory studies, Dr. Jack Stapleton and colleagues found that GBV-C inhibits HIV infection of white blood cells (abstract 156). GBV-C appears to alter the production of certain cytokines and chemokines (including RANTES, MIP-1a, MIP-1b, and SDF-1) that occupy the same cell surface receptor binding sites used by HIV, thus blocking HIV entry. It also seems to decrease the amount of the CCR5 receptors that certain strains of HIV need to enter cells. "[T]here may be multiple mechanisms by which GBV-C may help people who have HIV infection," suggested Dr. Stapleton.

Don't look for GBV-C to make its appearance as an HIV treatment anytime soon. Aside from the ethical issue of injecting someone with a new virus—which doesn't appear to cause disease, but which may in the future be associated with ill effects we don't yet know about—researchers are worried that introducing more GBV-C into people who already carry it could spur the immune system to clear the virus, leaving people with less protection than they started with. HCV/HIV-coinfected people face an additional quandary: the use of interferon to treat HCV may also promote clearance of HGV, leaving them more susceptible to HIV disease progression. Further study is clearly needed—understanding how GBV-C and HIV interact may provide insights that could lead to the development of new anti-HIV therapies in the future.

Retrovirus Conference Continued from page 1

infection. Of these, 92 (38%) showed evidence of prior HBV exposure and clearance, 17 (7%) showed evidence of current acute or chronic hepatitis B, and 38 (15%) had evidence of occult HBV (anti-HBc antibodies only, usually with undetectable HBV viral load). In this group, active hepatitis B was more common than in the population at large.

For HIV/HBV-coinfected people, tenofovir (Viread) continues to yield promising results. Dr. David Cooper of Australia and colleagues presented data from Gilead study 903 showing that adding both tenofovir and 3TC (lamivudine or Epivir) to an existing anti-HIV regimen suppresses HBV replication better than 3TC alone (abstract 825). The five patients who took tenofovir plus 3TC experienced an average 4.7-log decrease in HBV viral load after 48 weeks, compared to a 2.9-log drop among those taking 3TC without tenofovir. French researchers presented similar results (abstract 824). In their study, 10 patients who added tenofovir to their existing regimen experienced an average HBV viral load decrease of 4.5 logs after one year; three had undetectable HBV.

Liver Disease Progression and Mortality

Results from a European multi-center study of 492 HIV/HCV-coinfected patients confirm that HIV accelerates HCV disease progression in people with hepatitis C (abstract 830). Longer duration of HCV infection, age over 20 years at time of HCV infection, and history of heavy alcohol use—but not CD4 cell count, HCV genotype, HCV viral load, or use of anti-HIV therapy—were associated with more severe liver damage.

Likewise, researchers reported data showing that decompensated liver failure was more likely in people HIV/HCV-coinfected compared to those with HIV alone (abstract 823). This study—done in Taiwan, where hepatitis B is endemic—included 500 HIV-positive participants, 126 of whom were coinfecting with HBV. After a median of two years, 34% of the HIV/HCV-coinfected patients versus 18% of those with HIV alone developed acute hepatitis. Over 8% of the coinfecting participants developed decompensated liver disease, compared with just 0.5% of those with HIV alone. Nine coinfecting people died due to liver-related causes, versus zero with HIV alone.

Patients with and without hepatitis B responded similarly to anti-HIV therapy.

Dr. Yves Benhamou and colleagues from France presented results of a study looking at how prior exposure to HBV affects liver disease progression in people with HIV/HCV coinfection (abstract 822). It is known that chronic hepatitis B can worsen liver damage in people who also have HCV. Although most people exposed to HBV do not develop chronic infection, prior exposure to the virus may still have an effect on the liver. In this study of 145 patients, anti-HBc antibody positivity (indicating past infection) was associated with slower liver fibrosis. It is not known why past HBV exposure might have a protective effect.

Other News

Current guidelines recommend that susceptible HIV/HCV-coinfected people should be vaccinated against hepatitis A and B. A pilot study looked at immunogenic responses in HIV/HCV-coinfected people (abstract 826). One-third of those who received the hepatitis A vaccine produced anti-HAV antibodies, indicating protection had been achieved; vaccination was more likely to succeed in people with higher CD4 cell counts. About one-quarter of those vaccinated against hepatitis B produced anti-HBs antibodies.

Finally, new data confirmed that liver transplants can be successfully performed in people with HIV. Researchers from several transplant centers reported that HIV-positive people and HIV-negative recipients have similar post-transplant survival rates (abstract 155). Transplant outcomes in 23 HIV-positive people were analyzed. Survival rates were 90.9%, 75.9%, and 75.9% at 12, 24, and 36 months, respectively—somewhat higher than the comparable survival rates of 86.6%, 82.3%, and 79.2% in HIV-negative patients. HIV/HCV-coinfected people did worse than those who had HIV but not HCV, although their mortality rate was similar to that of HIV-negative transplant recipients with HCV. This study adds to the evidence that HIV status should no longer be considered a reason to deny someone a liver transplant.

See the HCV Advocate web site for a more detailed version of this report. For the complete Retrovirus conference program and abstracts, see www.retroconference.org/2003.

Clinical Trials

National Trials

ROCHE - 866-GO-WINGS

NIH - HALT-C (Cirrhosis)

800-411-1222

Northern California

University of California, Davis

Dr. Rossaro (916) 734-8696

University of San Francisco Medical Center

Stephanie Straley, PA (415) 353-2328

VA Hospital-UCSF

(415) 750-2105

California Pacific Medical Center

(415) 600-1100 or (415) 600-1106

San Francisco General Hospital

Athiana (415) 206-3725

San Francisco

Dr. Cazen (415) 565-6288

Stanford University Hospital

Stanford Liver Research Clinic (650) 724-7057

Quest Medical Research (HIV/HCV Coinfection)

Dr. Lalezari (415) 353-0800

East Bay Liver Clinic

Oakland, CA - Grant Young (510) 208-1777

Dr. John J. Jolley - San Rafael

Contact: Lynn Jolley

(415) 257-3030

Southern California

USC Hepatitis Research Clinic

Dr. Karen Lindsay, Susan Milstein, RN

(323) 442-5550

UC Irvine Medical Center

Dr. John Hoefs, Barbara Walker, RN

(714) 456-7821

VA Medical Center - Long Beach

Dr. Timothy Morgan, Julia Sanborn, RN

(562) 494-5933

Santa Barbara/Ventura Counties

Dr. Kip Lyche (805) 641-6525

HCSP

P.O. Box 427037

San Francisco, CA

94142-7037