

## AASLD Conference Highlights: *Part 1*



Alan Franciscus, Editor-in-Chief

The American Association for the Study of Liver Disease Conference was held on October 24 through October 28, 2003 in Boston, MA. AASLD conferences report on the most important research data on all forms of liver disease. This article is the first in a series that focuses on the most important and interesting findings on hepatitis B, hepatitis C and HIV/HCV coinfection, presented at the 2003 AASLD.

### HCV: TREATMENT FOR PEOPLE WITH PERSISTENTLY NORMAL ALTS

Approximately 30% of people with HCV present with persistently normal alanine aminotransferase (ALT). Most people with HCV and persistently normal ALTs do not progress to serious disease progression; if their disease does progress, it is very slow. However, it is important to remember that ALT levels do not accurately reflect the amount of inflammation or the disease state of the liver. In fact, two thirds of people with hepatitis C and persistently normal ALT levels present with some fibrosis that is usually minor but can be severe. Currently, the National Institutes of Health and European consensus conferences on hepatitis C both recommend not routinely treat-

ing these patients until more studies can be performed showing that treatment is safe and effective in this patient population.

Dr. Zeuzem and colleagues presented the results of a randomized controlled study to establish the efficacy of Pegasys (peginterferon alfa-2a ((40 KD) 180 µg/week Pegasys) plus Copegus (Roche's branded ribavirin) administered during 2 different treatment durations in chronic hepatitis C patients with normal ALT levels.

In this study, 491 patients were randomized (ratio 3:3:1) into three arms:

1. 212 were treated with PEG-IFN alfa-2a 180 µg/week plus ribavirin 800 mg/day for 24 weeks,
2. 210 received the same combination for 48 weeks, and
3. 69 patients received no treatment and were monitored for 72 weeks.

All patients were required to have chronic hepatitis C infection documented by positive anti-HCV antibody test and detection of HCV RNA by PCR (viral load). Persistently normal ALT activity was defined by at least 3 ALT determinations less than or equal to the upper limit of normal, a minimum of 4 weeks apart, with 1

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value within the 42-day screening time and 1 value 6 to 18 months before the study onset.

Patients with ALT levels greater than the upper limit of normal during the 18 months preceding baseline were excluded from the study. Liver disease consistent with chronic hepatitis C was confirmed by biopsy within 36 months before the study. Cirrhotic patients and patients with other chronic liver diseases or co-infected with human immunodeficiency virus were excluded from the trial. Sustained virological response (SVR) was defined as negative HCV viral load by PCR (< 50 IU/mL COBAS AMPLICOR® HCV Test v. 2.0) at the end of 24 weeks of untreated follow-up.

The demographics and baseline viral load measurements were similar in all three groups:

- \* Male gender: 42%, 39%, 38%;
- \* median age: 44, 44, 41 years, and
- \* median weight, 74 kg, 73 kg, 70 kg, respectively.

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# Depression:

## Part 3:



Lucinda K. Porter, RN, CCRC  
Eric Dieperink, MD

*This is the third and final installment of the Hepatitis C Support Project's newest publication, Coping with Depression and Hepatitis C. See last month's issue for Part 2.*

### PROFESSIONAL HELP

As mentioned previously, depression can be treated. There are a number of types of treatment for depression. The medical specialty for mental health diseases is called psychiatry. Psychiatrists can prescribe medications. Sometimes psychotherapy is recommended. Psychotherapy can be done individually or in a group. There are many types of psychotherapy and approaches vary widely. Shop around to find a therapist and style that suits you. Although some psychiatrists offer psychotherapy, patients are often referred to non-medical mental health professionals for this treatment. These can include psychologists, marriage and family counselors, licensed social workers or nurse specialists for this type of treatment.

***Important Note: If you have thoughts of suicide or hurting yourself or others, seek immediate professional help.***

### MEDICATION

Antidepressant medications are commonly used to treat depression. Studies have shown that antidepressants can help reduce depression associated with hepatitis C and interferon treatment. There are many different types of antidepressants. *Tricyclic antidepressants* were first-line medications during the 1960's through the 1980's. Over the past 10 years new antidepressants have been discovered that are as effective as the older ones but have fewer severe side effects. *Selective serotonin reuptake inhibitors* (SSRI's) primarily affect the neurotransmitter serotonin and include fluoxetine (*Prozac, Sarafem*), sertraline (*Zoloft*), paroxetine (*Paxil*), citalopram (*Celexa*),

***Antidepressants are not "uppers" or "happy pills," and they are not addictive.***

escitalopram (*Lexapro*) and fluvoxamine (*Luvox*). These medications are now considered first-line as they are safe, effective and are currently the most commonly prescribed antidepressants. Other antidepressants such as nefazodone (*Serzone*), venlafaxine (*Effexor*), mirtazapine (*Remeron*) and bupropion (*Wellbutri, Zyban*) have unique mechanisms of action but are also very effective.

### Antidepressant Side Effects

Antidepressant medications can cause side effects, usually these are mild, do not interfere with activities and often resolve over time. However, some side effects can be serious and those that are unusual, annoying, or affect your activities should be reported to your doctor right away. Common side effects of SSRI's include:

#### Headaches

Headaches may occur during the first one to two weeks, but usually go away after a short period of time.

#### Nausea

Nausea can also occur during the first one to two weeks and usually resolves after a short time.

#### Nervousness

Nervousness may also occur early on and go away after a couple of weeks.

#### Agitation

Agitation, or feeling jittery, occurs less frequently. Notify your doctor if it lasts longer than a day or two.

#### Sexual problems

Sexual problems may occur in both men and women. Although fairly common, these are reversible. Tell your doctor if you experience any

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## DEPRESSION

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sexual problems after starting an antidepressant, as there may be ways for your doctor to help.

*Some of the newer medications have unique side effects:*

**Nefazodone** should probably be avoided in people with hepatitis C because cases of life-threatening liver failure have been reported in association with this medication. However, all treatment decisions should be discussed with your doctor.

**Venlafaxine** has the typical SSRI side effects but may also cause *sweating* and has been associated with *high blood pressure*. Your blood pressure should be monitored.

**Mirtazapine** may be *sedating* at lower doses and can very rarely affect the white blood count.

**Bupropion** does not cause sexual dysfunction but should not be used in people who have or may be at increased risk for a seizure disorder. Bupropion may also cause *shakiness* and *trouble sleeping*. You should discuss these side effects with your doctor if they become troublesome. This drug is also used to help people stop smoking.

### WHAT TO EXPECT DURING ANTIDEPRESSANT THERAPY

Antidepressants often take some time before they are effective. Some people may notice improvement in their depressive symptoms in the first one to two weeks, but typically the medications must be taken regularly for six to eight weeks before their full effect is felt. Antidepressants should typically be continued for at least six to twelve months, but the length of treatment may vary.

Antidepressants are not “uppers” or “happy pills,” and they are not addictive. In order to be used effectively, antidepressants need to be taken on a regular basis. Never stop a medication without talking to your doctor. If you miss a dose of the medication take the next regularly scheduled dose; do not “double up” as this may cause increased side effects.

If you are taking antidepressants for the depression associated with interferon treatment, you should work closely with a healthcare provider who is knowledgeable about hepatitis C and interferon treatment. Avoid alcohol, since it can worsen depression and may interact with antidepressants and reduce their effectiveness.

All medications can cause allergic reactions. Tell your doctor about any allergies you might have. Antidepressants can also interact with certain drugs or other conditions. Inform your doctor about any over-the-counter or prescription medications, illicit drugs, or herbs you are using, since these may affect how the antidepressant works. Finally, notify your doctor if you experience any unusual or worsening symptoms.

Although antidepressants are often very helpful and can significantly improve your symptoms and quality of life, treatment should be individualized. Studies have shown that the best results occur when antidepressants are used in conjunction with psychotherapy. However, you should discuss treatment options with your healthcare provider to find the best treatment for you.

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*A special thanks to Liz Highleyman for her editorial contributions to this article.*

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# Signs of Cirrhosis



Kara Wright, PA-C

One of the most common questions from a patient with hepatitis C is: “How will I know if I get cirrhosis?” People always want to know what to look for. In reality, many patients with cirrhosis may not even know they have significant liver disease until further evaluated by a medical provider. Many patients may have cirrhosis and have no signs or symptoms at all. In this article, we will discuss the physical and laboratory signs of cirrhosis.

*Cirrhosis* is late stage liver disease. It is characterized by actual distortion of the liver architecture due to scarring of the liver and is generally considered irreversible. Once the liver cells become scarred, liver function declines which produces a number of physical as well as laboratory findings. Although these findings often indicate cirrhosis, they are not specific only to liver disease.

## Physical signs

*Ascites* is the accumulation of fluid in the abdominal cavity. In many cases, several liters of fluid can build up and cause severe abdominal distention. This is the most common complication of cirrhosis. Nearly 60% of all patients with compensated cirrhosis will develop ascites in 10 years.

*Spontaneous bacterial peritonitis (SBP)* is an infection of ascitic fluid. Manifestations of SBP include fever, abdominal pain, abdominal tenderness, and altered mental status. In the event of SBP, a provider must do a diagnostic paracentesis

(draining of the fluid from the abdomen).

*Hepatomegaly* is enlargement of the liver. The cirrhotic liver may be large, normal sized, or small. When it can be felt, it will have a firm and nodular consistency.

*Splenomegaly* is enlargement of the spleen and is common in patients with cirrhosis.

*Caput medusa* is noted when the veins in the abdomen are very prominent. This appearance has been said to resemble the head (caput) of the mythical Gorgon Medusa.

*Hepatic encephalopathy* is a potentially reversible disturbance in consciousness and behavior. Disturbance of sleep pattern is a common early feature that typically precedes overt neurologic features. Patients often feel very confused. Physical findings include asterixis. *Asterixis* is the bilateral but non-uniform flapping motions of outstretched hands.

*Fetor hepaticus* is a sweet, pungent smell to the breath of cirrhotic patients. It is caused by increased concentrations of a chemical, which is not being detoxified by the liver.

*Variceal hemorrhage* is a devastating complication that occurs in 25-40 percent of patients with cirrhosis. This occurs when a blood vessel has very high-pressure blood flow, which causes it to break and bleed.

*Jaundice* is the yellow coloring of the skin and mucus membranes that results from increased serum bilirubin.

*Spider angiomas*, also known as *spider telangiectasias*, are markings on the body, which, as indicated in the name, look like spiders. They have a central circular artery

with smaller vessels radiating from the center like spokes, or legs of a spider. The lesion is typically red or purple in color and the central part of the lesion may pulsate when compressed with a glass slide. Spider angiomas are most frequently found on the trunk, face and arms. As a

general rule, the number and size of the spider angiomas correlate with the severity of liver disease.

*Palmar erythema* is an exaggeration of the normal spotty redness on the palms of the hands. It is characterized by a deep redness on the fleshy part of the palm.

*Nail changes* are sometimes found. *Muehrcke's nails* are

***Compensated Cirrhosis means that the liver is heavily scarred but can still perform many functions; people with compensated cirrhosis exhibit few or no symptoms.***

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# Hepatitis A: What You Need to Know



Alan Franciscus, Editor-in-Chief  
Liz Highleyman

Hepatitis A is an inflammation of the liver caused by the hepatitis A virus (HAV); it was formerly known as infectious hepatitis. HAV is an RNA virus of the picornaviridae family; it is the most common type of viral hepatitis. Approximately 93,000 new HAV infections occur annually in the United States, and it is estimated that 33% of all people in the United States have been infected with HAV.

## HAV TRANSMISSION AND PREVENTION

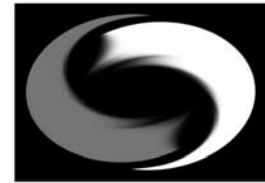
Hepatitis A is a highly infectious disease that is mainly spread through the fecal-oral route, that is, virus contained in feces is transferred to a person's mouth. The hepatitis A virus can also be spread by blood exposure but this is rare. Transmission of hepatitis A can happen through ingesting contaminated food or water, household contact (especially with infants or young children), and some types of sexual contact (e.g., analingus, or oral/anal sex) and rarely injection drug use. Workers in day care centers and long-term care facilities such as nursing homes have a higher risk of contracting HAV, as do international travelers to areas that do not have good sanitation or water processing facilities.

## RISK FACTORS ASSOCIATED WITH REPORTED HEPATITIS A (CENTERS FOR DISEASE CONTROL, 1990-2000, UNITED STATES):

- Unknown (46%)
- People who have household contact with an HAV-infected individual (14%)
- Men who have sex with men (10%)
- Other contact (8%)
- Injection drug users (6%)
- International travelers (5%)
- Food or waterborne outbreak (4%)
- Contact at day care centers (2%)

New HAV infections in the U.S. are most commonly observed among:

- Men who have sex with men
- People who practice oral/anal sex
- Injection drug users
- People who have household contact with an HAV-infected individual
- Employees of and children who attend day care centers
- Employees of and people who reside in long-term care facilities
- International travelers to areas with poor sanitation.



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- \* Genotype 1: 68%, 67%, 66%; and
- \* mean viral load: 1.2, 1.1 and  $1.3 \times 10^6$  IU/mL, respectively.

Overall SVR was 30% and 52% for the 24 and 48 week treatment groups, respectively, versus 0% for the untreated control group ( $p < 0.0001$ ). For genotype 1, SVR was 13% in the 24 week treatment group vs 40% in the 48 week treatment group ( $p < 0.001$ ). For genotypes 2 and 3— 24 weeks treatment had a SVR of 72% vs 78% in patients treated for 48 weeks ( $p = ns$ ). The safety profile was typical of interferon treat-

*Most people with HCV and persistently normal ALTs do not progress to serious disease progression*

ment but the incidence of the commonest interferon related adverse events was lower than in previous studies on abnormal ALT chronic hepatitis C patients. ALT values remained normal or near normal in the vast majority of patients from both treatment and control groups. Median ALT levels decreased from baseline in treatment responders.

Mild, transient ALT elevations were observed after end of treatment in relapsers from treatment groups. Only 2 patients, one treated for 24 weeks, and one from the control group, developed ALT flares (greater

than 10 times the upper level of normal).

The authors concluded that the effectiveness of Pegasys plus Copegus is comparable to those treatment results in patients with elevated ALT levels and that a duration of treatment according to genotype can be recommended following established algorithms.

### **HBV: A COMPARISON OF ADEFOVIR AND TENOFOVIR IN THE TREATMENT OF LAMIVUDINE-RESISTANT HEPATITIS B INFECTION**

Treatment for chronic hepatitis remains a challenge. Up until last year, interferon and Lamivudine were the only approved therapies for treating chronic hepatitis B. Usually, treatment with Lamivudine initially results in a decrease of HBV viral load, and an improvement in liver enzymes and liver histology. However, long term treatment with Lamivudine frequently results in a development of drug resistant mutants. Recently, Adefovir was approved for the treatment of chronic hepatitis B and is successful in treating individuals with lamivudine resistance. Tenofovir has been recently shown to have strong antiviral activity against lamivudine-resistant HBV.

Dr. van Bömmе and colleagues recently conducted a study that compared the antiviral effectiveness of Adefovir and Tenofovir. In this study fifty five patients with hepatitis B who developed resistance to Lamivudine after being treated for at least 24 months were studied. Of these patients, 19 were treated with Adefovir and thirty six were treated with Tenofovir for at least three months. HBV DNA (viral load), ALT and creatinine were measured during this study.

The authors reported that the hepatitis B viral load declined more rapidly in those patients treated with Tenofovir than in the patients treated with Adefovir. At the 6 month point, HBV viral load became negative in 69% of patients treated with Tenofovir compared to 37% of patients treated with Adefovir. The ALT levels declined significantly faster in patients treated with Tenofovir. Creatinine levels remained in normal ranges for both groups. No significant side effects were observed in both groups.

The authors concluded that Tenofovir seems to be superior to Adefovir in suppressing Lamivudine-resistant mutants.

### **HIV: PREDICTORS OF ANTIRETROVIRAL-RELATED HEPATOTOXICITY IN THE ADULT AIDS CLINICAL TRIALS GROUPS (AACTG)**

People with HIV are now living longer because of the successful use of HIV antiretroviral medications. However, these life saving drugs can potentially pose a risk of liver toxicity that could necessitate the discontinuation of HIV medications.

Dr. Servoss and colleagues recently reported the results of their retrospective analysis on the incidence of severe hepatotoxicity, liver failure and death in 21 Adult AIDS Clinical Trials Groups (AACTG) studies which enrolled subjects into arms that included single and multiple nucleoside reverse transcriptase inhibitors (NRTI), and triple drug regimens that included varying combinations of NRTI's, non-nucleoside reverse transcriptase inhibitors (NNRTI), and protease inhibitors (PI) (*Gastroenterology* 2001;120:A54). In this study the authors found that 10% of the patients developed severe hepatotoxicities

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measured by AST, ALT, and total bilirubin greater than 5 times the upper limit. When broken down by regime this was 12% single NRTI, 7.9% multiple NRTIs, 8.6% PI (-) triple drug, and 12% PI (+) triple drug.

The overall and liver-related death rates were 15% and 0.3%, respectively. Factors associated with severe hepatotoxicity were not included in their initial analysis. This current study report identified baseline predictors for severe hepatotoxicity in those receiving single NRTI, multiple NRTI, NNRTI, and PI-based regimens.

In this study, the data from 9,017 patients from AACTG studies were analyzed. The authors found that high AST levels (more than 1.25 times upper limit of normal) were

associated with early severe hepatotoxicity among all regimens. High triglycerides (more than 400 mg/dL) were associated with late severe hepatotoxicity among patients on single NRTI regimens.

Elevated creatinine (more than 1.5 times the upper limit of normal) and low platelets (less than 99,000/mm<sup>3</sup>) were risk factors for those on multiple NRTI regimens, as was nevirapine use for those on NNRTI-based regimens. Hepatotoxic potential of concomitant medications (CMEDS) predicted late severe hepatotoxicity for those on multiple NRTIs or indinavir. d4T was a predictor of early severe hepatotoxicity among patients on indinavir. Low CD4+ (less than 300 cells/mm<sup>3</sup>) was associated with a decreased risk of early and late severe hepatotoxicity for those on multiple NRTIs, while black race was

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Medical Writers' Circle is a publication of the Hepatitis C Support Project. It consists of a series of articles written by medical professionals about the management and treatment of hepatitis C. The articles are available for printing at the Hepatitis C Support Project website.

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## CIRRHOSIS

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characterized by paired horizontal white bands separated by normal color in the nail. Another nail disorder, *Terry's nails*, is seen in patients with cirrhosis. In this case, the two-thirds of nail plate closest to the hand

appears white whereas the furthest one-third is red.

*Gynecomastia* is benign growth of the tissue of the male breast. The tissue typically feels firm and rubbery. Up to two-thirds of patients with cirrhosis have gynecomastia. Men may also develop other features such as loss of chest or underarm hair and inversion of the normal male pubic hair pattern.

*Constitutional symptoms* such as weakness, fatigue, anorexia, and weight loss also occur. The fever of cirrhosis is typically low grade and continuous.

### Laboratory findings

Liver enzymes may provide the first clue to liver dysfunction. *Aspartate aminotransferase* (AST) and *alanine aminotransferase* (ALT) are usually moderately elevated in cirrhotic patients. AST is often more elevated than ALT, but levels can be normal in cirrhotics.

*Alkaline phosphatase* is usually elevated but less than 2-3 times the upper normal limit.

*Bilirubin* is often normal in well-compensated cirrhosis, but will rise as cirrhosis progresses.

*Albumin* is synthesized exclusively in the liver. Albumin levels

fall as the synthetic function of the liver declines due to worsening cirrhosis. Serum albumin levels can help to grade the severity of cirrhosis.

The liver synthesizes many proteins required for normal clotting. The *prothrombin time* (PT) reflects

the degree of liver dysfunction.

The PT increases as the ability of a cirrhotic liver to synthesize clotting factors diminishes.

*Anemia* may occur in cirrhotic patients due to a number of causes.

*Thrombocytopenia* (low platelets) is very common in cirrhotic patients and is often caused by an enlarged spleen, which can sequester up to 90% of circulating platelets.

If a patient has any of these signs, he or she should discuss them with a medical provider. These signs do not always indicate cirrhosis, but can help establish that diagnosis.

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associated with decreased risk of late severe hepatotoxicity for those receiving indinavir.

The authors concluded that in the largest U.S. HIV cohort ever studied:

- (1) there was a high rate of severe hepatotoxicity irrespective of ART class, with an overall rate of 10%;
- (2) among all ART regimens, high baseline AST and/or ALT (more than 1.25 times the upper limit of normal) were predictors of severe hepatotoxicity, confirming results from other cohorts;
- (3) nevirapine containing regimens were associated with both early and late severe hepatotoxicity;
- (4) previously unreported risk factors for severe hepatotoxicity among patients on multiple NRTIs included platelets less than 99,000/mm<sup>3</sup>, creatinine more than 1.5 times the upper limit of normal and concomitant hepatotoxic medications. Concomitant hepatotoxic medications, d4T use, and history of IVDU were risk factors for those on indinavir-based regimens.

The authors concluded that the findings suggest that in addition to baseline ALT and AST, other factors should be considered prior to initiating ART. Identification of those patients that are predisposed to hepatotoxicity will lead to tailored anti-retroviral therapy that will help people stay on life saving HIV medications.

*Part two will focus on new HCV therapeutic developments*

***Decompensated cirrhosis means that the liver is extensively scarred and unable to function. People with decompensated cirrhosis often develop complications, such as varices (stretched and weakened blood vessels) in the esophagus (swallowing tube) and stomach, internal bleeding, ascites (fluid accumulation), and other potentially life-threatening conditions. They may also experience reversible mental confusion.***



# Viral Hepatitis Report from the 43<sup>rd</sup> ICAAC



Liz Highleyman

Hepatitis B and C, as well as HCV/HIV and HBV/HIV coinfection, received considerable attention at the 43<sup>rd</sup> Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), held September 14-17, 2003 in Chicago.

## HCV TREATMENT IN COINFECTED PATIENTS

S.L. Preston and colleagues (abstract V-780) analyzed a model to predict long-term response to therapy with interferon plus ribavirin in people with chronic HCV. Variables associated with good long-term response were HCV RNA viral load at week 4 and at week 12, HCV genotype, age, and creatinine clearance (a measure of kidney function). This study confirms that in people with HCV alone, patients who do not respond at week 12 could stop therapy, sparing them side effects and cost.

But HCV/HIV coinfecting people may need longer treatment. Two studies presented at ICAAC yielded seemingly conflicting results. J. Berenguer and colleagues (abstract V-1726) presented data indicating that if coinfecting people treated with interferon plus ribavirin do not achieve an early virological response (EVR, at least a 2-log decrease in HCV RNA at 12 weeks), they are unlikely to achieve a sustained virological response (SVR, an undetectable viral load six months after the end of therapy). In this study, about 32% of the 132 participants had genotype 1 and about 28% had genotype 3. Of the 48 patients (36%) who achieved an EVR, half went on to

achieve an SVR. But of the 40 patients (30%) who did not achieve an EVR, none achieved an SVR with continued treatment. The researchers concluded that it may be advisable to stop treatment after 12 weeks if an EVR is not seen—similar to Preston's recommendation for people with HCV alone.

In the second study, S. Kottlil of the National Institutes of Health and colleagues (abstract V-1724) treated coinfecting patients (88% with genotype 1 or 4) with Peg-Intron plus ribavirin. About 70% of the 29 patients achieved an EVR at 12 weeks. Among those who completed a full course of therapy, 50% achieved an end-of-treatment response (ETR, undetectable HCV viral load at the end of therapy), but only 15% achieved an SVR. The treated patients had improved biochemical markers, and those who had pre- and post-treatment liver biopsies showed improved histology scores, even if they did not achieve a virological response. The NIH team also hopes to determine whether HCV therapy influences patterns of gene expression and activity in responders and non-responders (this analysis is underway).

The results of these two studies are not strictly comparable, both because Berenguer used standard interferon while Kottlil used pegylated interferon, and because a higher proportion of patients in the second study had genotype 1, which is harder to treat. Nevertheless, it is interesting that while about half as many people in the first trial achieved an EVR (36% versus 70%), more went on to achieve an SVR (18% versus 15%). Previous

research has suggested that coinfecting people respond more slowly to therapy and may take longer to achieve an EVR than those with HCV alone. Kottlil suggested that the 12-week cutoff may be too soon for coinfecting patients, and more people might achieve an SVR with longer treatment.

Adding more fuel to the debate. A. Moreno and colleagues (abstract V-777) reported on a trial in which 50 patients with HCV alone and 34 HCV/HIV coinfecting patients (all with genotype 1 or 4) received Peg-Intron plus ribavirin. After six months of treatment, 60% of the patients with HCV alone and 38% of coinfecting patients achieved an end-of-treatment response. The authors concluded that HCV RNA decline at week 4 predicted the likelihood of an ETR at six months in both HCV monoinfected and HCV/HIV coinfecting people. But, they noted, HCV clearance was slower in the coinfecting patients.

Two studies looked at treating coinfecting patients with pegylated interferon, alone or in combination with ribavirin. In a Spanish study of 230 coinfecting patients (abstract H-829), about 50% achieved undetectable HCV viral loads after 12 weeks of therapy; after 24 weeks, about 64% were undetectable. The authors concluded that Pegasys with or without ribavirin "has a high early virological response rate with a good tolerability." In contrast, a French study of 74 coinfecting patients (abstract H-828) found that only about one-third responded after 24 weeks, whether they received Peg-Intron alone or with ribavirin, and nearly one-half discontinued thera-

**ICAAC** *continued*

py—"a very poor response," according to the authors. It is unclear why these teams obtained such disparate results. Most patients in the French study had genotype 1, while the Spanish researchers did not report genotype.

**HIV TREATMENT IN  
COINFECTED PATIENTS**

C. Quereda and colleagues (abstract V-778) reported that concomitant therapy for both hepatitis C and HIV may lead to low rates of response to HCV treatment. In this study, 27 coinfecting patients who were not on HIV therapy and 108 who were taking HIV drugs started HCV treatment. Those who were not on HIV therapy were more likely to achieve end-of-treatment response (60% versus 33%) and SVR (41% versus 19%) to HCV treatment. Although more of the patients not receiving HIV therapy had genotype 1 or 4 (37% versus 61%), a multivariate analysis showed that both genotype and use of HIV drugs helped explain the difference in HCV treatment response rates. Among those taking HIV medications, HCV therapy was less well tolerated, and more patients in this group either temporarily stopped interferon or had their doses adjusted.

Based on a retrospective review of medical record from 1,094 patients, D. Dieterich and colleagues (abstract H-831) reported that the HIV protease inhibitor drug nelfinavir (Viracept) appears to be a safe and effective component of a combination drug regimen for HCV/HIV coinfecting people. Compared with other protease inhibitors (including amprenavir, indinavir, ritonavir, and saquinavir), nelfinavir was linked to fewer cases of severe liver enzyme (ALT and AST) elevations.

**HEPATITIS B**

On the hepatitis B front, C.L. Lai and colleagues (abstract V-1723) reported promising results from a study of the experimental nucleoside analog telbivudine. In a Phase IIb trial of 104 patients, telbivudine appeared safe and effective after one year. Patients who received either telbivudine alone or telbivudine plus lamivudine (3TC or Epivir) had greater reductions in HBV DNA viral load than those taking lamivudine alone.

Two research teams, one from Germany (abstract V-784) and one from France (abstract V-783), found that tenofovir (Viread) lowered HBV DNA viral load in HBV/HIV coinfecting patients who used the drug as part of their anti-HIV regimen. In the French study, one-third of patients achieved undetectable HBV viral loads. Importantly, tenofovir was effective in patients with lamivudine-resistant HBV.

**OTHER REPORTS**

Confirming that chronic HCV and HBV progress more rapidly in people coinfecting with HIV, M.A. von Wichmann and colleagues (abstract V-782) reported that coinfecting patients had a short survival time once they develop ascites (accumulation of fluid in the abdomen), a symptom of decompensated cirrhosis. In patients with chronic viral hepatitis alone, the median survival period with decompensated liver disease is five years. This retrospective review of medical records from 43 HIV positive patients (41 coinfecting with HCV and 12 with HBV), revealed a median survival period of 123 days. Notably, this group had relatively advanced HIV disease, with a median CD4 cell count of 187. Centers that do liver transplants for HIV positive peo-

ple generally prefer patients with at least 200 CD4 cells.

A.A. Butt and colleagues (abstract H-1715) analyzed medical records from 33,280 HIV positive U.S. veterans and 38,232 veterans with HCV, and reported that those who were coinfecting with HIV and HCV were significantly more likely to develop diabetes. The results are not surprising, since it is known that both HCV and certain HIV drugs are associated with higher diabetes rates. In this study, older age and being African American or Hispanic were also associated with increased risk for diabetes (notably, other risk factors including obesity and family history of diabetes were not recorded). The results suggest that healthcare providers should be vigilant in screening coinfecting patients for diabetes.

C. Wang and colleagues (abstract V-773) reported that people with higher HCV viral load were more likely to have HCV in their saliva. The researchers collected saliva from 12 volunteers for 21 consecutive days, and found HCV in 21% of the samples. No one with an HCV viral load below 1 million copies had evidence of the virus in their saliva.

In addition, people who brush their teeth less often, and those whose gums bleed when they brush (a sign of gum disease) were more likely to have HCV in their saliva. Although the study does not directly provide information about HCV transmission, it does reinforce recommendations about maintaining good oral hygiene and not sharing toothbrushes.

ICAAC web site:

<http://www.icaac.org/ICAAC.asp>

ICAAC coverage:

[www.hivandhepatitis.com/2003icr/43\\_ICAAC/main.html](http://www.hivandhepatitis.com/2003icr/43_ICAAC/main.html)

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