

Report from DDW 2005

– Part 3



Alan Franciscus, Editor-in-Chief

HCV TREATMENT RESPONSE AMONG ASIANS

There are many factors that influence HCV treatment response. It is well known that genotype, viral load, body weight, degree of fibrosis and adherence to HCV medicines are important factors that affect treatment response. It is also known that some racial or ethnic groups respond better to treatment than others. For example, African Americans do not respond as well to HCV medicines as Caucasians. In some small studies it has been shown that Asians may respond better to treatment than other racial or ethnic groups. A study released at DDW may shed some light on the difference in treatment response between Asians and Caucasians.

In a retrospective study by S.B. Missiha and colleagues 472 previously untreated patients from a large multicenter trial were analyzed to determine the predictors to sustained virological response (SVR – undetectable HCV RNA (viral load) during and at least 24 weeks after the completion of therapy). All the treated patients received peginterferon alfa-2a (Pegasys-180 µg – once a week) plus ribavirin (800 mg/day). It should be noted that now the standard dose of ribavirin

is higher for genotype 1 patients – 1000/1200 mg).

The analysis found that 47.5% of the 417 Caucasians and 67% of the 55 Asians achieved an SVR ($p = 0.0022$). Breaking it down by genotype it was found that in patients with genotype 1, 65% of the Asian group achieved an SVR compared to 35% of the Caucasian group. Interestingly, there were no differences in SVR rates in both groups when it came to people with genotypes 2 or 3.

The authors noted that Asians achieved 80% of ribavirin dose accumulation due to lower body mass index or weight which would in part explain the higher response rates in Asians. However, even after taking into consideration the lower weight of the Asian patients there was a dramatic difference in SVR among the genotype 1 patients between the two groups. It was concluded by the authors that their analysis suggests that there is a genetic or racial influence in treatment outcome between Asians and Caucasians.

U.S. VETERANS

Diabetes & HCV

More and more evidence is



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pointing to a link between hepatitis C and diabetes mellitus (type II diabetes). Although the direct link between HCV and type II diabetes has not been proven, many studies have found a higher prevalence of type II diabetes in people infected with hepatitis C. A recent study released at DDW by V. Khurana and colleagues adds to this growing body of evidence linking type II diabetes and HCV.

Data using the VISN 16 Veteran's Administration database of 480,306 veterans was analyzed. The patient characteristics of the veterans were 91.7% males with an average age of 61.1 ± 14.8 years. A total of 103,256 (21.5%) of veteran patients had type II diabetes and 14,021 (2.92%) of these patients had HCV infection. Based on the analysis the researchers found that HCV infection was a significant risk factor for type II diabetes. Other co-factors in this population for increased risk of type II diabetes include age and body mass index – all known co-factors for type II diabetes.

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Liver Steatosis: *Recent Research*



Liz Highleyman

Steatosis – also known as fatty liver – is a condition in which lipids, or fats, accumulate in the liver. Fatty liver is common in people with chronic viral hepatitis. While estimates vary, it is thought that perhaps half of patients with hepatitis C have steatosis, and the risk is significantly higher for those with genotype 3 HCV. Recent studies have found steatosis rates of 30-50% for individuals with genotype 1, 60-80% for those with genotype 3, and 40% for HIV/HCV coinfecting patients.

Steatosis can also occur in people without viral hepatitis, especially those who are obese or heavy drinkers of alcohol. (The combination of steatosis and liver inflammation in people who do not drink heavily is called nonalcoholic steatohepatitis, or NASH.)

The symptoms of steatosis are non-specific (including elevated liver enzyme levels), and many people with steatosis are asymptomatic. As with fibrosis, the definitive way to diagnose steatosis is by way of a liver biopsy.

Because steatosis contributes to the progression of liver fibrosis, increases the risk of hepatocellular carcinoma (liver cancer), and inhibits response to hepatitis C

treatment, experts have devoted increasing attention to understanding the causes of fatty liver and how to prevent or manage it. Several recent medical journal articles have reported on steatosis in people with chronic viral hepatitis.

What Causes Steatosis?

The cause of steatosis is not completely understood, but the condition is associated with a metabolic syndrome characterized by high body mass index (a measure of obesity), altered blood fat levels

“The symptoms of steatosis are non-specific (including elevated liver enzyme levels), and many people with steatosis are asymptomatic.”

(e.g., triglycerides, cholesterol), elevated blood glucose (sugar), insulin resistance, and type II diabetes. In the July 2005 *Journal of Hepatology*, Adam Gordon and colleagues from Australia reported on a study of 74 hepatitis C patients and 17 hepatitis B patients who underwent liver biopsy. They found that waist circumference, the presence of serum C-peptide (a byproduct of insulin production), and genotype 3 HCV were all independent predictors of steatosis grade.

A study by Laetitia Fartoux and colleagues published in the July 2005 issue of *Gut* found that steatosis patients with genotype 1 had greater insulin resistance than those with genotype 3, suggesting that insulin resistance is a cause – rather than a consequence – of steatosis and fibrosis in individuals with that genotype. Other research suggests that insulin resistance may be linked to steatosis even in individuals who are not overweight. And, as reported by R. D’Souza in the July 2005 *American Journal of Gastroenterology*, insulin resistance itself is associated with fibrosis progression and poor response to hepatitis C therapy.

Adding to the evidence, Elizabeth Powell and colleagues reported in the July 2005 issue of *Hepatology* that steatosis acts as a cofactor promoting liver damage in people with chronic hepatitis C, heavy alcohol use, or other types of liver disease. They noted that the mechanism of liver injury in obesity-related steatosis appears to involve a number of different pathways, including oxidative damage, increased susceptibility to apoptosis (programmed cell death), and altered liver cell regeneration.

In the May 2005 issue of the same journal, Nicole Seidel and colleagues reported data from a study showing that among HCV positive people, caspase (an enzyme that regulates apoptosis) activity was

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HealthWise:

Pharmacology Made Simpler



Lucinda K. Porter, RN, CCRC

Reading drug product information (PI) was the subject of last month's Healthwise column. Part of taking medication is knowing how to read the fine print. Some basics were covered last month. Using the two major hepatitis C (HCV) drugs, ribavirin (COPEGUS® and REBETOL®) and peginterferon-alfa (PEGASYS® and PEG-Intron®) as examples, this month's column will discuss more complicated terms and concepts and try to simplify them.

The *description* is one of the first sections in the prescription information.¹ PEG-Intron's® PI gives us the scientific name of the drug, peginterferon-alfa-2b, along with chemical information. It tells us that it is a white or off-white powder, a protein, and that it was genetically engineered. Other ingredients that are mixed in with PEG-Intron® are listed. These additives help stabilize a drug or make it more usable by the body. We are told the weight and that PEG-Intron® is a subcutaneous medication, meaning that it is given by injection into the layer of fat near the surface of the body. We also see that PEG-Intron® is sold in two different forms, one of which is the Redipen®. The different strengths are listed. It needs to be reconstituted, which means mixed with water, which is supplied. Also helpful to know is that after the drug has been reconstituted there is a little more in the vial than is actually used in order to ensure accurate dosing.

The PI for COPEGUS® tells us that the scientific name is ribavirin. We are told that ribavirin is a *nucleoside analogue* with *antiviral activity*. This tells us how the drug is classified, much as oranges are classified as citrus fruit. The formula for COPEGUS® is described and illustrated. The weight and ingredients of COPEGUS® are mentioned. We are told that it is a pill, what it looks like and that it is to be taken orally (by mouth).

Listed next in the PI for both brands of ribavirin is

the *mechanism of action*, or how the drug works. We are told that ribavirin is combined with interferon to treat HCV but we really do not know how it works.

Clinical Pharmacology is the next section. Two major sub-headings of pharmacology are *pharmacodynamics* and *pharmacokinetics*. Pharmacodynamics is about what a drug does to our body. Pharmacokinetics is what the body does to the drug.

In the PIs for both peginterferons we are told how this drug acts in a test tube, known as *in vitro*. *In vivo* tells us how the drug works in people. In both cases, we learn that peginterferon seems to have a number of biological actions. The pharmacodynamic section of PEG-Intron® gives some description of how the body is stimulated. Some proteins and body temperature increase; platelets (the part of our blood that helps us clot) and white blood cells (part of our immune system) temporarily decrease. The importance of this is not known in either PEGASYS® or PEG-Intron®.

Pharmacokinetics (PK), how drugs behave once they are in the body, has four parts:

1. *Absorption* – The process of how the drug is absorbed in the body.
2. *Distribution* – Where the drug is distributed after it enters the body.
3. *Metabolism* – How the drug is broken down by the body.
4. *Elimination* – How the drug leaves the body.

PK information is hard to read. To the untrained, the terms are complicated and abbreviations are used. If you do not have a good working knowledge of science, the information has no frame of reference. However, there are some basic concepts that are useful to know and that you can ask your medical provider. These are:

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The authors noted that there were limitations in their retrospective study but that the strength of the database (the number of people) analyzed helped to overcome some of the limitations. The authors concluded that HCV infection is associated with a 48% increased risk of having type II diabetes after controlling for age and body mass index (BMI).

Treatment in Veteran Centers

U.S. Veterans are one of the largest populations infected with hepatitis C. Fortunately, VA medical centers offer a wide spectrum of services for HCV infected veterans. However, there are many barriers to HCV treatment such as active

injection drug use, alcohol abuse, uncontrolled illnesses, housing and other issues. Furthermore, even after some of these barriers to treatment are removed there are many patients who do not seek HCV treatment. Others still are good treatment candidates who initially seek treatment but later decide that they do not want to be treated.

A study by Sue L. Currie and colleagues reviewed data from 24 VA Medical Centers throughout the United States between December 1999 and December 2000 to examine site variations in the number of people who are HCV treatment candidates who may initially agree to treatment, but who later decide not to start treatment.

Data from 4,084 patients was analyzed from 17 out of the 24 VA Medical Centers.

Patient Characteristics

Age, year (IQR)	49.0 (46-53.0)
Male gender	97.2%
Ethnicity	
Caucasian	56.6%
African-American	29.4%
Hispanic	9.5%
Served during Vietnam Era	76.7%
≤12 years of education	47.1%
Income \$10,000 or less	39.0%
Consumed 3 or more drinks/day	73.6%
Injection drug use	60.0%

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Eligibility criteria included a positive HCV antibody test and HCV RNA test (viral load), older than 18 years of age, a U.S. veteran receiving medical care at one of the participating study sites, previously untreated and under consideration for HCV treatment with IFN alfa-2b (standard interferon) and ribavirin.

Each study site had a trained hepatologist or liver specialist, and the patients were evaluated for HCV treatment candidacy using standardized criteria. In addition, each site had a dedicated study staff and HCV treatment resources available to the patients.

For patients who were considered HCV treatment candidates, data was collected on those who were offered treatment, including their acceptance, and whether or not treatment was actually started.

It was found that 32.2% of the participants were candidates for treatment according to standardized criteria and 40.7% were treatment candidates in the opinion of the treating clinician. The most common reasons for not being treatment candidates included ongoing recent substance use (20.2%), pre-existing psychiatric conditions and comorbid (existing) medical disease (17.9%).

Out of the 4,084 study participants, 1,624 patients were offered treatment. However, 377 (23%) patients declined to be treated. The most common reasons for delaying treatment were deferring treatment until a later date (51.4%) and concern about side effects (23.0%).

Of the 1,247 patients who agreed to treatment only 721 (58%) actually enrolled in treatment. Of the patients who initially agreed to be treated, 526 (42%) did not initi-

ate treatment.

The data was further analyzed by individual VA Medical Centers. The potential barriers including absolute contraindications to treatment, lack of local resources available to support patients on therapy and patient unwillingness to be treated were teased out in order to analyze the variation of treatment initiation among the participating VA sites. The participating sites were compared (17 of the 21 sites) and it was found that there was a statistically significant variation in treatment initiation rates among the VA Medical Centers – one site was found to be 12.5 times less likely to treat.

The authors concluded that “[s]trategies should be developed to improve initiation rates and reduce such significant variations in care.”

TREATMENT OF HCV-RELATED LYMPHOMA

People infected with the hepatitis C virus are at an increased risk for non-Hodgkin’s lymphoma (NHL). In fact, one recent study reported that people with hepatitis C are more than twice as likely to develop NHL as people in the general population. The standard treatment for NHL is chemotherapy, but it is less clear what the treatment should be for HCV-related NHL. In general, treatment of many of the extrahepatic diseases associated with HCV is with interferon with or without ribavirin. Some evidence exists to support this strategy with HCV-related NHL and a study recently released will add to the growing body of evidence to support the use of interferon (with or without ribavirin) for the treatment of HCV-related NHL.

J.P. Gisbert and colleagues recently analyzed 16 therapeutic studies where interferon with or without ribavirin was given to

HCV-infected patients with lymphoproliferative disorders (mainly low-grade, but also intermediate/high grade non-Hodgkin’s lymphomas) that included 65 HCV positive patients. The analysis found that 75% of the patients treated with interferon (with or without ribavirin) achieved a complete remission of the NHL. Of note, it was found that hepatitis C negative patients did not respond to the interferon therapy indicating that the effects of interferon on NHL was probably due to the eradication of HCV rather than interferon having a direct action against NHL. The authors noted that larger clinical trials are needed to determine the role of interferon plus ribavirin therapy for the treatment of NHL in people with HCV, but that the current therapy to treat HCV also appears to be an effective treatment of NHL in this patient population.

HIV/HCV COINFECTION

HCV Treatment and the Risk of Anemia

Liver disease has become a leading cause of hospitalization and death in people coinfecting with HIV and hepatitis C. In general HCV disease progression is faster in someone with both HIV and HCV. For this reason treatment of HCV may be more urgent in some patients coinfecting with both diseases. However, HCV treatment can cause anemia which is further complicated by the fact that people with HIV are at a higher risk for developing anemia.

The risk of HCV treatment induced anemia was examined in a small study of 89 HIV/HCV coinfecting patients by A. J. Uriel and colleagues. In this HCV re-treatment study (HRN 004), study participants were given pegylated

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interferon alfa 2a (Pegasys) plus optimized weight based ribavirin. The incidence of severe anemia (Hb (hemoglobin) < 10 g/dl), ribavirin dose reduction and treatment cessations due to anemia during the first 24 weeks of therapy were recorded to investigate the risk factors for the fall in Hb while on therapy.

The mean age was 48.5 years old, 84% were male, 87% had HCV genotype 1 or 4 and the median HCV RNA (viral load) was 694,812 IU/mL. The median CD4 count was 539 cells/mm³, 85% of the patients were on ART (anti-retroviral therapy), and 30% were on zidovudine (AZT). The median ribavirin dose was 13.1 mg/kg/day. The mean baseline Hb was 14.7 with a mean fall in Hb by week 8 of therapy of 2.63g/dl with a mean time to Hb nadir (lowest point) of 4 weeks. Using an intent to treat analysis of outcomes at week 24 of treatment, 12.5% of patients had a fall in Hb to < 10g/dl, 18% required a ribavirin dose reduction, and three patients discontinued therapy due to anemia. It was found that the ribavirin dose was not a significant predictor of anemia.

The authors concluded that the incidence of severe anemia was similar to that reported in the HCV mono-infected population and that only 3% of the patients required discontinuation of therapy due to anemia. Factors associated with increased risk of anemia included male gender, the use of AZT, and abnormal renal parameters. The authors recommended closer monitoring of these patients. Due to the higher rate of anemia in people taking AZT, the investigators recommended that HIV/HCV coinfecting patients should be switched to a

non-AZT containing regime before starting HCV therapy.

Steatosis

Steatosis is defined as fatty infiltrates of the liver and is a common finding for people infected with hepatitis C. For more information about steatosis in people with hepatitis C, see "Liver Steatosis: Recent Research" which appears in this month's newsletter.

A study by I. Gaslightwalla and colleagues comparing the development and severity of steatosis between HCV mono-infected patients and HIV/HCV coinfecting patients was reported at DDW. Seven hundred and eight patients were enrolled in this study - 154 patients with HIV/HCV and 554 with HCV alone. The mean age was 50.3 years old in both groups and there were no differences between the two groups in age or gender, although the coinfecting patients were more likely to be black (61.7% vs. 40.1%, $P < 0.001$) and weigh less (78.2 vs 88.4 kg, $P < 0.001$). In the coinfecting patients, the median CD4 count was 429 cells/mm³, 50.6% had undetectable HIV RNA (viral load), and 84.4% were taking HAART (highly active antiretroviral therapy). The steatosis was scored 0 (no steatosis), 1, 2, 3,) using the Brunt system.

Comparing the fibrosis score it was found that the coinfecting patients had more severe fibrosis (stage 3/4) - 43.6% vs 30.0%, ($P < 0.001$) and that steatosis was more common in the coinfecting group - 72.1% vs 52.0%, ($P < 0.001$) when compared to the HCV mono-infected group.

The steatosis score (0, 1, 2, 3) was significantly more severe ($P < 0.001$) in the coinfecting group (27.9%, 24%, 37%, 11%) than in the group with HCV alone (48%, 31.8%, 17.1%, 3.1%). It was also

found that the coinfecting patients were more likely to have a mixed or extensive steatosis compared to the HCV mono-infected patients.

Among the coinfecting group, the prevalence of steatosis was more common in patients with CD4 counts less than 350 cells/mm³ (83.1% vs 64.0%, $P = 0.009$), but there was no difference in the steatosis between patients with or without HIV RNA (viral load) or between the patients taking or not taking HAART.

The authors concluded that steatosis was significantly more common and advanced in coinfecting patients than in the HCV mono-infected.



PARTNERSHIP FOR PRESCRIPTION ASSISTANCE (PPA)

A new service was recently launched to help determine which patient assistance programs patients who lack prescription coverage may be eligible for in order to receive prescription coverage. This service is for all medications, but patients and providers who have questions regarding prescription coverage of hepatitis C medication can contact PPA for information on eligibility for hepatitis C medications. The manufacturers of pegylated interferon, Roche and Schering are members of PPA.

The program is available in English and Spanish and can be accessed on the web: <https://www.pparx.org>, or by calling 1-888-4PPA NOW (1-888-477-2669).



STEATOSIS

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greater in individuals with steatosis compared to those without. M. Romero-Gomez and colleagues reported in the May 2003 *American Journal of Gastroenterology* that levels of serum leptin (a hormone produced by fat cells that helps regulate body weight and metabolism) were higher in genotype 1 HCV patients with steatosis. Another fat-cell regulatory hormone, adiponectin, may also play a role in steatosis.

ROLE OF GENOTYPE 3

It is not yet clear how HCV contributes to the development of fatty liver, but the risk is greatly increased in people with genotype 3. Research suggests that metabolic cofactors play a more important role in the development of steatosis in people with genotypes other than 3; in the case of genotype 3, the risk of steatosis is elevated even in patients lacking these other cofactors.

Further, as reported by Thierry Poynard and colleagues in the July 2003 issue of *Hepatology*, sustained virological response (SVR) to interferon-based hepatitis C therapy can

lead to the reduction or even resolution of steatosis in patients with genotype 3, although this effect is typically not seen with genotype 1. Interestingly, a laboratory study conducted by K. Abid and colleagues (reported in the May 2005 *Journal of Hepatology*) revealed that while various HCV genotypes induced lipid accumulation in human liver cells, the effect was most pronounced with genotype 3a (about three times more fat accumulation than genotypes 1b or 3h).

However, as Gordon's team noted, increased steatosis grade is associated with increased fibrosis progression even in individuals with genotypes other than 3. Fartoux's study in *Gut* confirmed that while steatosis and fibrosis were more severe overall in individuals with genotype 3, severe steatosis was linked to worse fibrosis progression regardless of genotype.

STEATOSIS AND TREATMENT RESPONSE

Looking at response to hepatitis C treatment, S. Harrison and colleagues examined the medical records of 84 HCV patients in St. Louis who had evidence of significant (> 33%) steatosis or steatohepatitis, as well as 231 HCV positive patients without fatty liver;

results were reported in the June 2005 *Clinical Gastroenterology and Hepatology*. In the steatosis group, the overall SVR rate was 28%, compared with 44% for the non-steatosis group. Among patients with genotype 1, the respective rates were 23% vs 34%; in those with genotypes 2 or 3, the SVR rates were 42% and 78%. The authors noted that fatty liver had a detrimental effect on treatment response independent of body weight, and concluded that, "[o]verall SVR for patients with HCV and significant steatosis or [steatohepatitis] is considerably lower" than for HCV patients without the condition.

Likewise, in a study reported in the February 2005 *European Journal of Gastroenterology*, K.C. Thomopoulos and colleagues analyzed data from 116 chronic hepatitis C patients at a Greek hospital treated with either conventional or pegylated interferon plus ribavirin. Steatosis was present in about 45% of the subjects, and was associated with high body mass index. About 66% of subjects with no steatosis achieved SVR, compared with about 38% of those with any degree of fatty liver, leading the authors to conclude that steatosis was

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DONOR REGISTRY: NEW YORK

Did you know that after you die your skin can help burn victims? Your corneas can give sight to two people. In New York alone, more than 7,000 people are on the organ transplant waiting list. Hundreds of thousands more need tissue transplants. Your organs can save up to 8 lives and the donation of tissue can improve 12 lives. That is 20 lives you can help after you have died.

You can help people now while you are alive by arranging to donate tissue and organs upon your death. Residents of the state of New York can do this by calling the New York State Organ and Tissue Donor Registry at 1-866-NYDONOR (1-866-693-6667) or online at: www.health.state.ny.us/nysdoh/donor. Discuss your wishes with your closest family members and friends.

HEALTHWISE

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- How long will it take before the drug starts to work?
- When will it be at its peak?
- How long does it take the drug to leave the body?
- Should I take this drug with or without food?

A few more terms may be helpful. You will not always find information that will tell you what you want to know in an understandable form. However, occasionally these terms will be mentioned and some of them are used in the remaining article.

- *Half-life or terminal half-life* ($t_{1/2}$) – Length of time for one-half of a substance to be eliminated from the system. A short half-life is 4 to 8 hours and a long half-life is over 24 hours.
 - *Peak* – When the drug is at its highest in the blood.
 - *Trough* – When the drug is at its lowest in the blood.
 - *Bioavailability* – What percentage of the drug is available to be used after it enters the body.
 - *Clearance* – The elimination of a substance from the body.
 - *Steady state* – When the drug stays at a constant level in the body.
 - *Therapeutic Index (TI)* – This is a ratio between the average effective dose and the average toxic dose. The closer the ratio is to one, the greater the risk a drug can be toxic (potentially poisonous).

Looking at the pharmacokinetics section for PEG-Intron®, we learn that after a single dose, it takes about 4.6 hours for the drug to be

absorbed into the body. It reaches its maximum level in the blood in about 15 to 44 hours. This is sustained for 48 to 72 hours before the level starts to drop. After multiple doses, there is an increase in the bioavailability of PEG-Intron®. The average half-life is about 40 hours (ranges between 22 and 60). In short, half the drug is eliminated in about 40 hours. About 30% of the drug is eliminated through the renal system (kidneys). There is also information in this section that compares PEG-Intron® to the older form of interferon.

Looking at the pharmacokinetics section for COPEGUS®, we learn that after multiple doses and in combination with Peginterferon alfa-2a, it takes about 2 hours to reach its maximum level in the blood. COPEGUS® accumulates after multiple doses and the steady state is four times higher than that of a single dose. The average half-life is about 120 to 170 hours. Ribavirin is more bioavailable if taken with a high fat meal. It is not known how Copegus® is metabolized or eliminated.

Congratulations if you made it to the end of this article. Hopefully you learned something new. In time, technical information such as this will start to make more sense.

¹As was noted last month, the first information contained in the PI's for the hepatitis C treatment drugs is called black box information. Not all drugs have this.

PRIMARY CARE GUIDE

The Hepatitis C Support Project is very excited to announce a new educational tool recently posted to the HCV Advocate Web site:

Management of Hepatitis C by the Primary Care Provider: Monitoring Guidelines, by Drs. David H. Winston, M.D., PACP and Donna C. Winston, PhD, NP.

This comprehensive guide is the perfect tool for anyone working in hepatitis C. It was written to help guide providers and patients in the task of medically managing hepatitis C. Topics in the "Guide" include:

- * The HCV Virus
- * Natural History of HCV
- * Screening for HCV
- * Evaluating Patients with HCV
- * Counseling Patient with HCV
- * Treatment of HCV
- * Side Effect Management

This publication is the result of a joint venture by the Hepatitis C Support Project and the National Partnership for Wellness.



STEATOSIS

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“a strong independent factor for treatment failure.”

In another study by Fartoux and colleagues, published in the January 2005 issue of *Hepatology*, the researchers compared paired liver biopsy samples taken an average of 61 months apart from 135 untreated hepatitis C patients with initially mild liver damage (METAVIR scores of F0 or F1). Statistical analysis revealed that steatosis was the only factor independently associated with fibrosis progression. Although experts traditionally have not recommended hepatitis C therapy for patients with mild liver disease, the authors suggested that since steatosis is “a major determinant of the progression of fibrosis,” patients with steatosis and mild hepatitis C should be considered for treatment.

LIFESTYLE CHANGES CAN HELP

Fortunately, a healthy diet, exercise, and weight loss (or maintenance of a healthy weight) can help reduce and possibly eliminate steatosis. For example, Mary Ann Huang and colleagues reported in the May *American Journal of Gastroenterology* that an intensive program of nutritional counseling designed to promote weight loss and reduce insulin resistance led to histological (tissue health) improvements in patients with NASH. Among 15 subjects who completed the year-long dietary intervention and underwent paired liver biopsies, patients who showed improved liver histology scores had a significantly greater reduction in weight, waist circumference, AST and ALT levels, and steatosis grade. As Powell’s team concluded, “[a]ctive management of obesity

and a reduction in steatosis may improve liver injury and decrease the progression of fibrosis.”



NEW: PATIENT EDUCATION CENTER

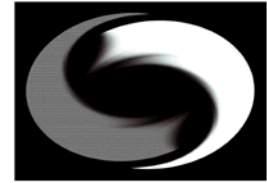
A new Patient Education Center has been launched on HCSP’s Web site (www.hcvadvocate.org) to complement our current on-line education center featuring CME and CEU web-based courses.

The launch of the Patient Education Center features the first in a series of self-paced study courses about hepatitis C. The first course is titled “A Basic Overview of HCV” and features a voiceover narration as well as text to follow along with the slide presentation. People who complete the on-line course will be issued a certificate of completion.

We would be very interested in your feedback to help with the design of future courses.

To access the module, go to http://www.hepeducate.org/pe_test/pe_course_list.php, or you can click on the Patient Education button on the front page of the Advocate website

Registration is required in order to access the on-line center. All registrant information is *strictly* confidential.



HEPATITIS C
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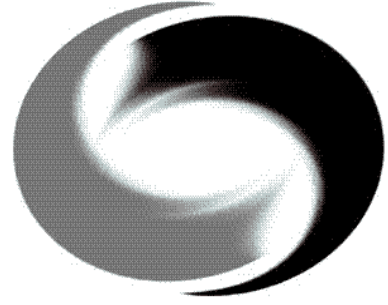
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