



A NEWSLETTER FOR THE HALT- C TRIAL

# HALT-C NEWS

Hepatitis C Antiviral Long-term Treatment against Cirrhosis

June 2002 Volume 2, Number 2

## TIPS FOR MANAGING SIDE EFFECTS

From the Coordinators at Saint Louis University

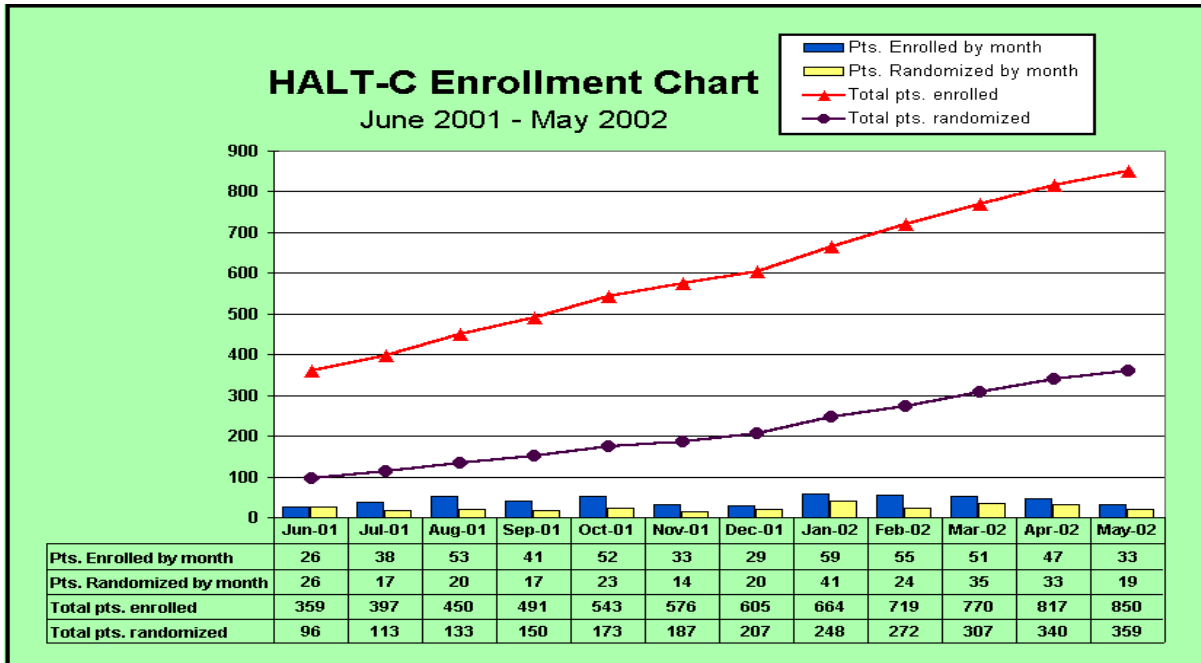
Below is a partial list of possible side effects of your therapy. Our patients have found the following suggestions to be helpful. Many thanks to Rhonda Hageman, NPC for her input.

- 1) Flu-like symptoms including fever, chills, headache, muscle aches, and fatigue.
  - a) One hour before your injection, take acetaminophen or ibuprofen. Consult your healthcare provider for dosing and daily limits.
  - b) Drink 24 ounces of water before your injection to combat dehydration.
- 2) Fatigue – symptoms include feelings of tiredness or weakness, poor memory or difficulty with concentration, becoming easily upset, feeling a lack of motivation.
  - a) Get enough rest (6 to 10 hours each night).
  - b) Continue or start light daily exercise. Weight bearing exercise, such as walking, helps

reduce muscle loss. (Muscle loss can cause increased fatigue).

- c) Drink plenty of fluids (without caffeine or alcohol).
  - d) Try drinking shakes made with protein powder.
  - e) Take a short “cat nap” in the afternoon.
  - f) You may need to alter your work schedule.
  - g) Laugh – Read a funny book, watch cartoons or a funny movie.
- 3) Irritability and depression – Signs of depression including feelings of deep and constant sadness, hopelessness, crying, major changes in mood, loss of interest in things you enjoy, trouble concentrating.
    - a) Learn relaxation and stress management techniques.
    - b) Avoid stressful situations if possible.
    - c) Include light exercise in your daily routine.
    - d) Laugh – Read a funny book, watch cartoons or a funny movie.

*Continued on page 3.*



# ISSUES OF INTEREST

Current topics from experts in the field

## LIVER BIOPSY AND THE HALT-C TRIAL

By Jules L. Dienstag, M.D.

Massachusetts General Hospital

Each of you has already undergone at least one liver biopsy, and many of you have suffered through this ordeal several times. Truth be told, your physicians who perform these biopsies do not enjoy putting you through this any more than you relish having the procedure done. Ultimately, however, the liver biopsy is felt to represent the “gold standard” for assessing the degree of liver injury and inflammation (grade) and the amount and pattern of liver scarring or fibrosis (stage). In persons with chronic hepatitis C, a liver biopsy is obtained typically before the initiation of antiviral therapy. This initial biopsy is usually part of an initial evaluation and provides information about injury and scarring that have occurred during the previous years of hepatitis C virus infection. In addition, knowing the degree of injury and scarring is helpful in predicting the future course of chronic hepatitis C and in providing some indication of the likelihood of a response to antiviral therapy. Of course, the liver biopsy is not the only important clinical indicator-predictor; however, when combined with such information as symptoms, findings on physical examination, laboratory tests on blood samples, and virologic features (level of HCV RNA and viral genotype), the liver biopsy rounds out a comprehensive assessment.

Chronic hepatitis C tends to be very slowly progressive, and this means that, for many of you, this liver disorder took many years to progress to its current level. Similarly, we expect the rate of clinical progression to be just as subtle and slow during the duration of the HALT-C Trial. Although we will collect information about clinical deterioration, we anticipate that most of what we will be measuring during your four years in the trial will be the rate of progression in your liver biopsies.

What can we tell from a liver biopsy? The core of tissue obtained at the time of a liver biopsy may measure only approximately a millimeter across and a few centimeters in length (1 inch = 2.2 centimeters), and it represents such a small fraction of the entire liver that it is not missed. Still, these biopsies provide a representative snapshot of inflammation, injury, and scarring (“fibrosis”) in the liver. Actually, the level of inflammation and injury tends to be uniform throughout the liver, while the degree of scarring can vary considerably throughout the liver; therefore, certainty about stage of scarring is limited somewhat by “sampling error.”

For you to understand what we look at, here is a quick

primer on microscopic liver structure, arranged into “lobules” (Figure 1).

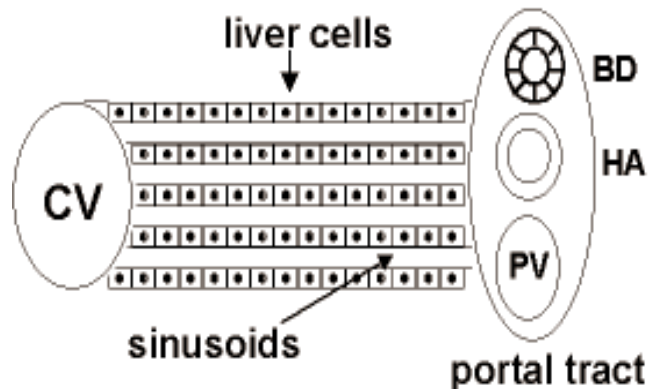


Figure 1.

The portal vein (PV) that carries blood with nutrients from the intestine and the hepatic artery (HA) that carries oxygenated blood from the lungs and heart both enter the liver in a structure called the portal tract. In addition to these “feeding” blood vessels, the portal tract contains the bile duct (BD), which carries bile (a detergent that helps us digest fat) made in the liver out into the gall bladder and intestines. Emanating like three-dimensional spokes of a wheel from the portal tracts are the liver cells arranged in neat cords surrounded by vascular structures called sinusoids, and these sinusoids feed into the central zone of the liver lobule. The central zone of the lobule contains the central vein (CV), which carries venous blood (after delivery of oxygen to the liver cells, after delivery of nutrients to the liver cells) back to the large blood vessels that return to the heart.

Each of the features of the biopsy - inflammation, liver cell injury, scarring - is assessed by an experienced pathologist and scored numerically. Inflammation and injury of liver cells are assessed in the portal tract, in the area of liver cells bordering the portal tract (“periportal” region), and in the area of liver cells between the portal tract and central vein. We use a scale of 18 points for these indicators, and these features represent the degree or “grade” of liver injury and inflammation. For the purposes of the HALT-C Trial, however, we are interested more in the “stage” of the liver disease than in the “grade” of inflammation. Although several numerical scales exist, the HALT-C Trial investigators have chosen a six-point scale for measuring scarring or fibrosis (Table 1).

*Continued on next page.*

## (Liver Biopsy continued.)

Table 1. Fibrosis scoring system

Score	Description of Fibrosis
0	No fibrosis
1	Fibrosis expanding some portal areas
2	Fibrosis expanding most portal areas
3	Fibrosis that forms a bridge between a few portal areas
4	Fibrosis that forms a bridge between many portal areas
5	Fibrosis that demarcates incomplete nodules of liver tissue (early or incomplete cirrhosis)
6	Sufficiently extensive fibrosis to demarcate many complete nodules of tissue and to alter the normal architecture of the liver (cirrhosis).

To be included in the HALT-C Trial, potential subjects must have had at least stage 3 fibrosis in a biopsy done prior to treatment in the HALT-C Trial, and the question we are trying to answer is whether long-term treatment can prevent or slow down the progression of fibrosis. Therefore, we will be re-evaluating liver biopsies every two years during the trial to see whether any difference in progression of fibrosis occurs between the treated and untreated group.

Liver biopsy would be less important were other clinical or laboratory tests available that could predict reliably the stage of fibrosis; however, to date, no such surrogates have been validated. In the future, potentially, new biochemical tests or even genetic tests might become available with which to measure fibrosis without the need for liver biopsy, and we hope to use serum and tissue obtained during the HALT-C Trial to validate one or more of these approaches when they become available. In addition, we will be asking you to give us permission to track down and evaluate all the previous liver biopsies you had prior to your joining the HALT-C Trial, and we will use these comparisons to define the rate of progression of fibrosis over time in chronic hepatitis C.

Finally, many of you have given permission to have genetic information (DNA) extracted from your blood cells and liver tissue during the HALT-C Trial. Techniques are being developed now that may allow us to look for genes that distinguish between study participants in whom fibrosis progresses and those in whom fibrosis remains stable (or even improves). Therefore, the amount of information that we can learn from the liver biopsies obtained during the HALT-C Trial could be magnified many times over and provide answers to very fundamental questions about the factors that promote scarring in the livers of persons with hepatitis C.

## Tips for Managing Side Effects Continued.

- e) Become a volunteer to help someone less fortunate than you.
  - f) Get professional help.
  - g) If feelings of irritability or depression persist, call the office; you may need a prescription for a mild antidepressant or anti-anxiety medication.
  - h) If you experience thoughts of harming or killing yourself or others, call the office immediately.**
- 4) Loss of appetite
- a) Eat small frequent meals, even when you are not hungry and nibble on healthy snacks throughout the day.
  - c) Take a 5-10 minute walk before meals to increase appetite and decrease nausea.
  - d) Drink plenty of water and clear juices such as apple, grape, or cranberry juice.
  - e) Try protein powder shakes, liquid milkshake supplements or Carnation Instant Breakfast on days you don't feel like eating.
  - f) Plan to eat some meals while socializing with friends.
  - g) Brush your teeth and/or use alcohol-free mouthwash several times a day to help eliminate the metallic taste in your mouth. It is also helpful to chew sugar-free gum or suck on lemon candy (preferably sugar-free) during the day.
  - h) Some people have found that eating a small amount of dark chocolate, yogurt, or honey before a meal helps to reduce the metallic taste. Fresh lemon in ice water and honey in tea are also helpful.

***Look for more tips for managing side effects in the next issue of the HALT-C News!***



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**Coming next Issue:  
The staff from the University of Texas  
Southwestern**

**About Massachusetts  
General Hospital**

Founded in 1811, the Massachusetts General Hospital (MGH) is the third oldest general hospital in the United States and the oldest and largest in New England. The MGH conducts the largest hospital-based research program in the United States. It is the oldest and largest teaching hospital of Harvard Medical School. MGH is also the largest nongovernment employer in the city of Boston, with more than 16,000 employees, including a nursing staff of 2,900. In addition, its 3,700-member medical staff includes physicians, dentists, psychologists, podiatrists, residents and fellows.



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The HALT-C News is a publication of New England  
Research Institutes and is published 4 times a year.

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