



A NEWSLETTER FOR THE HALT- C TRIAL

HALT-C NEWS

Hepatitis C Antiviral Long-term Treatment against Cirrhosis

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HOW DO YOU RELAX? TIPS FOR COPING WITH STRESS

Have you been told to “decrease your stress”, “try and relax” or “rest”? The next question is usually “how do I do that?” Before we talk about how “to relax” let’s discuss different ways people respond to stress. Stress can show up in our lives in ways that we may not identify as stress. Stress is defined as both an emotional and physical feeling of “tension”. Not all people perceive stress in the same way.

Some of the ways stress may be manifested:

Emotional - feelings of being depressed, sad, agitated, irritated, disappointed in yourself and cynical.

Physical - Headaches, backaches, fatigue, upset stomach or stomach aches, dizziness, muscle aches.

Behavioral - Sleeping too much or too little, over eating or not eating, sulking, explosive anger, snapping at people, grinding your teeth, clenching your fists.

Thought process - inability to concentrate, forgetfulness, worrying, “flight of ideas”(thoughts that race through your mind-sometimes good thoughts sometime bad)

It’s important to learn and know how your body responds to stress. This is important so you can intervene and keep your stress level “under control”. We know that each person responds differently to stress. And what works for one person may not work for another. We have listed some techniques and ideas to help deal with stress. When you “need a break” try one:

- Allow yourself to relax. You don’t have to do it all, and above all Don’t Feel Guilty!
- A hot bath (or shower) with the lights off and candles burning (lock the door!).
- Treat yourself to a massage. This is definitely worth doing.
- Aromatherapy - vanilla and cinnamon scents are the best!
- Sit outside in the sunlight, close your eyes and listen. If the weather doesn’t allow this, just open up the curtains and bring a chair to the window and sit in the sunlight.
- Exercise - a short 10-minute walk will do wonders.
- Spend some time with your hobby or start one.
- Laugh - “Laughter is the best medicine”.
- Slow down-this means your talking, walking, and eating (you can act relaxed even if you’re really not).
- Stop saying yes to everything and everybody.
- Allow your family and friends to “support you and to do things for you”.
- Make sure you eat healthy foods.
- Positive thinking

Stress will always be a part of our lives. By recognizing what stress is, how it affects us, and what we can do to manage it, stress will become a small part of our lives.



ISSUES OF INTEREST

Current topics from experts in the field

HCV-RNA: WHAT IS IT AND WHY DO WE MEASURE IT?

By Adrian M. Di Bisceglie, M.D.
Saint Louis University

Patients with hepatitis C may hear a lot about measurement of HCV RNA. HCV RNA stands for “**H**epatitis **C** **V**irus **R**ibo**N**ucleic **A**cid” and refers to a measure of the hepatitis C virus in the blood. Sometimes, different terms are used for the same thing, like “viral load” and “viral count”. The virus that causes hepatitis C (the hepatitis C virus, abbreviated HCV) consists of a very small particle made of proteins which enclose a core containing its genetic information. In the case of this virus, its genetic information is contained in an RNA molecule, very similar to the DNA which carries the genetic information of humans. The other difference between HCV and human genetic material is that the hepatitis C virus has only one gene, whereas humans have many hundreds of thousands.

Detecting and measuring the HCV RNA circulating in the blood stream of someone infected with HCV has become a very useful means of diagnosing infection with this virus. That is, if HCV RNA is present, that individual is infected with HCV. A similar type of testing is commonly used to diagnose infection with other viruses such as HIV (the virus that causes AIDS) and the hepatitis B virus (HBV). Note, though, that the test for HCV RNA is quite specific. There is virtually no risk of confusing a positive test for HCV with a positive result for HIV or HBV. Occasionally we will encounter “false positive” tests where the HCV RNA is positive but the person is not really infected with HCV. This is due to technical problems with the test used and can often be resolved by repeating the testing. All patients entering the HALT-C Trial must be positive for HCV RNA to start with.

It is also possible to measure the amount of HCV RNA in a blood sample. This is different from simply knowing whether it is present or not (a qualitative assay). The amount of HCV RNA can be reported as the number of copies (i.e. the number of virus particles) or the number of International Units per milliliter of serum. More recently, there has been a trend to report results in International Units as this is more standardized between different test kits made by different manufacturers. A test which measures the amount of HCV RNA is called a quantitative test, as it gives the quantity of virus in the blood. There is a wide range in the quantities of HCV RNA that might be found, from as little as only a few hundred to as much as several million International Units.

The amount of HCV RNA in the blood stream does not

correlate with how severe the hepatitis is. Thus, patients can have very severe hepatitis on liver biopsy and have a very low viral load and vice versa. What it does correlate with, to some extent, is how well the patient responds to treatment with interferon. The number of patients who successfully clear HCV from their system when treated with interferon is lower when the viral load is more than 1 to 2 million International Units per milliliter of serum. This difference is not quite as marked when interferon is combined with ribavirin and seems to play even less of a role when it is PEGylated interferon that is combined with ribavirin. Following the viral load may be a useful way of tracking the course of treatment with interferon and ribavirin. Thus, the hope is that the levels of HCV RNA decrease promptly and become negative on treatment. Becoming negative is much more important than just having a reduction in the viral load. Becoming negative defines one as a “responder” to treatment, whether it be at the end of treatment (an end-of-treatment responder) or more than 6 months after stopping treatment (a sustained responder). For patients to be enrolled in the HALT-C Trial, they should never have previously been a responder. That is, they should never have become negative for HCV RNA in serum while on treatment.

In the HALT-C Trial, blood is drawn at frequent intervals to measure HCV RNA. This testing is done at our central virology laboratory at the University of Washington in Seattle. First, though, the blood sample is centrifuged to separate the serum from red blood cells. The serum is then stored in a freezer at the local clinical center where it was drawn. Every week, a batch of serum samples is shipped to our central repository where most of it is kept in storage, but a portion is then shipped to Seattle for testing. The laboratory in Seattle does both quantitative and qualitative tests for HCV RNA. They do this testing in batches, and it may take several weeks for the result to return to the clinical center. One key blood sample is the one drawn at week 20. It is at this time point that an assessment is made whether the patient being treated is a responder or not. If the HCV RNA test is negative, the patient continues on PEGylated interferon and ribavirin for another 6 months. If, however, the HCV RNA still tests positive, the patient is then eligible for the main part of the HALT-C Trial, and they are randomly allocated to either continue PEGylated interferon (at a lower dose and without ribavirin) or to stop treatment but remain under close observation. The lab in Seattle strives to turn the results of the week 20 testing around very quickly because it is so important.

Continued on next page.

(HCV-RNA continued.)

Answers to some frequently asked questions:

If HCV RNA becomes negative on treatment, can it come back?

Yes, this happens quite frequently. We don't know why the test becomes negative – perhaps there is a very small amount of HCV RNA in the circulation which cannot be detected by the test or perhaps a small amount of the virus remains “hidden” in the liver and then emerges when the treatment is stopped. However, if HCV RNA remains negative for at least 6 months after stopping treatment, it usually (in more than 95% of cases) remains negative and that person seems to be cured of their hepatitis C infection.

How quickly does HCV RNA become negative on treatment?

Levels of HCV RNA begin to fall within hours of receiving a dose of interferon and then continue to fall over the next few weeks in those patients who will go on to become “responders”. Our experience tells us that if the HCV RNA is not negative by 12 weeks, there is only a small chance (less than 5%) that it will still become negative. It is for this reason that we have chosen 20 weeks as a decision point in HALT-C. If HCV RNA has not become negative by this time, it is unlikely to do so.

Can I still experience any benefit of treatment even if HCV RNA does not become negative?

Yes! We know that the liver biopsies of patients on treatment show less inflammation even when HCV RNA is still present. The aim of HALT-C is to determine whether this improvement in liver biopsy translates to more long term benefit with a lower risk of developing cirrhosis or its complications.

Why are the results of my HCV RNA testing not always available when I come back for my next visit?

Testing for HCV RNA is done in a central laboratory in Washington State. Testing is done in batches so there may be a wait of several weeks or even a month or two before the results are back. Remember that two tests often have to be done – both qualitative and quantitative. Even in clinical practice, outside of a research study like HALT-C, HCV RNA is usually only measured at a few time points, typically after 24 weeks but sometimes after 12 weeks of treatment.



Match 'Em Up!

Match the numbered terms with the definitions below.

- | |
|-----------------------------------|
| 1) Alanine aminotransferase (ALT) |
| 2) Hepatitis C |
| 3) Cirrhosis of the Liver |
| 4) Hepatologist |
| 5) Jaundice |
| 6) Nonresponders |
| 7) Antibody |
| 8) Clinical Trials |
| 9) Protocol |
| 10) Ascites |
| 11) Antigen |
-
- A) Fluid, within the abdomen (belly), sometimes caused by cirrhosis.
- B) A protein molecule produced by cells of the immune system in response to a foreign body, such as a virus or bacteria.
- C) A foreign substance that the body's immune system identifies as potentially harmful, resulting in the production of antibodies to fight it. A virus protein.
- D) Carefully controlled tests that are conducted in humans to learn the effectiveness and safety of new medical products (such as all new drugs) and techniques.
- F) An enzyme released from liver cells. Levels above normal may indicate liver damage.
- G) A step-by-step procedure followed to achieve an objective, such as the strictly followed methods used in clinical trials for new drugs.
- H) A doctor who specializes in the study and treatment of liver disease.
- I) Patients who do not respond to therapy within a specified time frame.
- J) A form of hepatitis that was previously known as non-A, non-B hepatitis. The Centers for Disease Control estimates 150,000 new cases each year.
- K) A condition characterized by yellowness of the skin and eyes.
- L) The result of long-standing inflammation and damage in the liver characterized by excess formation of scar tissue, also called fibrosis.

Answers on page 4.

MEET THE STAFF FROM...

Saint Louis University

Say hello to the staff at the Saint Louis University in St. Louis, Missouri

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Coming next Issue:
The staff from Massachusetts General Hospital, Boston, MA

Side Effects: Where Do They Come From?

Interferon

Common Side Effects

Fatigue	Loss of appetite
Flu-like symptoms	Weight loss
Headache	Depression
Dizziness	Low white blood cell count
	Low platelet count

Less Common Side Effects

Diarrhea	Shortness of breath
Seizures	Hair loss
Vision Changes	Aggravation of auto-immune disorder
Itching	Impaired concentration

Ribavirin

Common Side Effects

Anemia	Nausea
Dry mouth	Skin rash
Metallic taste	Cough
Shortness of breath	May cause birth defects
Fatigue	

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Check out the HALT-C Website:
WWW.HALTCRIAL.ORG

Answers to Match 'Em Up: 1) F 2) J 3) L 4) H 5) K
6) I 7) B 8) D 9) G 10) A 11) C