Marshfield Labs™
A division of Marshfield Clinic

1000 North Oak Avenue
Marshfield, WI 54449-5795

Hepatitis C Virus [HCV]

Background

It is estimated that 4.1 million (1.6%) Americans have been infected with HCV and 3.2 million of these are chronically infected. Acute infections are often asymptomatic and chronic HCV infections may eventually lead to liver cirrhosis or carcinoma. Hepatitis C is a leading indication for liver transplants in the U.S.

Patients at highest risk for HCV include: IV drug users or any needle stick with HCV infected blood, recipients of clotting factors made before 1987, hemodialysis patients, recipients of blood and/or solid organs before 1992, patients with undiagnosed liver problems, health care workers after possible exposure and infants age 12-18 months born to HCV infected mothers. HCV testing is indicated for all of these high and intermediate risk patients.

Since August 2012, the Centers for Disease Control is recommending that everyone born during 1945 through 1965 be screened for HCV.

Testing

Four questions can typically be answered by HCV testing:

1. Has the patient been exposed to HCV?
2. Does the patient have an active HCV infection?
3. What is the recommended therapy for patients with an active infection?
4. Is the antiviral therapy effective?

Recommended Testing

1. Hepatitis C Antibody Test [HCVAB].

   Anti-HCV can be found in 70% of symptomatic patients and in greater than 90% of patients within 3 months after symptoms begin. Remember, however, that many people who have hepatitis C have few or no acute symptoms.

   A negative HCVAB indicates that the patient has not developed an immune response against HCV, however two scenarios may give rise to a negative HCVAB result in an HCV infected patient. First, the patient may be immunosuppressed and not able to mount a detectable antibody response or second, the infection may be very recent and it is too early for an antibody response to be generated. Both of these patient groups would likely demonstrate a positive HCV RNA Quantitative PCR [HCVQT] result [see below].

   If the HCVAB test is positive, we recommend the quantitative HCVQT to determine if the patient has an active infection.

2. HCV RNA Quantitative PCR [HCVQT] (The HCVAB sample cannot be used for this testing).

   HCV RNA is extracted from serum, reverse transcribed and amplified by PCR. The result of this test may also be referred to as a viral load.

   If the HCVQT result is negative, the patient's infection may have resolved. Repeat HCVQT testing should be performed in 6-12 months to confirm resolution of infection.

   Positive samples are quantitatively reported if the viral load is between 15 and 100,000,000 IU/mL. Positive samples above or below this range are qualitatively reported as positive but >1.00E+08 IU/mL or <1.50E+01 IU/mL, respectively. If the patient has a positive HCVQT and is considered a candidate for treatment, HCV genotyping should be performed to guide treatment.

HCVQT testing should be performed periodically after initiation of antiviral therapy to evaluate treatment efficacy.

3. HCV Genotyping [HCVGEN] (The HCVQT sample may be used for this testing).

   HCV RNA must be present in the sample for genotyping; therefore, a documented positive HCVQT result with > 500 IU/mL must be demonstrated prior to HCVGEN testing. The 5' untranslated region of the virus is amplified by PCR and the nucleic acid sequence determined. This sequence is compared with that of previously genotyped HCV strains to identify the viral genotype.

   Viral genotype information is used to guide antiviral therapy. In general, infection with HCV genotypes 1 or 4 are less responsive to antiviral therapy and require a longer duration of treatment than genotypes 2 or 3. Of the four most common genotypes in the U.S., genotype 1 accounts for about 72% of cases, genotype 2 for 14%, genotype 3 for 6%, and genotype 4 for 1%.

One test that is **NOT** recommended is the HCV recombinant immunoblot assay (RIBA). This assay has been supplanted by improvements in the HCV Antibody Test and the availability of sensitive PCR tests. It retains a small niche in the evaluation of blood donors that test positive with the HCV Antibody Test Ordering the HCV RIBA test requires approval of a pathologist or Clinical Ph.D.

HCV treatment decisions are further based on a number of other parameters including the patient's health, viral load and liver test results. Current treatment recommendations using the results of all patient information are beyond the scope of this document. We recommend references 1 & 2 for further testing and treatment guidelines.

References

1. Scott JD, Gretch DR. Molecular Diagnostics of Hepatitis C Virus Infection A Systematic Review. JAMA. 2007;297:724-732.
2. Centers for Disease Control Guidelines for Laboratory Testing and Result Reporting of Antibody to Hepatitis C Virus* 2003 http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5203a1.htm Accessed 2/26/08
3. Centers for Disease Control document "Chronic Hepatitis C: Why Baby Boomer Should Get Tested" Accessed 03/12/13. http://www.cdc.gov/knowmorepehatitis/Media/PDFs/FactSheet-Boomers.pdf

Contact Information

Marshfield Labs Customer Service 800-222-5835.

Questions or Comments

Please refer any questions or comments to:

- Tim Uphoff, Ph.D., Clinical Consultant
- Thomas Novicki, Ph.D., Clinical Consultant
- Gene R. Shaw, M.D., Clinical Pathologist