CONFRONTING THE NEW EPIDEMIC IN PRIMARY CARE:
DIAGNOSIS AND MANAGEMENT OF HEPATITIS C

By

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The members of the committee appointed to examine the manuscript of JENNIFER EDMINSTER find it satisfactory and recommend that it be accepted.

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Acknowledgments

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ABSTRACT

Confronting the New Epidemic in Primary Care:
Diagnosis and Management of Hepatitis C

Chair: Lorna Schumann

Hepatitis C (HCV) is the most common blood-borne disease worldwide. Most cases of hepatitis C progress to chronic disease, with a significant portion of these ending in cirrhosis, liver failure and hepatocellular carcinoma. In the United States hepatitis C results in 8,000 to 10,000 deaths annually, and this figure is expected to triple in the next twenty years. There is no effective vaccine against hepatitis C, and efforts to develop a vaccine are hampered by the high degree of mutability exhibited by the virus. Current pharmacotherapy for HCV disease is limited to interferon alpha and ribavirin, and these drugs provide long-term remission of the virus in less than 50% of cases treated. Recent advances in HCV research demonstrate improved responses with the use of pegylated interferons, which have a longer serum half-life than interferon alpha. This paper provides an overview of the natural history and clinical findings of hepatitis C infection, as well as diagnostic testing and treatment schemes currently available.
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Introduction

Hepatitis C virus (HCV) infection, called non-A, non-B hepatitis, before the virus was isolated in 1989, is a disease of the liver spread parenterally, and to a lesser extent by sexual contact (Centers for Disease Control [CDC], 1998; National Institute of Diabetes and Digestive and Kidney Diseases [NIDDK], 2000). HCV has quickly become the most common blood-borne disease worldwide (CDC, 1998). It is caused by a Ribonucleic Acid (RNA) virus of the flaviviridae family, of which there are six genotypes and over 30 subtypes or “quasispecies” (Hoofnagle, 1997). HCV Type I, the genotype responsible for about 70% of HCV cases in the United States, is the type least responsive to antiviral therapy (DiBisceglie, Everson, Herrine, Lennox & Nikias, 1998). HCV Types IV, V and VI are also less responsive to antiviral therapy.

All of the numerous quasispecies of HCV have the propensity to mutate rapidly, and the resultant diversity in genetic make-up accounts for a variable clinical course and response to therapy (DiBisceglie et al., 1998). This genetic diversity also makes it difficult for the host’s immune system to sustain a defense against the virus and renders efforts to develop a vaccine equally challenging. To date, there is no effective vaccine against HCV (Ferri, 2001), although there are antiviral treatments available with variable success in slowing progression of the disease.

In 1997, HCV infection caused 8,000-10,000 deaths. The financial expense for diagnosis and treatment was estimated at four billion dollars (DiBisceglie et al., 1998). These numbers are rapidly increasing, virtually insuring that HCV will be regularly encountered and challenging to primary care providers today and in the near future. It is currently projected that the number of HCV-related deaths will triple in the next 10-20 years (DiBiscegli et al., 1998). Primary care
providers will undoubtedly encounter patients infected with HCV and should be familiar with its diagnosis and treatment.

Epidemiology

An estimated 4 million Americans and more than 170 million people worldwide are currently infected with HCV (CDC, 1998). Prevalence rates in the U.S. are highest among African-Americans (3.2%). The prevalence rate among Hispanics is 2.1% and Caucasians 1.5% (National Institutes of Health [NIH Consensus Statement], 1997).

The group with highest risk for HCV infection is illicit intravenous drug users (Figure 1), accounting for 50-60% of cases (CDC, 1998). People who received blood transfusions or organ/tissue transplants prior to July, 1992 are at increased risk for the disease, although they constitute a relatively small number. The risk of transmission via blood transfusions has virtually disappeared since the initiation of sensitive serological screening of donated blood in 1992. No new cases of transmission from donor blood have been reported in this context since 1994 (CDC, 1998). Long-term hemodialysis patients constitute a smaller group at risk, but within this population the prevalence of HCV infection averages about 10% (CDC, 1998).

There are a small number of health care workers, emergency and police personnel who have contracted HCV through needlesticks, blood-to-mucous membrane, and blood-to-blood contact. These account for 2-4% of hepatitis C cases (De Castro et al., 1998).

A history of multiple sex partners defines another high-risk category for HCV infection. The exact relationship between this phenomenon and HCV infection is unknown, confounded by variables such as drug use and infection with other sexually transmitted diseases. Long-term sexual partners of HCV-infected persons have a slightly higher incidence of infection than the general population, particularly female partners of infected males (CDC, 1998). Sexual
transmission accounts for about 7% of HCV cases, considerably less than the transmission rates found in hepatitis B (HBV) and human immunodeficiency virus (HIV) infections (CDC, 1998).

Maternal-infant transmission of HCV occurs in approximately 5% of cases, less than in other blood-borne viral infections. Breast-feeding is not considered to be a risk factor for transmission of HCV (NIDDK, 2000).

Most perplexing is the finding that over 40% of HCV cases in the United States have no known risk factors (Klaus & Grodesky, 1998). In most of these cases there is an association with low socioeconomic status, but the exact nature of this relationship is unclear (CDC, 1998). Body piercing, tattooing, and commercial barbering have not been reported to have an association with HCV transmission in the United States, although other countries have reported such an association (CDC, 1998).

Eighty-five percent of those infected will go on to develop chronic hepatitis C, with approximately 20% of these succumbing to hepatic failure (CDC, 1998). The majority of liver transplants are due to organ failure from this disease.

Natural History

After exposure to HCV, there is an average incubation period of 7 weeks before any symptoms occur (Hoofnagle, 1997). A majority of patients (60-70%) are asymptomatic in the acute phase of illness (CDC, 1998). In approximately 15% of cases the disease is self-limiting, indicated by normal liver enzymes and the absence of HCV RNA in serum, within one year of infection (DiBisceglie et al., 1998).

In most HCV cases (75-85%) viremia persists indefinitely, producing chronic hepatitis (Hoofnagle, 1997; NIDDK, 2000). In an insidious fashion, inflammatory cells invade the liver parenchyma and portal tracts, causing inflammation of hepatocytes and necrosis with varying
degrees of fibrosis (NIDDK, 2000). In approximately 20% of HCV cases the patient develops cirrhosis, characterized by diffuse fibrosis, bridging of portal tracts and nodular regeneration of the liver (NIDDK, 2000; CDC, 1998; Friedman, 2000). Symptoms are the result of hepatic cell dysfunction, portal hypertension and shunting to the systemic circulation. Cirrhosis leads ultimately to end-stage liver failure and, barring a liver transplant, to death. Hepatitis C accounts for 30% of liver transplants in the U.S. (Hoofnagle, 1997). HCV-infected persons are at increased risk for hepatocellular carcinoma, which occurs in 1-5% of patients, usually those with a 20-30 year history of chronic hepatitis and cirrhosis (Fallon, 1997). Figure 2 shows the clinical course for hepatitis C.

Acceleration in progress and increased severity of HCV disease appear to be related to age over 40 at the time of infection, alcohol use, and male gender (CDC, 1998). Coinfection with other viruses, notably hepatitis B (HBV) and human immunodeficiency virus (HIV), have also been found to exacerbate the progress of HCV disease (CDC, 1998).

Clinical Features

Initial symptoms of hepatitis C may include fatigue, malaise, anorexia, right upper quadrant tenderness and nausea. These symptoms are rather nonspecific and vague, making diagnosis challenging. Rising serum alanine aminotransferase (ALT) levels occur within a few weeks of exposure and continue to fluctuate between normal and up to ten times the upper limit of normal throughout the course of the illness (Hoofnagle, 1997). HCV RNA can be detected in serum in 90% of cases within 3 months after infection (NIH Consensus Statement, 1997).

As the disease progresses, patient signs and symptoms reflect the failure of normal liver functions. Bleeding problems can occur as a result of failure to synthesize vitamin K-dependent clotting factors. Bleeding tendency is further complicated by sequestration of platelets by an
enlarged spleen secondary to portal hypertension. Splenomegaly occurs in approximately 35-50% of all cases of cirrhosis (Friedman, 1997). Jaundice, pruritis, dark-colored urine and clay-colored stools reflect the liver’s failure to metabolize and excrete bilirubin. Ascites and peripheral edema develop when the liver can no longer generate sufficient albumin to maintain normal vascular osmotic pressure. Portal hypertension contributes to the process of ascites, as well as to the development of pulmonary edema and effusions, splenomegaly, and portal and esophageal varices. Inability to metabolize serum estradiol may result in gynecomastia in men, menstrual irregularities in women, and loss of libido. Spider angiomata may appear, particularly on the upper body, indicating inability of the liver to metabolize 17-ketosteroids. Hepatic encephalopathy occurs as a result of failure of the liver to detoxify noxious substances absorbed from the intestine, principally ammonia, leading to delirium and coma. Anemia and weight loss are also common manifestations of advanced stages of hepatitis. (Podolsky & Isselbacher, 1998).

Extrahepatic Manifestations

The most common immunologic complications of HCV infection is mixed cryoglobulinemia involving IgM and IgG. This condition occurs in approximately one-third of hepatitis C cases. Symptoms, which occur in only about 5% of these cases, include purpura on the lower extremities, glomerulonephritis, and peripheral neuropathy (NIDDK, 2000; Supa, 1999). Rheumatoid factor is elevated in the serum of 70% of hepatitis C patients. Other abnormalities include antinuclear antibodies seen in 20%, smooth muscle antibodies seen in 20%, and thyroid antibodies seen in approximately 20% (Fallon, 1997).

Dermatologic manifestations include lichen planus (5%) and porphyria cutanea tarda (5%), the latter being associated also with alcohol abuse (Fallon, 1997). Keratoconjunctivitis
sicca, a disturbance in lacrimal function causing dryness and irritation of the eyes, may also be associated with HCV infection (NIDDK, 2000).

Differential Diagnosis

The differential diagnosis of hepatitis C includes other viral forms of hepatitis, which may present signs and symptoms indistinguishable from those caused by HCV. These other viral forms include hepatitis A, spread through fecal-oral contact and hepatitis B, sexually transmitted, as well as blood-borne. A fourth form, hepatitis D, occurs only in conjunction with hepatitis B. A fifth variety, hepatitis E, is fecal-oral in transmission. It is not endemic in the United States, but is occasionally identified in people who have visited or immigrated from endemic regions (Alexander, 1998).

Noninfectious causes of liver inflammation include autoimmune hepatitis, alcohol- or drug-induced hepatitis, biliary obstructive disorders, and inherited storage disorders, e.g. hemochromatosis, Wilson’s disease, and alpha-1-antitrypsin deficiency (Friedman, 2000). These may be distinguished from viral forms of hepatitis by initial antibody- or viral RNA-detecting serology and confirmed by the appropriate serum assays, as well as by liver biopsy (Friedman, 2000).

Diagnostic Testing

Initial screening, prompted by symptoms of hepatitis and/or history of belonging to a high-risk category, should include an acute hepatitis panel and liver function panel. Table 1 describes the diagnostic tests used for the detection and monitoring of HCV. The hepatitis panel is useful in ruling out other forms of hepatitis and includes the following tests: HAV antibody IgM, HBV surface antigen (HbsAg), HBV core antibody IgM (IgM anti-HBc), and HCV
antibody (anti-HCV) (Pathology Associates Medical Laboratories, Spokane, WA, personal communication, August 2000).

Two HCV antibody tests are currently in use: the enzyme immunoassay (EIA) and the recombinant immunoblot assay (RIBA). The third generation EIA (EIA-3) incorporates three HCV antigens which enhances the test’s sensitivity compared to earlier versions, making earlier diagnosis possible. EIA-3 is the primary initial screening tool for patients suspected of carrying HCV, and it is currently approved by the Food and Drug Administration for blood donor screening (Supa, 1999). Mean sensitivity of the EIA-3 is approximately 97%, but false-positive results remain a problem in low-prevalence populations, such as blood-donors (Gretch, 1997).

Confirmation is usually made using the recombinant immunoblot assay (RIBA), which is more specific and more standardized than the EIA (Lok & Gunaratnam, 1997).

Qualitative detection of HCV RNA, using the reverse transcriptase polymerase chain reaction (PCR) and branched DNA (bDNA) assays, can be useful in detecting viremia and confirming infection in those cases which are EIA positive and RIBA indeterminate (Gretch, 1997). Quantitative PCR can determine viral load and is useful in monitoring response to antiviral therapy (Gretch, 1997). Optimal PCR assays can detect HCV RNA levels, as low as 100 copies per milliliter of plasma or serum (Gretch, 1997). Lack of standardization and reliability of the PCR methods is a major limitation of HCV RNA testing (Gretch, 1997).

The genotyping of HCV can be helpful in estimating response to treatment with interferon, since those patients with genotypes II and III have better documented response to interferon therapy than those with genotype I (CDC, 1998). Genotyping should not be used exclusively to disqualify patients from therapy, however, since patients with a low viral load of
genotype Ib have demonstrated satisfactory response to antiviral treatment (Lok & Gunaratnam, 1997).

Liver function studies to evaluate HCV typically include aspartate transaminase, (AST), alanine transaminase (ALT), alkaline phosphatase, albumin and total bilirubin measurements (NIDDK, 2000). The principal liver function test used for clinical monitoring of hepatitis C is the ALT. This serum indicator rises early in the course of the disease and shows intermittent, marked elevations, usually up to five times the upper limit of normal, with subsequent return to normal values (NIDDK, 2000). There is considerable variability in ALT elevations, the range being zero to twenty times normal (NIDDK, 2000). Serial ALT measurements, together with periodic HCV RNA assays, are the standard tests for monitoring response to interferon therapy. Total bilirubin levels may be elevated, and alkaline phosphatase levels may show mild increases, appearing early and remaining until late in the course of the disease (Alexander, 1998). Prothrombin time (PT) may be prolonged, indicating failure of the liver to synthesize vitamin K-dependent clotting factors. These complications tend to be evident only in more advanced stages of liver disease (Friedman, 2000).

Serum alpha fetoprotein (AFP) measurements provide a marker for hepatocellular carcinoma (HCC) and should be obtained in advanced cases of hepatitis C. Mildly elevated levels are also sometimes found in nonviral forms of hepatitis and cirrhosis, whereas HCC produces marked elevations, with a sensitivity of 90% (Jacobs et al., 1996). Serial AFP values can be helpful in monitoring the progress of liver neoplasms.

Until recently, liver biopsy has been considered the “gold” standard for confirming the diagnosis of hepatitis C and for tracking the histologic progression of the disease. Biopsies are also used to determine the appropriateness of antiviral therapy in particular cases and to monitor
response to treatment. The procedure is relatively expensive and is associated with bleeding risk and a 0.02% mortality risk (Wong, Bennett, Koff, & Paulker, 1998). The invasive nature of the biopsy procedure, as well as its expense and associated risks, may present a deterrent to some patients seeking antiviral treatment, thus excluding some candidates who would benefit from interferon therapy. For these reasons liver biopsy may not be considered essential in all cases (Wong et al., 1998).

Treatment

Current therapy for HCV infection involves discontinuation of all hepatotoxic substances, especially alcohol. Rest, with gradual resumption of activity, as signs and symptoms subside is recommended (See Table 2: Patient Teaching for HCV). Balanced nutrition with normal-caloric intake is advised. In early stages of chronic liver disease, an abundance of dietary protein is necessary to replenish muscle wasting, restore albumin, and aid in conversion of fats to lipoproteins for removal from the liver to avoid fatty infiltration. In advanced cirrhosis, however, protein restriction is necessary to avoid excessive accumulation of serum ammonia with resultant encephalopathy. Salt restriction is required in cases of edema. The largest meal of the day should be eaten in the morning, while antiviral medication, if used, should be taken in the evening to minimize nausea. Diphenhydramine 25 mg. taken orally three times daily or prochlorperazine 10 mg. two to four times per day may be used for control of nausea (Alexander, 1998). Hospitalization may be necessary if severe nausea and vomiting occur. Other indications for hospitalization include elevation of PT greater than 3-4 seconds above normal, mental status deterioration or absence of adequate caregiving resources in the outpatient setting (Alexander, 1998).
Treatment with the immune-modulator interferon (IFN) alpha is the first line of pharmacologic therapy for HCV infection, with standard dosing of 3 million units three times a week for 48 weeks (NIDDK, 2000). If no improvement in liver function tests is seen within 3 months of initiating therapy, there probably will not be an effective response and treatment should be stopped (CDC, 1998). Only about half of those treated respond to therapy, as indicated by normalization of ALT levels and clearance of HCV from the blood. Of those who do respond, more than 50% relapse and the remainder show a sustained remission of the disease one year following treatment, i.e. about 20-25% of those initially treated (CDC, 1998). One proposed reason for the modest therapeutic response to interferon is its very short half-life in the serum. It is postulated that, during troughs in serum concentration of IFN, the highly mutable HCV is able to generate resistance to IFN’s antiviral activity (Foster, 1998). A recent improvement in interferon therapy, now undergoing clinical trials, involves the addition of the protein molecule polyethylene glycol (PEG) to the interferon molecule. The pegylated interferon is as biologically active as the parent molecule, but less susceptible to proteolysis and has a longer half-life (Foster, 1998). Early data show improved sustained response rates to monotherapy with PEG-IFN-alpha, as well as significantly better toleration of side effects (Foster, 1998).

Side effects of alpha interferon, which is an inflammatory mediator active in influenza infections, are predictably flu-like symptoms, myalgias, arthralgias, fever, headache, nausea and vomiting and malaise. Acetaminophen or ibuprophen may be used to help relieve some of these discomforts. Most symptoms gradually diminish after the first few weeks of therapy. Bone marrow suppression can also occur, as well as cognitive changes, depression and irritability. Side effects resolve once patient is taken off the alpha interferon.
The addition of the nucleoside analog ribavirin (1000-1200 mg/d in 2 divided doses) to the treatment regimen for HCV infections appears in early trials to double the sustained response after 48 weeks, from 15-20% with interferon alone to 35-45% using combination therapy (NIDDK, 2000; McHutchison et al., 1998). Ribavirin does not affect the viral load, but does seem to act synergistically with interferon to lower ALT levels, enhance liver restoration and improve symptoms (Fallon, H., 1997). Combination therapy using interferon and ribavirin has been found to be effective either as initial treatment (Davis et al., 1998) or as treatment after relapse (McHutchison et al, 1998).

Side effects of ribavirin are less well tolerated than those of alpha interferon. In one study by McHutchison et al. (1998), 21% of patients receiving combination therapy withdrew from treatment because of severe side effects. Ribavirin induces hemolysis in a majority of recipients with resultant symptomatic anemia, reduction in hematocrit by up to 10%, and hemoglobin reduction of 2-3 g/dL (NIDDK, 2000). Pre-existing anemia or hemolytic syndromes should therefore not be treated with ribavirin. Since this drug is primarily excreted by the kidneys, hemolysis induced by ribavirin therapy may be life-threatening in patients with compromised renal function. Therefore those with serum creatinine levels above 2.0 mg/dL should not be given ribavirin therapy (NIDDK, 2000). Less serious, but nonetheless bothersome, side effects include irritability, skin rash and itching, and rhinitis. Ribavirin is also a known teratogen and should be excluded in treatment of women who are, or may become, pregnant (NIDDK, 2000).

Careful monitoring of hepatic, renal and hematologic changes, as well as cognitive depression, must be carried out in the management of antiviral therapy for HCV infection. Serum aminotransferase levels and complete blood count should be checked at weeks 1, 2, and 4.
and then at intervals of every 4 to 8 weeks thereafter. At 24 weeks, HCV RNA and aminotransferase levels should be obtained to evaluate adequate response to treatment. Patients with genotype I who continue to have unsuppressed levels of HCV RNA, should discontinue treatment at this point. Those who are HCV RNA negative may continue therapy for a total of 48 weeks. Patients with genotypes II or III may discontinue therapy, if seronegative at 24 weeks (NIDDK, 2000).

The cost of antiviral treatment is considerable: $2,150 for a 6-month course of interferon; and with the addition of ribavirin and a longer course of treatment, up to $8,600 (DiBisceglie et al., 1998). When compared to a liver transplant, however, which is estimated at $215,984 (DiBisceglie et al., 1998), or to the expenses incurred in treating cirrhosis and hepatoma, antiviral therapy must be considered cost-effective.

Because of the expense, potentially serious side effects and relatively low response rate, specific criteria for antiviral therapy have been designated to predict those patients who will be most likely to respond satisfactorily to treatment (Table 3).

Primary Prevention

Avoidance of risk factors where possible is the most obvious means of HCV prevention. Since the major attributable cause of HCV infection is illegal intravenous drug use (60%), efforts should be made to counsel I.V. drug users to be screened for blood-borne diseases and to enter drug rehabilitation programs. If the client is unwilling to submit to such measures, he/she should participate in needle exchange programs, using only clean or sterile supplies and not sharing needles with other users.

Improved screening methods have sharply reduced the incidence of blood transfusion-acquired Hepatitis C, with no new cases being detected since 1994 (CDC, 1998). Current
practice includes screening all donors of blood, semen, organs and tissues for high-risk behaviors and serologic markers. Other standards of practice include use of viral inactivation of plasma, clotting factors and immunoglobulin products.

For primary prevention of HCV transmission in hemodialysis units, in addition to standard body fluid precautions, health care workers are required to glove for any contact with patients or hemodialysis equipment, to disinfect all nondisposable equipment after each use, and to refrain from sharing medication vials or supplies among patients. Members of high-risk groups, as well as those already determined to be HCV positive are highly encouraged to be vaccinated against HBV and HAV, to prevent additional insult to the liver in the case of infection with these diseases.

Much controversy exists over the risk of sexual transmission, but there is some increased incidence (5-10%) in long-term sex partners of patients with hepatitis C. Screening should be offered to spouses of HCV-infected persons and the use of condoms is recommended, although data on their effectiveness in preventing HCV transmission are lacking (CDC, 1998).

Secondary Prevention

Persons who have known percutaneous exposure to HCV-infected blood should be tested for HCV antibody and ALT activity. If positive, the person should be referred by the primary care provider to a specialist for management. Immunoglobulin and antiviral agents are not currently recommended for prophylaxis of those exposed to HCV, although the latter may be used following the acute phase of the disease.

Children born to HCV-infected mothers need not be screened for HCV antibody before 12 months of age, after which passive maternal antibody is no longer present (CDC, 1998). Those who test positive should be followed by a specialist to monitor ALT levels. Neither
antiviral nor immunoglobulin therapy is recommended for these children until they demonstrate liver disease.

Conclusion

Hepatitis C infection is an increasingly prevalent infection leading in most cases to chronic liver disease. Serious sequelae include cirrhosis, hepatocellular carcinoma and liver failure. Current treatment consists of interferon-alpha, usually in combination with ribavirin, with unsatisfactory results in most cases. Ongoing clinical trials using pegylated interferon offer some hope for improved response to therapy.

Improvements in the diagnosis and management of HCV infection depend on increasing our understanding of the pathogenicity of the virus, as well as host factors which lead to greater severity and chronicity of disease. Further research is needed to develop serological tests for antibody and viral detection which are less variable and more specific. Improved methods of assessing liver damage and dysfunction are also needed. It is hoped that future research will provide an effective vaccine and more effective therapy for this potentially fatal illness.
References


<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Cost</th>
<th>Turnaround Time</th>
<th>Preparation</th>
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<tbody>
<tr>
<td>Anti-HCV (EIA)</td>
<td>97%</td>
<td>False+ in autoimmune hepatitis &amp; up to 50% screened blood donors (Ferri, 1999)</td>
<td>$232.00</td>
<td>24-48 HRS.</td>
<td>NONE</td>
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<td>Anti-HCV (RIBA)</td>
<td></td>
<td>More specific than EIA</td>
<td>$235.00</td>
<td>4-6 DAYS</td>
<td>NONE</td>
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<td>HCV-RNA PCR</td>
<td></td>
<td></td>
<td>$236.75</td>
<td>7-10 DAYS</td>
<td>NONE</td>
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<tr>
<td>LIVER FUNCTION TESTS</td>
<td></td>
<td></td>
<td>$24.35</td>
<td>24 HRS</td>
<td>NONE</td>
</tr>
<tr>
<td>Alanine aminotransferase (ALT)</td>
<td>++</td>
<td>Increases w/obesity, some drugs</td>
<td></td>
<td></td>
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<tr>
<td>Aspartase aminotransferase (AST)</td>
<td>+</td>
<td>Also elevated in skeletal muscle disease; ETOH abuse</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Bilirubin, total and direct</td>
<td></td>
<td>Elevations in advanced liver damage</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Albumin &amp; Total protein</td>
<td></td>
<td>Normal except in advanced cirrhosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prothrombin Time</td>
<td></td>
<td>Normal except in advanced cirrhosis</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Alkaline Phos.</td>
<td>NI - &lt;3X NI</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>CBC with platelets</td>
<td></td>
<td></td>
<td>$16.45</td>
<td>24 HRS.</td>
<td>NONE</td>
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<tr>
<td>Alpha fetoprotein (AFT)</td>
<td>90% sensitive for HEPATOMA (&gt;10,000 mcg/L assoc. with poor prognosis)</td>
<td>Also may be elevated in viral or toxic hepatitis or traumatic injury</td>
<td>$2,159.00</td>
<td>7-10 DAYS</td>
<td>DC ASA &amp; NSAIDS 7 days prior; pre-op labs; Bleeding risk; 0.1% mortality</td>
</tr>
<tr>
<td>Liver Biopsy</td>
<td></td>
<td>Useful in monitoring histologic damage in already diagnosed HCV disease</td>
<td></td>
<td></td>
<td>DC ASA &amp; NSAIDS 7 days prior; pre-op labs; Bleeding risk; 0.1% mortality</td>
</tr>
</tbody>
</table>

Table 1 - Tests Used in the Diagnoses and Monitoring of Hepatitis C
Table 2: Patient Teaching for HCV

Life-Style Modifications

- If you drink alcohol, stop. Even small amounts put a strain on your diseased liver.
- Eat a well-balanced diet with plenty of protein, but limit the salt. Eat your largest meal in the a.m.
- Avoid contact sports, heavy lifting or strenuous activity to avoid any further injury to your liver.
- Get plenty of rest.

Measures to Prevent the Spread of Hepatitis C

- HCV positive women do not need to avoid pregnancy or breastfeeding. Only about 5% of babies born to infected mothers become infected, and there is no treatment available to prevent this from happening.
- Do not donate blood, semen, body organs or tissues.
- Do not share razors, toothbrushes, dental appliances or any personal items that may have even a tiny amount of blood on them.
- Cover any cuts or sores and avoid skin contact of broken skin with others.
- HCV is not spread by sneezing, coughing, hugging, or casual contact.
- You might be worried about transmitting the disease to your sex partner. While sexual transmission is rare, some cases have occurred. If you have multiple sex partners, you are at increased risk for STDs. Use a condom!
- Children who are infected with HCV should not be excluded from schools or daycare.
Table 3: Prediction of Patients Who Will Respond to Interferon/ Ribavirin

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Description</th>
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<tbody>
<tr>
<td>Age 18-60 years</td>
<td></td>
</tr>
<tr>
<td>HCV-RNA (&lt;3.5 million genomes/ml)</td>
<td></td>
</tr>
<tr>
<td>Repeatedly elevated ALT levels</td>
<td></td>
</tr>
<tr>
<td>Liver biopsy positive for fibrosis or moderate degrees of inflammation and necrosis</td>
<td></td>
</tr>
<tr>
<td>Cessation of alcohol and illicit drug use</td>
<td></td>
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<tr>
<td>Absence of depression or psychiatric illness</td>
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</tr>
<tr>
<td>Absence of autoimmune disease (e.g. rheumatoid arthritis, lupus erythematosis or psoriasis)</td>
<td></td>
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<tr>
<td>Absence of pre-existing cytopenia</td>
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<tr>
<td>Absence of thyroid disease</td>
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<tr>
<td>Absence of cardiovascular or cerebrovascular disease</td>
<td></td>
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<tr>
<td>Ability to use contraceptives effectively (NIH, 1998)</td>
<td></td>
</tr>
</tbody>
</table>
Figure 1: Risk Factors for HCV Infection

- Sexual Transmission: 7%
- Perinatal Transmission: 5%
- Occupational Hazard: 1%-4%
- Unknown Source: 40%
- I.V. Drug Use: 50%-60%