THE HEPATITIS C CLINIC

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Because of its high cost and potential for failure, treatment of chronic hepatitis C infection requires careful patient evaluation and close follow-up. This clinic uses a multidisciplinary approach to achieve high quality, cost-effective care.

Hepatitis C virus (HCV) infection has become a medical and financial challenge to both the U.S. health care system in general and the VHA in particular. Currently the most widespread chronic bloodborne infection in the United States, HCV is estimated to be more than three times as prevalent among VA patients than among the general U.S. population.[1]

Aside from its frequency, HCV infection has a number of characteristics that combine to make management problematic. Chronic infection progresses slowly, with complications developing gradually over decades. And while therapies have evolved rapidly in recent years, sustained response rates still are relatively low. Plus, these treatments are expensive: At present, the pharmaceutical cost alone of treating one VA patient for chronic HCV infection over the course of one year is about $15,000. This amount increases substantially when you figure in the costs of laboratory tests; clinic resources; medical personnel; and, if the patient develops serious complications, hospital admission and additional treatment (such as blood transfusions).

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Given these facts, it's believed that a health care system such as the VA can optimize the use of its resources by ensuring that all candidates for HCV treatment are educated about the disease and its management, evaluated carefully for any factors (such as viral genotype, pretreatment viral load, alcohol or substance use, and history of adherence[2]) that might affect their therapeutic response, treated for any conditions that represent a barrier to HCV therapy, and monitored closely throughout the course of treatment.

To perform these tasks effectively and efficiently, a clinic was established at the West Side campus of the VA Chicago Health Care System (VACHCS) in Chicago, IL. Since 1999, this hepatitis C clinic, part of the facility's gastroenterology clinic, has been working to provide a full spectrum of care—based on education, evaluation, and monitoring of patients with HCV—according to the VA's latest HCV treatment recommendations.[2] After outlining some pertinent facts

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Table 1. Risk factors that may warrant testing for hepatitis C virus (HCV) antibody[6,7]

- Past or present intravenous drug use (even one incident)
- Blood transfusion or solid organ transplant prior to 1992 or from a known infected donor
- Unequivocal blood exposure on skin or mucous membrane
- Chronic hemodialysis (current or past)
- Unexplained liver disease or abnormal alanine aminotransferase level
- Intemperate alcohol use*
- Accidental injury with infected needle
- Birth to HCV-infected mother
- Military service during the Vietnam war era†
- Past or present tattoo or repeated body piercing†
- Past or present intranasal cocaine use†
- History of multiple sex partners†,‡

*Defined by the VA as over 50 g/day for 10 years or more.[6] †Testing recommended by the VA, but not necessarily by other sources (such as the CDC). ‡Defined by the VA as more than 10 lifetime sexual partners.[6]

about chronic HCV infection and briefly reviewing its treatment, this article details the setup of the VACHCS hepatitis C clinic, describes the clinical pathway followed by the staff to optimize HCV care, and discusses the clinic's progress thus far.

HCV AT A GLANCE

HCV is a positive strand RNA virus transmitted primarily through exposure to infected blood. Its prevalence in the United States is approximately 1.8% and the number of new cases per year is estimated to be between 25,000 and 35,000.[3,4] The total cost of HCV infection in the United States in 1997 was estimated at $5.46 billion, about 67% of which was attributed to indirect expenses.[5]

Commonly recognized risk factors for HCV infection include intravenous drug use, blood transfusion or organ transplant prior to 1992, hemodialysis, and occupational exposure to infected blood (Table 1).[6,7] The VA also considers Vietnam era military service, tattooing or repeated body piercing, multiple sex partners, and intranasal cocaine use as indications for HCV antibody testing.[6]

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Between 60% and 85% of all HCV infections become chronic.[4] Of these cases, about 10% to 20% progress to cirrhosis and 1% to 5% develop hepatocellular carcinoma.[7,8] On average, clinically significant hepatitis takes 10 years to develop; cirrhosis, 21.2 years; and hepatocellular carcinoma, 29 years.[9]

What impact does HCV infection have on public health? The disease is associated with approximately 40% of all chronic liver disease in the United States and about 10,000 deaths annually.[4,7] Five and 10 years after clinical decompensation of liver function, survival rates are 50% and 30%, respectively.[10] Furthermore, HCV-related cirrhosis is the leading indication for liver transplantation.

THE CHALLENGE OF HCV TREATMENT

In the early 1990s, HCV treatment consisted of interferon alfa monotherapy, which yielded disappointing rates of sustained virologic response, on the order of 15% to 25%.[11] The addition of ribavirin to the regimen increased these response rates to between 40% and 50% for patients with genotype 2 or 3 HCV infection and to 30% for patients with genotype 1 HCV infection.[12]

Most recently, a modified form of interferon alfa, known as pegylated interferon, has been introduced. Researchers found that by attaching a polyethylene glycol (PEG) moiety to interferon they could extend its half-life, thus delaying elimination and cutting down the frequency of administration from three times to once a week. Two forms of pegylated interferon (peginterferon alfa-2a and peginterferon alfa-2b) have been approved by the FDA for treating

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Table 2. Contraindications to hepatitis C treatment according to guidelines of the VA Chicago Health Care System

- Nonadherence to medication or clinic appointments
- Decompensated liver disease
- Uncontrolled psychiatric conditions
- Immunocompromise following solid organ transplant
- Life limiting nonhepatic disease
- Significant substance abuse or alcohol intake in the past six months
- Pregnancy or inability or refusal to practice contraception
- Unstable cardiovascular disease
- Presence of uncontrolled autoimmune disease, antinuclear antibodies, or hepatitis B surface antigen; or elevated levels of thyroid stimulating hormone, glycosylated hemoglobin, or ferritin
- Abnormal results of complete blood cell count, including white blood cell count less than 3,000/mm, platelet count less than 75,000/mm, or hemoglobin levels less than 13 g/dL in men or 12 g/dL in women in the presence of coronary artery disease

chronic HCV infection, alone or in combination with ribavirin. When used with ribavirin, sustained response rates for the pegylated interferons are better than those of standard interferon plus ribavirin.[2]

All of these antiviral agents are associated with potentially severe adverse effects. Both standard and pegylated interferons can cause flulike symptoms (such as fatigue and myalgia), exacerbate autoimmune disease, and induce bone marrow suppression. Neuropsychiatric effects include irritability, cognitive changes, lack of motivation, and depression. Patients with previously diagnosed depression (or other mood disorders) may find their condition worsened during interferon therapy. Ribavirin has been associated with hemolytic anemia, which can be life threatening in patients with cardiovascular disease or preexisting anemia. It's also a teratogen. During therapy with these agents, therefore, patients should be monitored for adverse effects through regular laboratory testing. A decrease in dosage or discontinuance of therapy is required if bone marrow suppression or hemolytic anemia is found and can't otherwise be treated.

A complete medical history and laboratory workup is required for every patient with HCV infection prior to initiation of treatment.

A number of medical and psychiatric conditions have been identified as contraindications to HCV therapy. At the VACHCS, these include uncontrolled psychiatric conditions; recent, significant substance abuse or alcohol intake; uncontrolled autoimmune disease; and unstable cardiovascular disease (Table 2). For this reason, a complete medical history and laboratory workup is required for every patient with HCV infection prior to initiation of treatment.

CLINIC BASICS

Although there have been significant advances in recent years regarding our knowledge and treatment of HCV, there is still much we don't know—and the disease remains a threat to the general U.S. population. For many patients, a diagnosis of HCV carries with it many questions: How did I contract the disease? How badly damaged is my liver? Can the disease be transmitted to my family? And most important, can it be treated? We established the VACHCS hepatitis C clinic with the goal of answering such questions, in the form of an individualized patient education program, while at the same time preventing and controlling HCV infection according to the specific needs of our veteran population.

Ideally, a hepatitis C clinic should involve a hepatologist, a nurse practitioner, and a clinical pharmacist. Due to budgetary and staffing constraints, however, the VACHCS hepatitis C clinic currently is run by a clinical pharmacist, in conjunction with a gastroenterologist. The primary objective is to make sure patients with HCV are being evaluated in a timely manner,

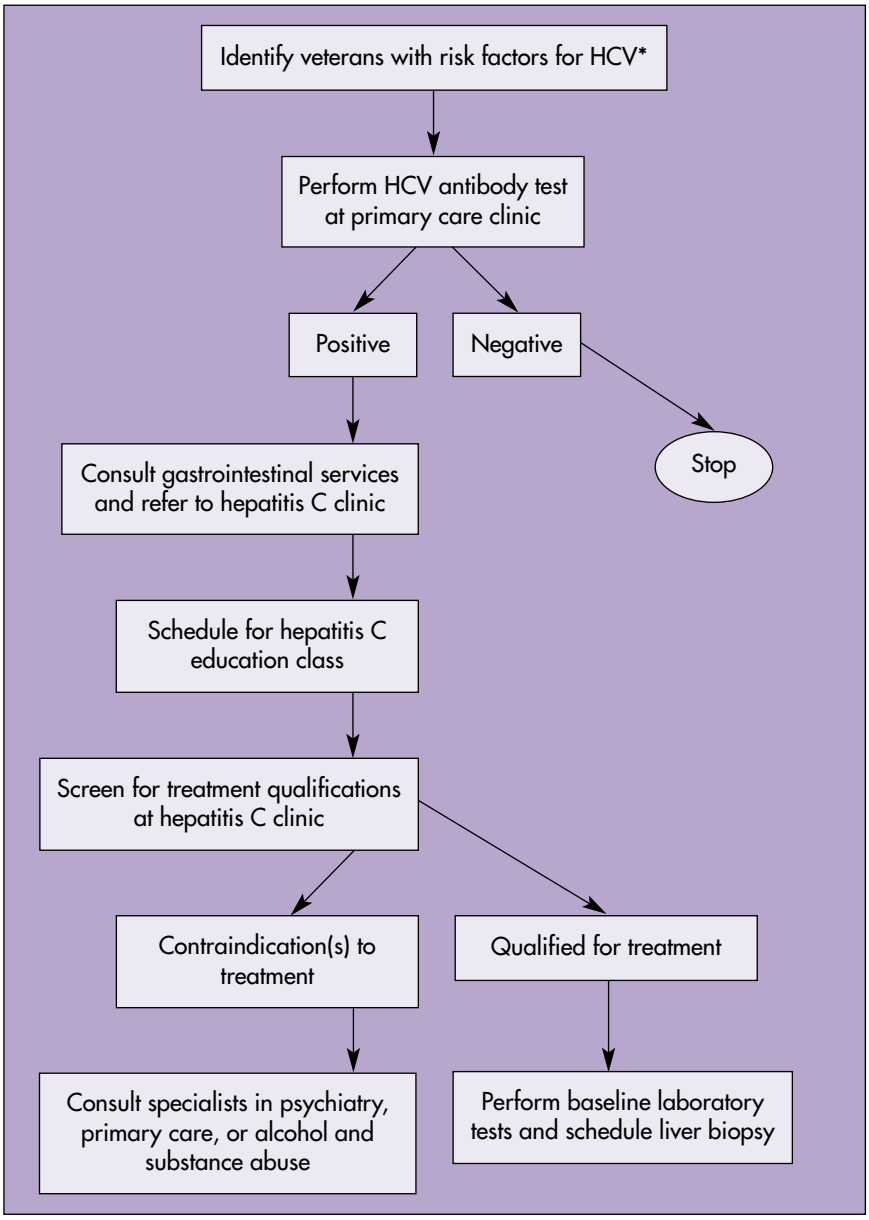

Figure. Hepatitis C clinic pathway at the VA Chicago Health Care System, Chicago, IL. *HCV = hepatitis C virus.

after which they can be redirected to the appropriate area of treatment or counseling.

At the VACHCS, primary care providers screen their patients for HCV risk factors and perform appropriate testing during routine appointments (Figure). Patients who test positive for HCV are referred to the hepatitis C clinic. Prior to an individualized clinic appointment, the patient is scheduled to attend one of the clinic's hepatitis C education classes, which are held monthly and taught by the clinical pharmacist.

During this class, the instructor outlines HCV risk factors (including modes of disease transmission and prevention), reviews how the disease is diagnosed, describes the clinical presentation, and discusses treatment issues (including potential adverse effects). The instructor explains both the effects of being coinfected with HCV and HIV and the dangers of alcohol use for HCV patients—which include earlier disease progression and a higher risk of hepatocellular carcinoma (see "The Impact of Alcohol on Hepatitis C" on page 31).[13] This class also gives patients an opportunity to ask questions about their infection and receive individualized answers.

After attending the class, patients are scheduled for a one-on-one appointment with the clinical pharmacist, who evaluates their eligibility for treatment. If no contraindications are found, baseline laboratory tests and a liver biopsy are performed at the gastroenterology clinic.

Among these baseline laboratory assessments are tests for HCV genotype and viral load. It's necessary to obtain these results prior to treatment because they help the clinician predict treatment response and cost-effectiveness and determine the course and duration of therapy. Consistent with VA recommendations, the total duration of HCV therapy is 48 weeks in patients with genotype 1 HCV infection and 24 weeks in those with other HCV genotypes.[2] The documented sustained response rates for these courses of therapy are 28% and 69%, respectively.[14,15]

Recent data regarding early virologic response rates now allow clinicians to evaluate a patient's response to treatment as early as 12 weeks. Current recommenda-

tions are to consider withdrawing treatment if the patient is still viremic, or if viral load fails to decrease by 2 $\log_{10}$, after 12 weeks of therapy. Treatment also is discontinued in patients with genotype 1 HCV infection who have detectable HCV-RNA levels after 24 weeks of therapy.[2]

The hepatitis C clinic also is closely involved in the patient's care once treatment has begun. During therapy, the patient is scheduled for monthly clinic visits to monitor adherence to the treatment regimen, treatment response, adverse effects, and laboratory test abnormalities. The monthly interval was adopted to help clinic staff stay in frequent contact with patients without imposing too heavily on the patient's regular activities. If an appointment is missed, the patient is contacted to reschedule the evaluation, medication refill, and laboratory tests. The hepatitis C clinic staff are responsible for following up with laboratory results and taking appropriate action if anemia or other abnormalities become evident.

ADDRESSING CONTRAINDICATIONS TO THERAPY

Initially, all patients with a diagnosis of HCV are candidates for treatment. Due to the significant adverse effect profile of current HCV medications, however, we routinely screen all HCV-positive patients for contraindications to treatment. Criteria for indications and contraindications to treatment have been established by the VA.[2] At our facility, these criteria have been adopted and expanded with regard to our patient population's specific characteristics.

Not all of these contraindications to HCV treatment, however, are absolute, and many—such as recent substance abuse or heavy alcohol use, uncontrolled psychiatric conditions, nonadherence to treatment, an uncontrolled nonhepatitic medical condition, and abnormal complete blood cell count—may be overcome through intervention. Therefore, when such barriers to treatment are identified at our hepatitis C clinic, we enlist the help of appropriate specialists (such as substance abuse clinic staff, alcohol treatment counselors, general practitioners, and psychiatrists). Through the work of these multidisciplinary teams, some patients can be cleared for HCV therapy. Once such a patient begins HCV treatment, the team continues to work in concert to make sure the problem doesn't return.

The Impact of Alcohol on Hepatitis C

At the VACHCS, patients with hepatitis C virus (HCV) infection who are using alcohol actively don't qualify for treatment. This is because of the reduced HCV treatment response rates and accelerated progression of liver disease that have been shown to occur in such patients.

Alcohol is an independent risk factor for liver disease. The risks of cirrhosis and of liver cancer associated with alcohol use in patients with HCV infection have been postulated to result from alcohol enhancing viral replication or increasing liver cell susceptibility to viral injury.[1,2] Viral loads are higher in HCV-positive patients who use alcohol heavily than in those who use none. These levels can drop dramatically, however, when such individuals are able to abstain from alcohol before beginning therapy.[3,4]

Therefore, at the VACHCS, addiction specialists from the alcohol treatment program are called in to work closely with HCV-positive patients who still are using alcohol at the time of clinic evaluation for HCV treatment. The goal is to help patients make a commitment to abstain from alcohol in order to optimize their HCV treatment and prevent or delay the complications of their disease. Once the patient has been alcohol free for at least six months, HCV treatment can be initiated.

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For patients with potential contraindications that can't be changed through intervention, the risks and benefits of initiating treatment must be considered. If the risk of a potential adverse event of treatment outweighs the benefit, the patient will not be offered treatment.

Perhaps the most important function of the clinic is to coordinate the ongoing evaluation and monitoring of at-risk patients.

In the VA population, it's not uncommon for patients with HCV infection to have such potential contraindications to therapy as psychiatric disorders and recent history of drug or alcohol abuse. This is why a highly organized, collaborative, multidisciplinary approach is crucial to the success of the VACHCS hepatitis C clinic. Perhaps the most important function of the clinic is to coordinate the ongoing evaluation and monitoring of at-risk patients who are candidates for or recipients of HCV therapy.

THE CLINIC IMPACT

Since its implementation, our hepatitis C clinic has had a positive impact on our ability to care for patients with HCV. Patients now know more about their infection. Uncertainty and anxiety have been replaced with determination to overcome any contraindications and to make themselves good candidates for treatment.

To date, 1,600 HCV-positive patients have been enrolled and scheduled for the hepatitis C education class. Of these patients, 900 (56%) attended the class and were scheduled for a clinic appointment. In that group, about 700 patients (78%) were evaluated for HCV treatment, and of those, about 500 were referred to a specialist—250 (50%) to an alcohol and substance abuse counselor, 150 (30%) to a psychiatrist, 50 (10%) to a primary care provider, and 50 (10%) to other appropriate fields of care—so that psychological or medical issues could be resolved and HCV therapy, if appropriate, could begin.

A GROWING NEED

In 2002, the National Institutes of Health reported that the age group with the highest prevalence of HCV infection was 40 to 59 years[4]—a population that includes veterans who served in the Vietnam war era. As these patients age, and the disease continues its slow progression, more complications are expected to arise. That's why, over the next 10 to 20 years, the costs and number of deaths attributable to HCV-related chronic liver disease is expected to rise dramatically.[4]

These factors, combined with the current high prevalence of HCV infection among veterans treated at VA medical centers (estimated at between 8% and 10%[16]), have made developing a system to manage chronic HCV imperative. Multidisciplinary hepatitis C clinic programs, such as the one we've implemented at the VACHCS, can help the VA—and other large health care systems—meet the challenge of providing for the complex needs of patients with HCV. ●

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