

REVIEW

Management of chronic hepatitis C

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Hepatitis C virus (HCV) infection is transmitted primarily through percutaneous exposure to blood, and most infections are associated with injection drug use. Progression to chronic HCV occurs in 55% to 86% of infected people, and persistent infection is a major cause of cirrhosis, end stage liver disease, and hepatocellular carcinoma. The detection of HCV antibodies should be performed initially to screen at risk populations. In those who are seropositive, HCV viraemia should be assessed to determine if chronic HCV is present. The HCV genotype should also be determined, as this is the strongest predictor of response to available treatment. A liver biopsy is very often helpful because it can estimate degree of hepatic fibrosis, identify concurrent diseases that might contribute to hepatic injury, and aid in selection of patients for treatment. The decision to start antiviral therapy should take into account potential contraindications to therapy, patient motivation, severity of disease, age, and HCV genotype. Combination therapy with weekly subcutaneous pegylated interferon and daily oral ribavirin is the standard of care for treating patients with chronic HCV.

SCOPE OF THE PROBLEM

Infection with HCV is an important public health problem in both developing and developed countries.¹ Despite the introduction of laboratory tests to screen national blood supplies, HCV remains the most common cause of post-transfusion hepatitis worldwide because unselected blood and blood products are still used in many developing countries or economies in transition.^{1–9–11} The World Health Organisation estimates that 200 million people, or about 3% of the world's population, have been infected with HCV, making this one of the most common blood borne infections globally.^{9–11} However, most people are asymptomatic and unaware that they are infected. About 170 million people are estimated to be living with chronic HCV and are at risk of advanced liver disease.^{9–11} Three to four million new HCV infections occur each year, and about 250 000 annual deaths throughout the world result from HCV associated chronic liver disease.¹ As knowledge of the infection continues to increase among the general public, more people will probably be tested for and diagnosed with chronic HCV in the future.

NATURAL HISTORY AND CLINICAL FEATURES OF CHRONIC HCV

In up to 45% of cases, acute HCV infection completely resolves, and this seems to be associated with a younger age at infection, female sex, and possibly certain major histocompatibility complex genes.^{6–8 12} However, about 55% to 86% of HCV infected patients develop chronic infection, manifested by the persistence of detectable HCV in the serum, and this has been primarily attributed to the propensity of HCV to mutate and evade host defences.^{6–8 13 14}

Chronic HCV is usually characterised by a lack of symptoms or only fatigue or vague abdominal pain. Extrahepatic manifestations of chronic HCV may be identified, and these are associated primarily with autoimmune or lymphoproliferative states (table 1).¹⁵ Increases in serum alanine aminotransferase (ALT) reflect hepatocyte injury, but these values typically fluctuate over time and may be even normal on occasion.⁵

The major complication of chronic HCV infection is progressive hepatic fibrosis leading to cirrhosis, which develops in about 20% of those with chronic HCV.^{6 7} The natural history of chronic HCV is variable, and progression of chronic liver disease is insidious in most patients. About one third of patients with chronic HCV develop hepatic cirrhosis 15 to 20 years after infection (“rapid fibrotic progressors”), one third

Infection with the hepatitis C virus (HCV) is a leading cause of liver disease worldwide.¹ This disorder was first recognised in the mid-1970s and was categorised as “non-A, non-B hepatitis”.² HCV was subsequently identified in 1988 as a ribonucleic acid (RNA) virus,³ and it can cause persistent infection in susceptible hosts after parenteral or percutaneous transmission.^{4 5} Progression to chronic hepatitis C occurs in most people acutely infected with HCV, and persistent infection is an important cause of cirrhosis, end stage liver disease, and hepatocellular carcinoma.^{1 6 7} Liver disease attributable to HCV currently represents the main indication for liver transplantation.^{5 8} Thus, early detection and treatment is of great importance.

Primary care physicians play a key part in the management of patients with chronic HCV by (1) identifying those chronically infected with the virus, (2) educating such people about the nature of the disease (particularly transmission, progression, and interaction with alcohol), and (3) assisting in treatment decisions. This article reviews the epidemiology, natural history, and clinical characteristics of chronic HCV infection to better assist clinicians in this endeavour. The diagnostic evaluation and current treatment regimens are also discussed.

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Abbreviations: HCV, hepatitis C virus; RNA, ribonucleic acid; ALT, alanine aminotransferase

Box 1 Extrahepatic manifestations of chronic hepatitis C virus infection

Autoimmune diseases

- Arthritis
- Autoimmune thyroiditis
- Diabetes mellitus
- Idiopathic thrombocytopenic purpura
- Myasthenia gravis
- Sjögren's syndrome

Dermatological manifestations

- Erythema multiforme
- Erythema nodosum
- Lichen planus
- Porphyria cutanea tarda
- Pruritus
- Psoriasis
- Vasculitis

Haematological disorders

- Aplastic anaemia
- Essential mixed (type II) cryoglobulinaemia
- Monoclonal gammopathy
- Non-Hodgkin's lymphoma

Neurological disease

- Peripheral neuropathy

Ocular diseases

- Mooren's corneal ulcers
- Scleritis
- Uveitis

Pulmonary disease

- Idiopathic pulmonary fibrosis

Renal disease

- Membranoproliferative glomerulonephritis

develop cirrhosis 20 to 30 years after infection ("intermediate fibrotic progressors"), and one third develop it only after 30 years of HCV infection ("slow fibrotic progressors").¹⁶ Patients with persistently normal values of serum ALT have a lower risk for fibrotic progression.¹⁷ However, a number of factors can accelerate progression to advanced liver disease, most notably alcohol consumption,^{17–22} coinfection with HIV^{23–26} or hepatitis B virus,^{27–28} and older age at the time of infection.^{14–17} In particular, heavy alcohol intake (>50 grams per day) in patients with chronic HCV has been shown to increase fibrosis progression, rates of cirrhosis, and risk of death.^{17–22} The adverse effects of light and moderate amounts of alcohol intake on HCV infection have not been thoroughly evaluated, but one retrospective study assessing patients who drank less than 40 grams per day of alcohol found that fibrosis correlated with greater alcohol use and more frequent drinking.²⁹ Obesity and hepatic steatosis are also emerging independent predictors of more severe liver fibrosis.^{30–35}

Chronic HCV infection is associated with an increased risk of hepatocellular carcinoma, but this occurs primarily in patients with cirrhosis.^{4–5–36} Factors that increase the risk of hepatocellular carcinoma among HCV infected people include male sex,³⁶ older age,³⁶ chronic hepatitis B infection,^{28–36–37} and

heavy alcohol ingestion (>50 grams/day).^{22–36–38} Once cirrhosis is established, the incidence of hepatocellular carcinoma is 1% to 4% per year.³⁹ Death from chronic HCV typically occurs because of decompensated cirrhosis or hepatocellular carcinoma. Figure 1 summarises the natural history of HCV infection.

APPROACH TO THE EVALUATION OF THE PATIENT WITH HEPATITIS C

A systematic approach to the evaluation of patients with HCV infection should include an assessment of pertinent risk factors for HCV transmission; a thorough history emphasising concomitant medical illnesses, ongoing substance misuse, and neuropsychiatric disorders; and a careful physical examination to identify stigmata of end stage liver disease. Additional laboratory tests should then be performed to further determine the need for antiviral therapy.

Risk factors for HCV infection

Primary care physicians should obtain a history of high risk exposures associated with the transmission of HCV. HCV is transmitted primarily through percutaneous exposure to blood,^{12–40–42} and risk factors associated with transmission of HCV include:

- *Injection and other illicit drug use*—currently, most new HCV infections are associated with injection drug use, and this accounts for about 60% of HCV transmission.⁴³ About 65% of injection drug users are infected within one year of initiation of injection behaviour.⁴⁴ Intranasal cocaine use has also been associated with acquisition of HCV.⁷
- *Transfusion and organ transplantation*—the introduction of HCV antibody testing in 1992 made transmission of HCV by these routes rare, but recipients of blood transfusions and organ transplants before this date remain at particular risk.⁴⁵
- *Haemodialysis*—the prevalence of HCV antibodies among haemodialysis patients is about 8%,⁴⁶ and the infection is presumed to have been transmitted by inadequate infection control practices.⁴⁰
- *Health care workers*—needlestick injury is the primary risk factor for HCV transmission among health care workers, and the incidence of seroconversion after such an injury is 3% to 4%.^{8–47} Transmission of HCV from blood splash to the conjunctiva has also been reported.^{48–49}
- *Sexual activity*—sexual transmission of HCV occurs at low frequency. Based on seroprevalence studies using genotyping or sequence analysis to evaluate antibody concordant couples, the estimated prevalence of HCV among heterosexual couples in monogamous relationships is 2.8% to 11% in south east Asia, 0% to 6.3% in northern Europe, and 2.7% in the USA.⁵⁰ In addition, persons in long term monogamous relationships are at lower risk of HCV acquisition (0% to 0.6% per year) compared with persons with multiple partners or those at risk for sexually transmitted diseases (0.4% to 1.8% per year).⁵⁰ This difference may reflect differences in sexual risk behaviours or in rates of exposure to non-sexual sources of HCV, such as injection drug use, intranasal cocaine use, tattooing, or sharing of razors and toothbrushes.⁵⁰ Monogamous couples do not need to use barrier protection but should be advised that condoms may reduce the already low risk of HCV transmission.^{12–40–42} HCV infected people who have multiple sexual partners or who are in short term relationships should be advised to use condoms to prevent the transmission of HCV (as well as other sexually transmitted diseases).^{12–40–42}

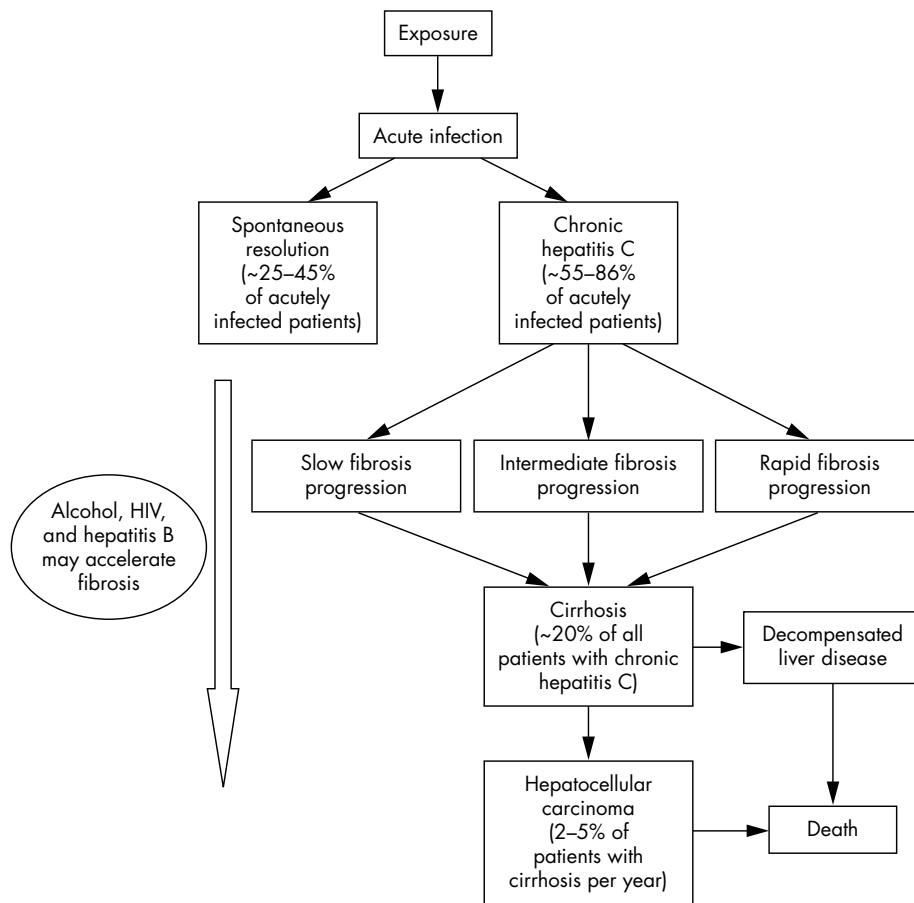


Figure 1 Natural history of hepatitis C virus infection. Adapted from National Institutes of Health Consensus Development Conference Statement: Management of hepatitis C: 2002-June 10-12, 2002. *Hepatology* 2002;36(suppl 1): S3-20.

- *Tattooing/body piercing*—contaminated equipment or supplies associated with these activities have been implicated in HCV transmission.^{7 51}
- *Vertical transmission*—the incidence of HCV infection is 5% to 6% among infants born to HCV infected women,⁵² but the incidence rises to about 20% among children born to mothers coinfecting with both HCV and HIV.⁵³ Infants born to HCV infected women should have their blood tested for either HCV RNA at six months of age or HCV antibody at 15 months of age (after maternal antibodies have waned).¹² Breast feeding does not seem to transmit HCV.⁵⁴
- *Alternative routes of transmission*—there is no evidence that casual contact, such as kissing, hugging, or sharing eating utensils, is associated with HCV transmission.^{12 40-42} However, sharing household items that may be contaminated with blood, such as razors, toothbrushes, or nail grooming equipment, should be avoided.^{12 40-42}

History and physical examination

Clinicians should identify symptoms that may be attributable to chronic HCV, such as lethargy, malaise, abdominal pain, and arthralgias, as well as symptoms of severe liver disease (such as confusion, easy bruising, and ascites). Ongoing drug and alcohol misuse that could exacerbate liver damage associated with chronic HCV and lead to lack of adherence to HCV therapy should also be determined.^{12 41 42} Comorbid conditions that might influence the suitability for treatment, such as neuropsychiatric illnesses, cardiovascular disease, and autoimmune disorders, should also be ascertained during the initial assessment.⁵⁵ Physical examination should focus on identifying any stigmata of advanced liver disease.

Laboratory evaluation

A number of tests are useful in the evaluation of HCV infection:

- *HCV antibody*—the detection of HCV antibodies is recommended as the initial test for the identification of HCV and is useful for screening at risk populations.¹² Box 2 lists the patients who should be considered for HCV screening.

Box 2 Patients for whom HCV testing is recommended*

- Persons who have injected illicit drugs (even only once)
- Persons with conditions associated with a high prevalence of HCV infection:
 - HIV infection
 - Haemophilia (especially if received clotting factor concentrates before 1987)
 - Haemodialysis
 - Unexplained abnormal aminotransferase activities
- Children born to HCV infected mothers
- Health care, emergency, and public safety workers who experience a needlestick or mucosal exposure to HCV positive blood
- Current sexual partners of HCV infected persons

*Adapted from Strader DB *et al.* *Hepatology* 2004;39:1147-71.

The primary serological test used for the detection of HCV antibody is an enzyme immunoassay (third generation), which is comparatively inexpensive, reproducible, and carries a high sensitivity (99%) and specificity (99%).¹² It can detect antibodies 4 to 10 weeks after infection.⁸ A negative enzyme immunoassay is usually sufficient to exclude the diagnosis of HCV infection in immunocompetent patients.¹² However, the test can be falsely negative in those with immunodeficiencies or end stage renal disease.^{8, 12} Once patients seroconvert, they usually remain positive for HCV antibody.⁸ Thus, the presence of HCV antibody may reflect remote or recent infection.

- **HCV RNA assays**—assays based on the molecular detection of HCV using polymerase chain reaction or other gene amplification techniques are available. A qualitative HCV RNA assay can confirm viraemia in patients with a positive enzyme immunoassay result as well as in those with a negative test in whom infection is still suspected.⁸ The quantitative HCV RNA assay can help predict treatment response (patients with HCV viral loads exceeding 2 million copies/ml (or 800 000 IU/ml) respond less well to treatment) and is useful in monitoring the response to HCV therapy.^{12, 55, 56} However, HCV RNA values provide no information about disease severity or risk of progression, so serial monitoring of HCV viral loads in untreated patients is unnecessary.
- **ALT and assessment of liver function**—ALT activities may be useful in monitoring HCV infection but are insensitive in predicting disease progression to cirrhosis.³⁷ ALT activities may be normal or fluctuate in those with HCV infection, and a single normal value does not exclude active infection, progressive liver disease, or cirrhosis.³⁷ Liver function tests, which include prothrombin time, bilirubin, and albumin, should also be performed.
- **Genotype**—worldwide, six genetically distinct groups of HCV isolates, called genotypes (numbered 1 through 6), have been identified.⁵⁶ There is little difference in the mode of transmission or natural history of infection among the different genotypes. However, cure rates with antiviral therapy are notably higher with genotypes 2 and 3, and the duration of HCV therapy is shorter for these genotypes.⁵⁸ Thus, HCV genotype is an important parameter to determine in the evaluation of chronic HCV infection. Genotype does not change during the course of infection and should only be evaluated once.⁵
- **Liver biopsy**—as ALT abnormalities cannot accurately predict the degree of hepatic inflammation and fibrosis,⁵⁷ histological evaluation of a liver biopsy specimen remains the gold standard for reliably estimating the stage of hepatic fibrosis and degree of hepatic inflammation in patients with chronic HCV.^{12, 41, 42, 57, 59, 60} Thus, the liver biopsy can determine the relative urgency of HCV therapy. The most validated method for evaluating the degree of hepatic fibrosis is the METAVIR classification system, which divides liver fibrosis into five discrete stages (0 = no fibrosis; 1 = mild fibrosis (portal fibrosis without septae); 2 = moderate fibrosis (a few septae); 3 = severe fibrosis (numerous septae without cirrhosis), 4 = cirrhosis).⁶⁰ A liver biopsy may identify concurrent disease processes (for example, steatosis, iron overload) that can contribute to hepatic injury. It aids in the selection of chronic HCV patients for treatment and helps to correctly time therapeutic interventions.³⁶ The liver biopsy can also determine the presence of cirrhosis, which may increase the risk of toxicity with therapy even in HCV genotypes 2 and 3. Clinicians routinely obtain a liver biopsy in patients with HCV genotype 1 infection to guide recommendations for treatment. As patients infected with HCV genotypes 2

or 3 have a high likelihood of response, some advocate treating such patients without a liver biopsy.^{12, 42}

- **HIV screening**—many risk factors for HCV transmission are shared by HIV infection.^{7, 45} However, results from a recent cross sectional study show that a high percentage of HCV infected patients are not being tested for HIV.⁶¹ Patients with HCV who are at risk for HIV should be offered testing with appropriate pre-test and post-test counselling.
- **Hepatitis A and B screening**—as coinfection with hepatitis B virus accelerates the progression to cirrhosis^{27, 28} and increases the risk of hepatocellular carcinoma,^{28, 36, 37} patients with chronic HCV should also undergo serological testing for hepatitis B virus. Hepatitis A serology should also be performed as superinfection with this virus could result in higher morbidity.⁶²
- **Hepatocellular carcinoma screening**—patients with HCV induced cirrhosis may be evaluated for hepatocellular carcinoma with a serum α fetoprotein and abdominal ultrasound every six months,⁶³ although data on the optimal screening strategy are lacking.
- **Antinuclear antibody**—patients with chronic HCV infection have been found to have a higher rate of autoantibodies in the serum.⁶⁴ As a result, determination of the antinuclear antibody has been recommended before starting HCV therapy.⁵⁵ Although the presence of an antinuclear antibody does not adversely affect the outcome of HCV therapy, such patients should be monitored carefully for the development of autoimmune diseases (for example, thyroiditis, rheumatoid arthritis, and psoriasis) during the use of interferon.⁶⁵
- **Thyroid function tests**—thyroid disorders are common in patients with chronic HCV, and interferon induced thyroid disease is among the most common adverse events associated with HCV treatment.⁶⁶ Thyroid stimulating hormone concentrations should therefore be checked before starting HCV therapy.⁵⁵

TREATMENT OF CHRONIC HCV INFECTION

Support and education

Support and education are central to the management of patients with chronic HCV, and healthcare providers should distribute additional educational materials and offer referral to support groups to those undergoing evaluation for established HCV infection. Patients with chronic HCV should be referred to an infectious diseases physician or hepatologist

Table 1 Possible adverse effects of pegylated interferon and ribavirin therapy*

Pegylated interferon	Ribavirin
Alopecia	Cough, dyspnea
Anaemia	Gout
Autoantibodies	Haemolytic anaemia
Bronchospasm	Insomnia
Depression/mood lability	Nausea
Diarrhoea	Pharyngitis
Influenza-like symptoms (headaches, fatigue, fever, myalgias, arthralgias, anorexia)	Pruritus
	Rash
	Teratogenicity
Injection site pain/erythema	
Loss of libido	
Retinopathy	
Sleep disturbances	
Thrombocytopenia	
Thyroid dysfunction (hyperthyroidism/hypothyroidism)	
Weight loss	

*Adapted from Lauer GM, Walker BD. *N Engl J Med* 2001;**345**: 41–52.

with expertise in HCV to provide more information about diagnosis, natural history, and therapeutic options. Clinical management should subsequently be multidisciplinary, with input from advanced practice nurses, psychiatrists, pharmacists, dietitians, and addiction management experts.

Treatment of neuropsychiatric disorders

Neuropsychiatric disorders, particularly depression, are common among patients with chronic HCV and are frequent adverse effects of interferon therapy.⁶⁷⁻⁶⁸ Identification and treatment of neuropsychiatric disorders should be pursued before and during HCV therapy.¹² Referral to a psychiatrist should also be considered.

Immunisation against hepatitis A and B

As acute infection with hepatitis A or B in those with underlying chronic HCV infection can result in high morbidity,^{28,62} hepatitis A and B vaccination should be performed in those who are seronegative for these viruses. These vaccines are safe and effective in patients with chronic HCV and may prevent poor outcomes.⁵⁵

Avoidance of hepatotoxins

Heavy alcohol consumption can worsen the course and outcome of chronic HCV and may seriously compromise treatment by decreasing adherence or interfering with the antiviral action of interferon based therapy.²² Efforts to diagnose and treat alcohol misuse should be performed before beginning HCV therapy. Treatment for drug and alcohol misuse should be made available to all patients who want and need it. Data are inadequate to provide definitive recommendations regarding the effect of light to moderate alcohol use in patients with chronic HCV. Safe levels of alcohol consumption in patients with chronic HCV remain unclear, and even moderate levels of consumption may accelerate disease progression.¹² Alcohol abstinence is therefore recommended before and during therapy.^{12,41,42} In addition, the use of all over the counter drugs and herbal agents that may have hepatotoxic effects should also be determined.⁶⁹

Pegylated interferon and ribavirin therapy

Combination therapy with pegylated interferon and ribavirin (Copegus, Hoffmann-La Roche; Rebetol, Schering-Plough) is currently the standard of care for treating patients with chronic HCV. The primary goal of treatment is to eradicate (that is, cure) chronic HCV,^{12,41,42} but therapy can also

decrease hepatic inflammation and fibrosis, slow disease progression, and reduce the risks for cirrhosis and hepatocellular carcinoma even in the absence of cure.⁷⁰⁻⁷⁴ Two types of pegylated interferons, pegylated interferon alfa-2a (Pegasys, Hoffmann-La Roche) and pegylated interferon alfa-2b (Peg-Intron, Schering-Plough), which differ in their pharmacokinetic and chemical properties, have been developed.⁷⁵ Both formulations are given weekly via subcutaneous injection. Ribavirin is dosed by weight for genotype 1 (1000 mg per day if <75 kg and 1200 mg per day if ≥75 kg), whereas 800 mg per day is sufficient for genotypes 2 and 3, regardless of weight.⁵⁸

Cure is determined by a sustained virological response, defined as the absence of detectable HCV RNA six months after the withdrawal of HCV therapy. Pegylated interferon alfa-2a (180 µg per week) plus ribavirin produces an overall sustained virological response rate of 56% to 63%,^{58,76} while pegylated interferon alfa-2b (1.5 µg/kg per week) plus ribavirin produces a similar sustained virological response rate of 54%.⁷⁷ HCV genotypes 2 and 3 are more responsive to HCV therapy (cure rates 78% to 84%) and require only six months of treatment compared with HCV genotype 1 (cure rates 42% to 52%), which requires 12 months of therapy.^{58,76,77} Referral to an infectious disease physician or hepatologist should be performed to ensure appropriate monitoring during therapy as there are a number of adverse effects associated with both drugs (table 1).

Among those who are coinfecting with both HIV and chronic HCV, the efficacy and safety of HCV treatment with pegylated interferon and ribavirin has recently been determined.⁷⁸⁻⁸⁰ The AIDS pegasys ribavirin international coinfection trial (APRICOT)⁷⁸ and the AIDS clinical trials group study 5071⁷⁹ evaluated the use of pegylated interferon alfa-2a (180 µg weekly for 48 weeks) plus ribavirin (different ribavirin dosing regimens were used in these studies). Subjects with HCV genotypes 2 and 3 were found to be more responsive to HCV therapy (cure rates 62% to 73%) compared with those with HCV genotype 1 (cure rates 14% to 29%). A third study, the French ANRS HC-02 RIBAVIC trial,⁸⁰ examined the use of pegylated interferon alfa-2b (1.5 µg/kg weekly for 48 weeks) combined with ribavirin 800 mg daily in HIV/HCV coinfecting patients. Cure rates in this trial were substantially lower, and subjects with HCV genotypes 2 or 3 had a sustained virological response rate of 43%, while those with HCV genotype 1 had a sustained virological response rate of only 11%. HCV therapy did not compromise treatment of HIV infection in these studies. Close monitoring for adverse effects during HCV therapy is strongly advised.

Indications for chronic HCV therapy

The decision to treat chronic HCV should be made on an individual basis and take into account potential contraindications to therapy (table 2), patient motivation and readiness, severity of disease, age, and HCV genotype.

Patients with chronic HCV who should be considered for treatment include those who have at least moderate fibrosis (that is, METAVIR stage ≥2) on liver biopsy, HCV genotype 2 or 3, persistent symptoms (for example, fatigue), and extrahepatic manifestations.^{12,41,42} Special attention should be given to people who traditionally have not been considered candidates for treatment, including those who are coinfecting with HIV, have controlled depression, or have a history of substance misuse but are currently in recovery. Observation with regular follow up every 6–12 months is recommended for patients with HCV viraemia, raised or persistently normal ALT activities, but only minimal or no histological evidence of fibrosis.^{12,42} A repeat liver biopsy in five years may be useful in these patients to assess the rate of progression of hepatic inflammation and fibrosis.⁸¹

Table 2 Potential contraindications to pegylated interferon and ribavirin*

Contraindications	
Pegylated interferon	Active substance misuse (particularly alcohol) Autoimmune disorders Decompensated cirrhosis Hyperthyroidism Neutropenia Pregnancy Severe psychiatric disease Thrombocytopenia Uncontrolled diabetes mellitus Uncontrolled hypertension Uncontrolled seizure disorder
Ribavirin	Anaemia Cerebrovascular disease Coronary artery disease End stage renal disease Haemoglobinopathies Pregnancy

*Adapted from Lauer GM, Walker BD. *N Engl J Med* 2001;**345**:41–52.

SUMMARY

HCV is transmitted primarily through percutaneous exposure to blood, and most infections are associated with injection drug use. Progression to chronic hepatitis C occurs in 55% to 86% of people acutely infected, and persistent infection is a leading cause of advanced liver disease. The detection of HCV antibodies should be performed initially to screen at risk populations. If this test is positive, an HCV RNA assay (to determine if chronic HCV is present) and an HCV genotype test (as genotype is the strongest predictor of response to therapy) should be performed. A liver biopsy can estimate the degree of hepatic fibrosis, identify concurrent disease processes that might contribute to hepatic injury, and aid in the selection of patients for treatment. Patients with chronic HCV should be counselled to reduce alcohol consumption, as it accelerates liver injury, and should be vaccinated against hepatitis A and B viruses, if seronegative for these infections. Combination therapy with weekly subcutaneous pegylated interferon and daily oral ribavirin is currently the standard of care for treating patients with chronic HCV. Close monitoring of patients during HCV therapy is required as there are a number of adverse effects associated with both drugs.

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This course will be held on 19-22 September 2005 at the University of Warwick. Further information is from Dr Charlotte Moonan, Department of Biological Sciences, University of Warwick, Coventry CV4 7AL, UK. Tel: 024 7652 3540; email: Charlotte.Moonan@warwick.ac.uk.