An overview of hepatitis C
clinical management in opiate pharmacotherapy settings

'Since becoming Director of the Alcohol and Drug Service at St. Vincent's Hospital in Sydney in 1982, I have seen an increasing number of patients develop serious complications from chronic hepatitis C. In 2008, over half of all our patients on methadone or buprenorphine have chronic hepatitis C infection. Alcohol and Drug doctors, nurses and other clinicians should regard HCV prevention and treatment as part of our core business. Treatment regimens for HCV continue to steadily improve. Indeed for people who have HCV (apart from genotype 1), our treatment cure rates are now clearly over 70%. This is great news. We should be more willing to recommend HCV treatment to our patients. Only then will they be more willing to consider treatment themselves.'

Dr Alex Wodak
Director Alcohol and Drug Service
St. Vincent's Hospital, Darlinghurst NSW 2010

ashm

NATIONAL CENTRE IN HIV EPIDEMIOLOGY AND CLINICAL RESEARCH

Contents:

Introduction..... 1
Transmission..... 1
Pre- and post-test discussion of HCV in the drug and alcohol (D&A) setting..... 2
Initial testing – differentiating chronic and cleared infection.... 2
Assessment and monitoring of someone with chronic HCV infection..... 3
Liver biopsy..... 5
New tests for staging liver disease..... 5
Antiviral treatment for HCV..... 5
Side effects..... 5
Contraindications to treatment.... 6
Monitoring for complications, including cirrhosis..... 6
General management for people with chronic HCV 6
Discrimination..... 7
References..... 7

Introduction

Around 40,000 people in Australia receive opiate replacement pharmacotherapy (methadone or buprenorphine) at any one time, and approximately 50% of them have chronic hepatitis C virus (HCV) infection. Studies have shown that viral eradication or cure rates following treatment for HCV infection are comparable between people on opiate pharmacotherapy to those not. Additionally, a review of the literature has shown that treatment adherence rates are often higher than expected in this population. The barriers to HCV treatment are coming down, with the exclusion criterion of active injecting drug use removed in 2001 and the requirement for liver biopsy to prove liver damage removed in 2006. But, despite all this, few people on opiate replacement pharmacotherapy access HCV treatment.

The burden of HCV disease is increasing. By the end of 2006, it was estimated that more than 200,000 people were living with chronic HCV infection.[1] An estimated 5,400 of them were living with HCV-related cirrhosis and without effective therapeutic intervention this figure is likely to double by 2020.[2] Complications related to chronic HCV infection are now the most common indication for liver transplantation in Australia, and there are approximately 250 deaths every year from advanced HCV liver disease. Disturbingly, this number is increasing each year, and is more than double the number of deaths from HIV/AIDS. However, there is still widespread misunderstanding about the progression of HCV disease and how successful treatment can be.

The most important factors associated with risk of more advanced HCV liver disease are:

- heavy alcohol intake
- long duration of infection (more than 20 years)
- coinfection with HIV or HBV
- obesity/insulin resistance/diabetes

Where one or more of these factors are present, a formal assessment of HCV liver disease stage should be done, with consideration given to treatment. Even in the absence of these factors, people with chronic HCV should be assessed for liver disease. Current treatment involves pegylated interferon (a weekly injection) and ribavirin (a capsule swallowed twice a day). Treatment duration is either 24 or 48 weeks, depending on HCV genotype. The biggest factor associated with treatment success is a patient's genotype. In Australia the two most common genotypes are 1 (50-55% of all HCV infections) and genotype 3 (35-40% of all HCV infections).[3] Approximately 50% of those with genotype 1 and 70-80% of those with genotype 3 can be cured with treatment. Yet less than 2% of all people with chronic HCV infection receive treatment each year.

Drug and alcohol practitioners are in a unique position to assess, refer and become involved in the treatment of their patients with chronic HCV infection. With an increasing burden of disease, it is essential they are able to identify those most at risk of complications from their HCV, and those most in need of HCV treatment. This booklet provides an overview of the important issues, to enable practitioners to feel more comfortable in answering questions from their patients about HCV and HCV treatment, and ensure that those most in need of HCV treatment are identified and provided with the opportunity to access it.

Transmission

HCV transmission occurs predominantly through blood-to-blood contact.[4] The most common mode of transmission in Australia is injecting drug use.

The provision of needle and syringe programs to injecting drug users (IDUs) is vital. While the largest risk is associated with the sharing of needles or syringes, there appears to be some evidence for transmission from other shared injecting equipment, such as spoons, filters and tourniquets.

Sexual HCV transmission is uncommon, particularly in the context of heterosexual relationships but may occur

if there is blood-to-blood contact during sexual activity.[5] There is also evidence transmission risk may be higher in those who are co-infected with HIV or other STIs.[6]

The risk of perinatal HCV transmission is approximately 5%.[7] Coinfection with HIV increases the risk two-fold.[8] No changes have been recommended in Australia for the management of pregnancy or labour in women with HCV, nor for the management of the neonate. Currently there is no indication for elective caesarean section in HCV-positive mothers.[9] Despite HCV RNA being detectable in breast milk, breastfeeding has not been directly linked to transmission of HCV.[10] Australian guidelines recommend breastfeeding should be encouraged.

Household transmission (e.g. via razors or toothbrushes) can occur but is considered rare.

Pre- and post-test discussion of hepatitis C in the D&A setting

Drug and alcohol practitioners play an important role in providing pre- and post-test discussion as part of diagnostic testing for HCV.

Pre-test discussion

The discussion should include:[11]

- risk assessment and discussion of the reason for testing
- how to reduce the risk of becoming infected or infecting others, for example information about safer injecting when this is relevant
- possible desirability for other BBV testing and/or STI testing
- information about confidentiality and privacy
- information about the testing process, including how results are to be provided, and the window period
- information about what happens to test results (i.e. the notification process)
- seeking informed consent for the test to be conducted
- assessment of the person's preparedness to be tested
- information about what a negative or positive result means including basic printed information about HCV
- assessment of support mechanisms while waiting for the test result and/or if the result is positive.

Post-test discussion

Please refer to the National Hepatitis C Testing Policy for advice on post-test discussion if the test result is negative.

If the test result is positive, ensure discussion occurs at an appropriate time and includes issues such as:

- immediate needs and support including written referral information– available from 1300 437 222 (1300 HEP ABC)
- safer behaviours – education, information and support including needle and syringe programs if appropriate
- legal requirements for disclosure and how or if to disclose to family and friends
- managing or understanding strong emotions, feelings, reactions and changes
- options in drug treatments and medical management
- ongoing counselling or therapy if required
- complementary/alternative management options
- ways to deal with loss and grief, depression, anger and anxiety
- strategies for managing HCV which are flexible and appropriate to the person's needs
- legislative requirements (notification, contact tracing, storage and coding)
- Referral to State and Territory hepatitis organisations via 1300 437 222 or www.hepatitisaustralia.com

People diagnosed with hepatitis C infection may need continuing support, particularly in the period immediately after they learn their test result. They may benefit from the provision of written material which includes key information and contact details of local support services. The Hep C in Brief patient fact sheet is available for download from the ASHM website (available in eight community languages) at http://www.ashm.org.au/hepc-factsheet/. Also available from the ASHM website is a Hepatitis C Fact Sheet for Clients of Pharmacotherapy Services. Refer to the Contact section in this booklet.

Initial testing – differentiating chronic and cleared infection

When assessing someone with possible HCV infection, an HCV antibody test should be performed. A positive test indicates ***exposure*** to HCV, but ***does not prove active infection***. A HCV RNA test, such as a PCR (polymerase chain reaction) test documents viraemia, and thus active infection. HCV PCR tests can either be qualitative (result being positive or negative) or quantitative (result providing viral load). The presence of a positive antibody test and an elevated ALT (alanine aminotransferase) level, particularly in the setting of risk factors for transmission, is highly suggestive of active HCV infection.

HCV Ab test	If positive shows evidence of previous exposure to virus. Importantly, does NOT provide immunity against reinfection with the HCV virus. Remains positive following viral clearance.
HCV PCR test	If positive shows active infection (i.e. viraemia)
ALT	If elevated in context of positive HCV Ab, generally indicates some level of liver disease from HCV virus and likely active HCV infection.

Cleared infection

Approximately 25% of people with acute HCV infection spontaneously clear the infection without treatment, generally within the initial 3-6 months.[12] In individuals with persistently normal ALT levels, a qualitative HCV PCR test should be carried out to determine whether the infection has cleared.[13]

A patient can be considered to have cleared HCV infection if they have two negative PCR tests, carried out at least 3 months apart.

A qualitative HCV PCR test in these conditions is rebatable under Medicare. HCV antibody positive patients found to be HCV RNA negative should be reassured that they have been exposed to HCV in the past, but have cleared infection.

It is recommended that patients with normal liver function and no detectable HCV RNA have repeat PCR testing for detection of HCV reinfection on an annual basis if there is ongoing risk behaviour such as injecting drug use. Repeated antibody testing will not reveal a new infection in this group, as their existing HCV antibody will remain positive, despite having cleared infection. Neither does their positive HCV antibody confer any protection against HCV reinfection.

Chronic infection

Approximately 75% of people infected with HCV progress to chronic HCV infection.

A patient can be considered to have chronic HCV infection if they have documented active infection for more than six months. This means a positive PCR test 6 months or more after initial infection.

The outcomes for people with chronic HCV infection are variable. There are particular factors which are significantly associated with a greater likelihood of progression to liver damage/fibrosis and ultimately cirrhosis. These are: heavy alcohol consumption, long duration of infection, coinfection with HIV or HBV, and obesity/insulin resistance/diabetes. In addition, individuals with elevated ALT levels have a higher risk of disease progression than those with consistently normal ALT levels, although the latter group may still develop significant fibrosis.

After 20 years of infection about 7% of people with chronic HCV infection will have developed liver cirrhosis, with this figure increasing to 20% after 40 years. After 40 years of infection, about 4% will have developed liver failure or liver cancer.

Assessment and monitoring of someone with chronic HCV infection

It is recommended that a person with chronic HCV infection is seen every 6 to 12 months. The main aims for any D&A health professional are to:

- educate about behaviours that risk re-infection and transmission to others
- identify and address any modifiable risk factors (e.g. excessive alcohol consumption)
- identify those most at risk of chronic HCV infection complications and decide which individuals are appropriate for antiviral therapy
- educate about treatment and assess desire for treatment
- ensure referral to a specialist for HCV treatment assessment is made at an appropriate time
- ensure monitoring for cirrhosis and advanced liver disease complications (such as liver failure, liver cancer) where appropriate
- determine need for support services
- evaluate and recommend shared-care responsibility

Identifying those most at risk of disease progression

One of the most important things to establish in monitoring a person with chronic HCV infection is whether or not they are likely to develop any serious liver damage.

The following factors must be documented, as there is very good evidence that they are associated with higher risk of cirrhosis:

- heavy alcohol intake (more than 4 standard drinks/day)
- duration of infection (over 20 years)
- coinfection with HIV or HBV

Additionally, there is increasing evidence that the following are linked to disease progression:

- Obesity/insulin resistance/diabetes

Alcohol intake

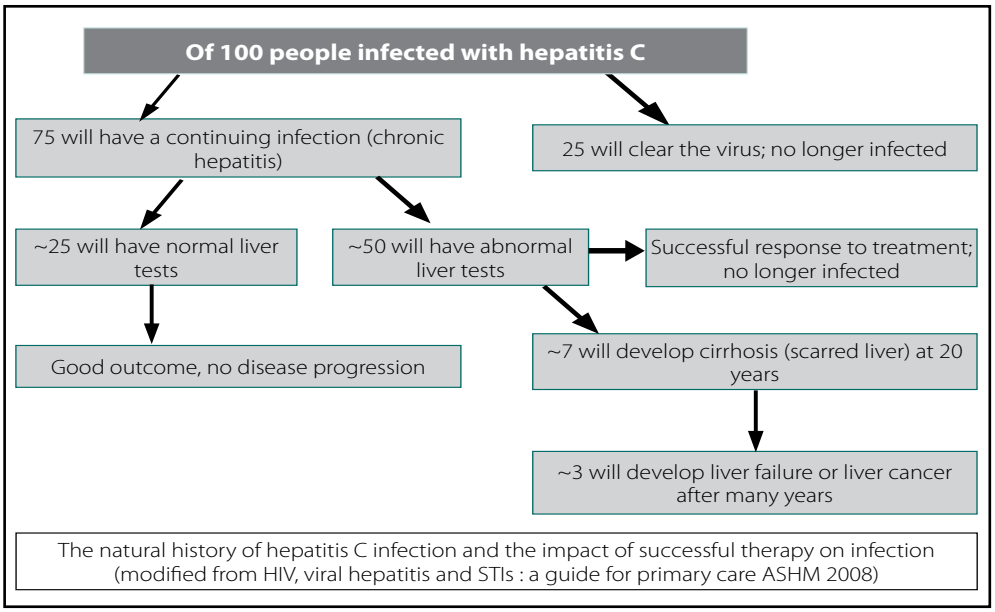
This is discussed further in subsequent section, 'General management for people with chronic HCV infection'. Broadly speaking, heavy alcohol intake is associated with increased risk of liver damage. Any person with excessive alcohol consumption (more than 4 standard drinks per day) should be advised of their increased risk of disease progression, and supported wherever possible to reduce their alcohol intake. General advice about alcohol intake should be guided by your assessment of their stage of disease and risk of progression.

Duration of infection

It is not always possible to determine the exact duration of infection. It is important not to assume that the date of first HCV Ab test is the date of infection. A good rule of thumb is to determine the year of the first injection, and assume infection two to three years subsequent to that. Some people who acquired HCV prior to the availability of HCV testing in 1990 will have been diagnosed with non-A non-B hepatitis. Other people, given the often asymptomatic nature of the disease, will not have been aware of their infection and so not been tested for some time following exposure. A person's age alone is often a very good indicator of duration of infection.

Most people who have acquired HCV through injecting drug use in Australia and are now over the age of 40 years are likely to have been infected for 15 or 20 years. It is good practice to be thinking about HCV treatment assessment for any person over 40 years and on methadone who you see in your practice.

Chronic hepatitis C outcomes chart (natural history)



The natural history of hepatitis C infection and the impact of successful therapy on infection (modified from HIV, viral hepatitis and STIs : a guide for primary care ASHM 2008)

Coinfection with HIV or hepatitis B virus infection (HBV)

Any person coinfected with HCV and HIV or HBV (HBsAg positive) is at increased risk of disease progression. They should be closely monitored, and treatment considered.

Obesity/insulin resistance/diabetes

There is increasing evidence of an association between obesity and insulin resistance/diabetes and HCV liver disease progression. People with chronic HCV infection and obesity should be supported to lose weight and take regular exercise. This is discussed in the section 'General management for people with chronic HCV infection'.

ALT level

Too often ALT testing is used as a primary tool to determine prognosis. Although people with elevated ALT levels have a higher risk of liver disease progression than those with consistently normal levels, the latter group may develop significant liver fibrosis. In addition, among those with elevated ALT levels, the extent of elevation correlates poorly with disease progression risk. Despite these limitations, regular liver function testing (every 6-12 months) is recommended to determine the extent of liver inflammation and assess synthetic function – see 'Pathology tests' below.

Factors associated with progression of liver disease

- heavy alcohol intake (more than 4 standard drinks per day)
- long duration of infection (20 years or more)
- coinfection with HIV or HBV
- obesity/insulin resistance/diabetes

NB: Most people over 40 years of age with chronic HCV infection in Australia are likely to have been infected for 15 or 20 years. They should be more strongly considered for HCV treatment assessment.

At each visit for HCV monitoring, a clinical examination as well as pathology tests should be performed. These will allow you to evaluate current disease severity and estimate risk of progression to fibrosis and cirrhosis.

Clinical examination

Clinical examination will focus on detecting evidence of more advanced liver disease. The following should be looked for:

- palmar erythema
- ascites
- spider naevi
- encephalopathy
- scleral icterus
- asterixis
- jaundice

Pathology tests

Regular monitoring should include full blood count and liver function tests.

Liver function tests every 6-12 months can provide information about extent of liver inflammation and assess synthetic function. Reduced albumin and raised bilirubin are important markers of advanced liver disease. A reduced albumin, particularly if combined with low platelet count suggests underlying cirrhosis. Other indicators of cirrhosis include elevated bilirubin (although if isolated may indicate Gilbert's syndrome), prolonged prothrombin time (PT), an AST/ALT ratio of >1.0, and an AST/platelet ratio of >1.5. However, cirrhosis may be present in the setting of normal markers of synthetic function such as albumin, bilirubin, platelet count and PT. Cirrhosis may also be present in the setting of normal ALT levels.

HCV genotype

HCV genotype impacts on length of treatment and likely response. Genotypes 2 and 3 require shorter (24 weeks) treatment and have higher likelihood of success (70-80%), whereas genotypes 1 and 4 require longer (48 weeks) treatment and have lower likelihood of success (~50%). HCV genotype testing is Medicare funded for anyone considering treatment. HCV genotype testing may assist both people with HCV and their clinicians with treatment-related decision-making, and need not be delayed until specialist review.

People with HCV genotype 2 or 3 can be informed that they have a high chance of eradicating the virus with just six months of treatment. People with HCV genotype 1 can be counselled that, while treatment length is longer and the likelihood of eradicating the virus is lower, this should not dissuade them from attempting treatment.

The HCV viral load also provides important information in relation to treatment success, particularly for those with HCV genotype 1. If the HCV viral load is <400,000 IU/ml in a person with HCV genotype 1, treatment success approaches that for HCV genotype 2 and 3. **However, HCV viral load does not correlate with liver disease progression risk and does not need to be monitored regularly.**

Decision-making about treatment

In determining whether a person is appropriate for antiviral treatment, the drug and alcohol health professional is in a good position to also consider the person's social situation. This includes looking at their living arrangements and availability of support, their mental health and current income/work situation as well as current drug use. All of these may impact on how well the person may manage any HCV treatment. Of note, a recent review of the literature supports the effectiveness of treating HCV among people on methadone.[14] Specifically it showed that outcomes, in terms of successfully completing treatment and viral eradication, are comparable between people on methadone and those not. Five of the six studies reviewed showed excellent rates of adherence to treatment (72-100%).

Any person with chronic HCV infection at risk of liver disease progression should be advised of the potential benefits of antiviral therapy. Where treatment is appropriate, much of the assessment should be related to choosing the best timing of therapy. Persons at highest risk of progression (based on risk factors listed) should be encouraged to consider therapy as soon as practicable. For others, timing of treatment can be based on lifestyle issues such as work, social circumstances, control of substance use, and desire for pregnancy.

While most treatment is based in public hospitals at present, there is an important trend towards treatment in the community. This will involve drug and alcohol clinicians, as well as primary care clinicians, taking on a greater role in the support and monitoring of people on HCV treatment. Many hospitals have put together shared-care packages with specific information and guidelines about patient management during HCV treatment. In addition, a small number of GPs in NSW, ACT and Victoria have been approved to prescribe combination therapy for HCV as part of a Section 100 (PBS) community prescribing program.

Liver clinics usually offer additional services that may be of benefit to patients. Such services include clinical nurse consultants, psychologists, psychiatrists, social workers and dieticians. Referral to a liver clinic, which can be made at any time, is necessary for specialist pre-treatment assessment and initiation of treatment.

Local hepatitis C councils or drug user groups may provide information and peer support for people considering treatment (refer to Contacts section).

Liver biopsy

A liver biopsy is no longer required before someone may receive hepatitis C treatment.

A liver biopsy may be performed to determine the severity of inflammation and fibrosis and guide treatment decisions in those with evidence of chronic HCV infection. There are several systems in use for recording the degree of fibrosis based on biopsy findings. Most of these use a scoring system ranging from stage 0 (no fibrosis) to stage 4 (definite cirrhosis). The finding of early liver disease, minimal disease activity and no or minimal fibrosis (stage 0-1) in a person with >15 years chronic HCV infection suggests a low likelihood of disease progression. Consequently, the person may be reassured, and treatment deferred. Some people with early liver disease may still wish to proceed with antiviral therapy, particularly if they have a favourable HCV genotype (2 or 3). On the other hand, people with moderate fibrosis (stage 2), severe fibrosis (stage 3), or cirrhosis should be offered antiviral therapy, provided no contraindications are present. Liver biopsy remains a very useful procedure for confirming or excluding significant fibrosis, but is not required for access to government-funded antiviral therapy.

New tests for staging liver disease

New and non-invasive methods of assessing disease stage have recently been developed, including the FibroScan® measurement of liver elasticity. The FibroScan® technique can be used to quantify hepatic fibrosis. It is a simple and pain-free procedure with no contraindications. A mechanical pulse is generated on the skin surface, and velocity of the wave used to determine the degree of 'stiffness' of the liver. A higher degree of stiffness correlates with a greater degree of hepatic fibrosis. It is easily performed in an outpatient clinic and gives immediate results in the form of a numerical score. It appears to have the highest sensitivity in detecting little or no fibrosis or in early cirrhosis, with less reliability when moderate or severe fibrosis is present. While not yet widely available, it is likely to replace liver biopsy-based assessment in the future.

Antiviral treatment for HCV

Previously in Australia, antiviral therapy was funded only for people with significant liver fibrosis. However, with increasing data to support the efficacy of antiviral therapy, it is now available to any previously untreated person 18 years or older with chronic HCV infection and compensated liver disease who agrees to effective contraception.

A liver biopsy is no longer a specific requirement for treatment. Active IDU is no longer an exclusion criterion.

Antiviral therapy is available in Australia under Section 100 of the Pharmaceutical Benefits Scheme (PBS) for any patient who fulfils all the following criteria:

- 18 years or older
- Documented chronic HCV infection (repeatedly positive HCV Ab and HCV PCR positive)
- Compensated liver disease
- No prior treatment with interferon alfa or pegylated interferon alfa
- Effective contraception

The major aim of treatment is to achieve viral eradication. In HCV, viral eradication or cure is defined by the achievement of a sustained virological response (SVR).

SVR = negative HCV RNA by a sensitive qualitative test six months after the completion of therapy.

The most effective therapy for HCV is a combination of subcutaneous pegylated interferon administered once a week plus oral ribavirin taken twice-daily. The combination of pegylated interferon and ribavirin produces an overall sustained virological response of greater than 50%.[15,16] This is a significant improvement over the SVR rates achieved with interferon monotherapy (10%) or standard interferon (given three times a week) plus ribavirin (40%).

The likelihood of response is much higher in people with HCV genotype 2 or 3 (70-80% SVR rate after six months of combination pegylated interferon and ribavirin) than genotype 1 or 4 (50% SVR rate after 12 months of therapy). While HCV genotype is the most powerful predictor of response, other predictors of SVR include low viral load, minimal hepatic fibrosis, female gender and age (younger than 40 years). Recently the rapidity of on-treatment response has emerged as a major factor in predicting sustained virological response.

By monitoring on-treatment response, people can be informed of their likelihood of a SVR. Those who have a greater than 2 log (100-fold) reduction in viral load by week 12 (termed an early virological response) have an approximately 70% chance of sustained virological response.[17] Conversely, those who fail to achieve a greater than 2 log drop in viral load at week 12 should have their treatment ceased, as there is a negligible (1-2%) chance of SVR. Additionally, those with genotype 1 who achieve undetectable HCV RNA at week 4 of therapy (termed a rapid virological response) have a 80-90% chance of viral eradication and may be able to shorten their treatment duration.[18]

There is currently significant effort being directed at determining whether measurement of early on-treatment virological responses may allow some patients to have treatment duration shortened, and whether others may benefit from longer duration of therapy.

The benefits of achieving an SVR include a reduced risk of liver disease progression for people at all stages of disease. In addition, there have been reports of significant regression of fibrosis, even in people with cirrhosis.

Genotype	Duration of treatment	Likely cure rate of treatment
1	48 weeks	~50%
2	24 weeks	70-80%
3	24 weeks	70-80%
4	48 weeks	50-60%

People who have failed to respond to either interferon monotherapy or combination interferon plus ribavirin in the past, are now also eligible for further treatment under Section 100 guidelines. Therapy may be for six or 12 months duration, depending on HCV genotype.[18]

Side effects

Side effects are common but, importantly, ***do not usually require discontinuation of treatment***. However, people on treatment do require significant support and encouragement. Adverse effects of therapy

include flu-like symptoms, irritability, weight loss, insomnia, vomiting, depression and anxiety, mild hair loss, rash, cough, myelosuppression and the development of certain autoimmune conditions, most notably thyroid disease.

Ribavirin treatment always induces a degree of intravascular haemolysis, which results in a fall in haemoglobin in many people. This anaemia may result in tiredness, shortness of breath and precipitation of myocardial ischaemia in those at risk. Ribavirin dosage may be reduced, depending on degree of haemolysis, or erythropoietin prescribed.

Interferon causes serotonin depletion which may result in depression, and selective serotonin reuptake inhibitors (SSRIs) may be considered for management or prophylaxis. It is the interferon which also commonly causes flu-like symptoms, which tend to peak early in the course of treatment. Interferon may also lower platelet count (a concern among people injecting) and white blood cell count.

Given the wide range and potential seriousness of side effects, people on treatment must be closely monitored. Currently, most treatment is provided through public hospitals where there is ready access to nurse specialists to provide advice and support. In general, people on treatment are seen every two weeks for the first month, and then each month until the end of treatment. Blood counts and biochemistry are evaluated at each visit. Dose-modification guidelines are followed when side-effects or laboratory changes require intervention.

The majority of people DO complete a full course of treatment for HCV once they have begun. Only a small minority actually cease their treatment early because of side-effects.

Contraindications to treatment

The major contraindications to therapy include:

- decompensated liver disease
- major psychiatric conditions, particularly severe depression
- autoimmune disease
- significant cardiac disease
- pregnancy (ribavirin is a teratogen – ***patients and their partners must avoid pregnancy during therapy and for six months after cessation of treatment due to the possibility of birth defects)***

Although interferon is contraindicated in people with depression, it may be used safely in patients with controlled depression and anxiety disorders or controlled seizure disorders. If the person is being treated by a psychiatrist or neurologist, discussion with them is recommended before the initiation of interferon therapy.

Monitoring for complications, including cirrhosis

Not all people will be appropriate for, or interested in, treatment. Regular clinical monitoring must continue, with a focus on those most at risk of progression.

Thrombocytopenia, prolonged prothrombin time (PT) or hypo-albuminaemia all suggest the presence of cirrhosis with some degree of hepatic decompensation and portal hypertension. However, people with well-compensated cirrhosis due to chronic HCV infection may have a completely normal platelet count, PT and serum albumin level for many years. Hepatic ultrasound may show features of cirrhosis or fatty infiltration but is commonly normal.

Markers of cirrhosis include:

- prolonged PT or international normalised ratio (INR)
- low albumin
- elevated bilirubin
- low platelet count (thrombocytopenia)
- AST/ALT ratio > 1.0
- AST/platelet ratio (APRI) > 1.5

People with HCV-associated cirrhosis should be monitored for deteriorating liver function and for the development of hepatocellular carcinoma (HCC). Often a specialist is involved in the care of a person with cirrhosis but they may attend their drug and alcohol health practitioner when new symptoms develop.

Concerning features include:

- falling serum albumin levels
- prolongation of prothrombin time
- development of jaundice
- development of other clinical signs (e.g. peripheral oedema, ascites, muscle wasting)

People with these features should be referred to a specialist hepatologist. HCC is becoming a major clinical problem in patients with HCV-associated cirrhosis. The current recommendations regarding screening for HCC include ultrasound and alpha feto protein (AFP) levels every six months for those people with chronic HCV infection who have diagnosed or suspected underlying cirrhosis. This is to detect small lesions that may be amenable to curative treatment including liver transplantation.

General management for people with chronic HCV infection

Vaccination

Coinfection with more than one hepatitis virus may be associated with more severe liver disease. Super infection with hepatitis A viral infection in a person with chronic HBV or HCV, or acute HBV in a person with chronic HCV, may precipitate the development of acute liver failure. In the long term, people with HBV and HCV coinfection tend to be more likely to progress to cirrhosis and to develop hepatocellular carcinoma.

HAV and HBV vaccination should be offered to all people with chronic HCV infection if they have no evidence of immunity.

Lifestyle issues/alcohol intake

The possibility of lifestyle modification needs to be discussed, particularly in relation to alcohol consumption and drug use.

Alcohol intake ideally should be minimal. Excessive alcohol consumption (>40 g/day) is associated with higher risk of disease progression and a poorer response to treatment. For those who continue to drink, advice about alcohol intake should be tailored to their stage of disease and risk of progression. For example, someone with early liver disease, no risk factors for progression, a consistently normal ALT, and normal clinical examination could be advised to drink alcohol in accordance with the safety advice given to the general population. In contrast, a person with significant fibrosis will have an increased need for moderation of alcohol intake. Individuals with cirrhosis should certainly be encouraged to stop drinking alcohol altogether.[5]

Advice about alcohol intake should be tailored to your assessment of their stage of disease and risk of progression.

There will be individuals who continue to inject drugs and who require ongoing care and monitoring. They are not only at risk of superinfection with other HCV genotypes, but may be putting others at risk through their injecting practices. Drug and alcohol health professionals play a key role in their care. They are able to identify and counsel those most at risk from their HCV, they may play an integral role in assisting someone to become ready for HCV treatment, and they can investigate and deal with other aspects of a person's medical care, including opiate replacement pharmacotherapy.

Nutrition and body weight

For most people with chronic hepatitis C, dietary recommendations are the same as for the general population. These include encouraging:

- grilled rather than fried food
- lean meats and fish
- reduced-fat products
- wholemeal bread and pasta
- vegetables and fruit
- minimisation of fat for spreading and cooking

Overweight or obese patients should be advised of a gradual weight reduction program, particularly as there is increasing evidence of interaction between HCV, obesity and type 2 diabetes in accelerating progression to fibrosis. Those who may have fatty liver need to avoid a precipitous fall in weight as this can induce deterioration in liver function. Obesity is also associated with poorer responses to HCV treatment.

Fatigue and other symptoms

People with chronic hepatitis C may report fatigue, malaise, headache, rash, and aching muscles and joints. Consideration should be given to specific food and drinks that may be triggering symptoms, as well as work, family or other commitments, which may exacerbate stress and fatigue. Patients may benefit from planning rest periods during the day or incorporating light to moderate exercise into their routines to reduce fatigue.

Complementary therapies

There is no evidence that herbal medicines have an antiviral effect despite many patients reporting some symptomatic improvement and the ability of some agents to induce a fall in ALT.

Most preparations are safe but some have reported hepatotoxicity and should be avoided (e.g. mistletoe, valerian, heliotropium, kombucha tea and kava). Close monitoring of liver biochemistry is recommended at the commencement of any herbal medicine. Hepatitis Councils have further information regarding complementary therapies.

Discrimination

Australian Commonwealth law prohibits discrimination against someone with an infectious disease, unless the discrimination can be shown to be necessary to protect public health. Most states and territories have laws in the same terms as the Commonwealth law.

Hepatitis C is a highly stigmatised condition and many people living with the disease experience discrimination. The Anti-Discrimination Board of NSW found that discrimination in health care settings may take many forms and results in unfair treatment of patients.[19]

Discriminatory behaviours in this setting may include:

- refusal of care or treatment
- lack of pre- and post-test discussion
- giving a lower standard of treatment

Behaviours which reflect stigmatisation towards a patient can also reduce the standard of health care received and lower the quality of life for people with hepatitis C. Such behaviours include:

- breaches of confidentiality and disclosure related to hepatitis C, even among health care workers
- assumptions about how people acquired hepatitis C
- assumptions about people's past or present drug use

Health care workers should respect the rights of people with hepatitis C regardless of how they were infected. Everyone living with hepatitis C should have access to care and services regardless of transmission route, gender, race, culture, sexual orientation or lifestyle issues (such as drug use).

Discrimination and stigmatising behaviours can be avoided by:

- ongoing health care worker education and continuing medical education
- ensuring standard infection control procedures are followed, thus reducing the need for disclosure or differential treatment
- ensuring people's privacy and confidentiality are protected

As stated in ***A Model of Care for the Management of Hepatitis C Infection in Adults,***[20] the suggested items below may limit and prevent discrimination:

- take a holistic approach, such as treating the client as a whole person with many potential interacting aspects rather than a person with one disease
- be non-judgmental and have a respectful attitude towards the client's needs, treatment preferences and lifestyle
- provide advice and information on the full range of medical and non-medical approaches to managing hepatitis C
- empower clients with sufficient information to make informed decisions that best suit their lifestyle, occupational and social responsibilities, personal needs and preferences
- develop rapport and mutual trust

The National Hepatitis C Project

The National Hepatitis C Project is an Australian Government-funded, 18-month initiative based with the Multicultural HIV/AIDS and Hepatitis C Service (MHAHS).

The Project aims to address identified gaps in relation to hepatitis C in Culturally and Linguistically Diverse (CALD) communities.

The priority target groups for the Project are the general community, young people and injecting drug users. A written resource – *Hepatitis C is Everybody's Business* – has been produced in 15 languages, including English.

For more information and/or regular Project updates, contact the Project Officer at MHAHS on (02) 9515 5030.

References

1 National Centre in HIV Epidemiology and Clinical Research. HIV/AIDS, viral hepatitis and sexually transmissible infections in Australia Annual Surveillance Report 2007. Sydney: National Centre in HIV Epidemiology and Clinical Research, The University of New South Wales, 2007.

2 Razali K, Thein H H, Bell J, Cooper-Stanbury M, et al. 'Modelling the hepatitis C virus epidemic in Australia'. Drug Alcohol Depend 2007;91:228-235.

3 Bowden DS, Berzsenyi DM (2006). 'Chronic hepatitis C virus infection: genotyping and its clinical role'. Future Microbiol 1: 103–112.

4 Crofts N, Dore G, Locarnini S. 'Hepatitis C: An Australian Perspective'. Melbourne: IP Communications, 2001:209.

5 ASHM. 'HIV,Viral Hepatitis and STIs: a guide for primary care', 2008 Edition:15.

6 MacDonald M, Wodak A. 'Preventing transmission of hepatitis C. Hepatitis C Update. A management guide for general practitioners'. AFP 2003;28(Dec):10.

7 Ceci OM, Marello F, Francavilla R, Loizzi P, et al. 'Vertical transmission of hepatitis C virus in a cohort of 2.447 HIV-seronegative pregnant women: A 24-month prospective study', Journal of Paediatrics, gastroenterology and nutrition, 2001; 33, 570-575.

8 Gibb DM, Goodall RL, Dunn DT, Healy M, Neave P, Cafferkey M, Butler K. 'Mother to child transmission of hepatitis C virus: evidence for preventable peripartum transmission', Lancet, 2000; 356, 904-907.

9 Alric L, Costedoat N, Piette JC et al. ' Hepatitis C and pregnancy', Revue de Medecine Interne 2002: 23(3), p. 283-91

10 Resti M. 'Mother-to-infant transmission of hepatitis C virus', Italian Journal of Gastroenterology & Hepatology, 1999; 31, 489-93.

11 Department of Health and Ageing: National HCV Testing Policy 2007, 24-27. [Online] [access 2008]. Available from http://www.health.gov.au/internet/main/publishing.nsf/Content/phd-hepc-testing-policy-may07

12 Micallef JM, Kaldor JM, Dore. GJ. 'Spontaneous viral clearance following acute hepatitis C infection: a systematic review of longitudinal studies', Journal of Viral Hepatitis, 2006; 13, 34-41.

13 Department of Health and Ageing: National HCV Testing Policy 2007, 32. [Online] [access 2008]. Available from http://www.health.gov.au/internet/main/publishing.nsf/Content/phd-hepc-testing-policy-may07

14 Novick DM, Kreek MJ. 'Critical issues in the treatment of hepatitis C virus infection in methadone maintenance patients'. Addiction, 2008; June 103(6), 905-918.

15 Manns MP, McHutchison JG, Gordon SC et al. 'Peginterferon alfa-2b plus ribavirin compared with interferon alfa-2b plus ribavirin for initial treatment of chronic hepatitis C: a randomised trial'. Lancet 2001;358:958-65.

16 Fried MW, Shiffman ML, Reddy KR et al. 'Peginterferon alfa-2a plus ribavirin for chronic hepatitis C virus infection'. N Engl J Med. 2002;347:975-82.

17 Davis GL, Wong JB, McHutchinson JG, Manns MP, Albrechtr J. 'Early virologic response to treatment with pegylated interferon alfa-2b plus ribavirin in patients with chronic hepatitis C'. Hepatology 2003; 38:645-652.

18 Jensen DM, Morgan TR, Marcellin P, Pockrus PJ, Reddy KR, Hadziyannis S, et al. 'Early identification of HCV genotype 1 patients responding to 24 weeks peginterferon -2a(40kd) ribavirin therapy', Hepatology 2006; 43:954-960.

19 Anti-discrimination Board of New South Wales. C-Change: Report of the enquiry into hepatitis C-related discrimination. Sydney:2001(Nov).

20 Australian National Council on AIDS, Hepatitis C and Related Diseases. A Model of Care for the Management of Hepatitis C Infection in Adults. July 2003.

Contacts- Hepatitis C and related organisations/groups can be contacted for further resources and support information

AUSTRALIA – HEPATITIS C COUNCILS

Hepatitis Australia
National
Tel: 61 2 6232 4257
Fax: 61 2 6232 4318
Web: www.hepatitisaustralia.com

Australian Capital Territory
Tel: 02 6257 2911
1300 301 383 (Hepline)
Fax: 02 6257 1611
Web: www.acthepc.org

New South Wales
Tel: 02 9332 1599
1800 803 990 (Freecall country)
Fax: 02 9332 1730
Web: www.hepatitisc.org.au

Northern Territory
NT AIDS and Hepatitis Council
Tel: 08 8941 1711
1800 880 899 (Freecall)
Fax: 08 8941 2590
Web: www.ntahc.org.au

Queensland
Tel: 07 3236 0610
1800 648 491 (Freecall country)
Fax: 07 3236 0614
Email: admin@hepatitisc.asn.au
Web: www.hepqld.asn.au

South Australia
Tel: 08 8362 8443
1300 437 222 (cost of a local call)
Fax: 08 8362 8559
Web: www.hepccouncilsa.asn.au

Tasmanian Council on AIDS, Hepatitis and Related Diseases
Tel: 03 6234 1242
1800 005 900 (Freecall country)
Fax: 03 6234 1630
Web: www.tascahrd.org.au

Victoria
Tel: 03 9380 4644
1800 703 003 (Freecall country)
Fax: 03 9380 4688
Web: www.hepcvic.org.au

Western Australia
Tel: 08 9227 9800
08 9328 8538 (Infoline)
1800 800 070 (Freecall country)
Fax: 08 9227 6545
Web: www.hepatitiswa.com.au

AUSTRALIA – RELATED

Australian Injecting and Illicit Drug Users League (AIVL)
Tel: 02 6279 1600
Email: info@aivl.org.au
Web: www.aivl.org.au

Australasian Society for HIV Medicine (ASHM)
Tel: 02 8204 0700
Email: ashm@ashm.org.au
Web: www.ashm.org.au

Australian Drug Foundation
Tel: 03 9278 8100
Email: adf@adf.org.au
Web: www.adf.org.au

Gastroenterological Society of Australia
Tel: 02 9256 5454
Email: feedback@gesa.org.au
Web: www.gesa.org.au

National Centre for Education and Training on Addictions
Tel: 08 8201 7535
Email: nceta@flinders.edu.au
Web: www.nceta.flinders.edu.au

National Centre in HIV Epidemiology & Clinical Research (NCHECR)
Tel: 61 2 9385 0900
Fax: 61 2 9385 0920
Web: www.nchecr.unsw.edu.au

Funded by
Australian Government
Department of Health and Ageing

Produced and Distributed by:
NATIONAL CENTRE IN HIV EPIDEMIOLOGY AND CLINICAL RESEARCH
ashm
Australasian Society for HIV Medicine Inc

ashm
National Viral Hepatitis Education Program
ISBN: 978-1-920773-62-5
ABN: 48 264 545 457
Revised September 2009
Print more copies of this supplement from: www.ashm.org.au/publications

For additional copies of this resource and the Hepatitis C Fact Sheet for Clients of Pharmacotherapy Services contact:

Australasian Society for HIV Medicine Inc (ASHM)
LMB 5057 Darlinghurst NSW 1300
Tel: 61 2 8204 0700
Fax: 61 2 9212 2382

National Centre in HIV Epidemiology & Clinical Research (NCHECR)
Tel: 61 2 9385 0900
Fax: 61 2 9385 0920