Over the past decade hepatitis C virus (HCV) has been one of Australia’s most commonly notified infectious diseases. By the end of 2010, it was estimated that 297,000 people living in Australia had been exposed to the virus, of whom 221,000 were living with chronic HCV infection. The number of new HCV infections is estimated at 10,000 per year.

Chronic HCV infection can cause long-term liver disease, including cirrhosis and hepatocellular carcinoma (HCC). While understanding of the infection has increased rapidly there is still no vaccine for HCV. Prevention of transmission depends on decreasing exposure to infected blood, particularly by injecting drug use. Treatment is rapidly improving such that the majority of people living with hepatitis C can now be cured. However this requires appropriate testing, assessment and referral.

One of the priority actions in the National Hepatitis C Strategy 2010-2013 is to increase the participation of general practitioners (GPs), nurses and other members of primary healthcare teams in the management of hepatitis C, including the delivery of treatment.

GPs have a vital role in diagnosis, support, assessment, referral and treatment of people living with chronic hepatitis C.
**The virus**

Hepatitis C is a ribonucleic acid (RNA) virus, discovered in 1989, belonging to the flavivirus family. There are six genotypes of hepatitis C with approximately 40 different subtypes. Currently, genotype is the best predictor of treatment responsiveness but new agents will change this.

**Natural History**

A few patients will experience symptoms of acute hepatitis at the time of infection, however most people will remain asymptomatic. Figure 1 illustrates the natural history of hepatitis C infection. Of 100 people who are infected with hepatitis C, between 25 and 45 will clear the virus up to 12 months (usually within 3-6 months) after infection. Those that do not clear HCV are described as having chronic hepatitis C. Most will experience few symptoms but when present they may include fatigue, nausea, headaches, depression, upper abdominal pain and intolerance to fatty foods and alcohol. After 20-40 years some patients will experience progressive liver fibrosis and may develop signs and symptoms of cirrhosis, liver failure or liver cancer (HCC).

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**Figure 1: Natural history**

This chart shows the different potential outcomes for untreated chronic hepatitis C. It does not show the outcome for individual people. Factors such as alcohol intake, age when hepatitis C was acquired and current level of inflammation may all influence an individual’s outcome.

Adapted from G Dore/Hepatitis NSW (2012)

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**Table 1: Role of the GP**

| Prevention         | Improved health care of injecting drug users.  
|                    | Reduce sharing of injecting equipment.  
|                    | Vaccination for hepatitis B (and hepatitis A if at risk).  
|                    | Psycho-social support including alcohol and other drug counselling.  
|                    | Drug substitution treatment – methadone or buprenorphine  
| Diagnosis          | Identify people at risk of chronic hepatitis C and offer testing.  
|                    | Think: could this patient have chronic hepatitis C? Most of the risk of having chronic hepatitis C can be assessed by the question – “Have you ever injected drugs?”  
| Assessment and further care | Support and good comprehensive primary care. See RACGP ‘Red Book’ Guidelines for preventive activities in general practice (7th edition) 2009 for details.  
|                    | Perform basic investigations. Refer to Figure 2 and Table 2.  
|                    | Determine:  
|                    | Acute or chronic infection.  
|                    | Active or resolved.  
|                    | Presence of other causes of liver disease.  
|                    | Presence of complications e.g. cirrhosis.  
|                    | Lifestyle:  
|                    | Alcohol / drug use – advise minimal alcohol use.  
|                    | Smoking – advise that quitting will lead to improved general health.  
|                    | Weight and exercise – obesity is associated with a poorer response to treatment.  
| Treatment:         | Provide information about treatment.  
|                    | Referral to specialist for assessment and possible treatment.  
|                    | Refer to patient support organisations.  
|                    | Provide support before, during and after treatment.  
|                    | Detection and treatment of side effects of treatment e.g. depression.  
|                    | Shared care for chronic hepatitis C treatment – consider attending ASHM hepatitis C prescriber training courses.  

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2 General Practitioners and Hepatitis C
Transmission

Hepatitis C transmission occurs predominantly through blood-to-blood contact. The most common mode of transmission in Australia continues to be injecting drug use (IDU). The continuation and expansion of needle and syringe programs for injecting drug users is vital to assist in reducing the spread of HCV. While contaminated needles and syringes are most infectious, there is some evidence for transmission from other shared injecting equipment, such as spoons, filters and tourniquets.

The evidence at this time suggests a very low rate of transmission through sexual contact. Transmission may occur if there is blood to blood contact during sexual activity. It is clear that sexual transmission rates are higher if the patient is coinfected with HIV and possibly other STIs.

The risk of perinatal transmission of HCV varies from 0 to 11% and averages 5%. Coinfection with HIV increases the risk at least two-fold. To date, the National Health and Medical Research Council has not recommended changes to obstetric practice during antenatal care, delivery and post partum care or in management of the neonate. Currently, there is no indication for elective caesarean section in HCV-positive mothers. Despite HCV RNA being detectable in breast milk, breastfeeding has not been directly linked to transmission of HCV. Australian guidelines recommend breastfeeding should not be discouraged unless there are cracked and bleeding nipples.

Household transmission (e.g. via razors or toothbrushes) is considered rare. Nevertheless, because the possibility of blood contact exists, these items should not be shared.

There is NO risk of viral transmission of hepatitis C through the sharing of cups and plates or via hugging and other such personal contact.

Hepatitis C Testing

Informed Consent and Conveying HCV Test Results

General practitioners and other primary health care professionals play an important role in testing for HCV. All testing for HCV should be done after a discussion with the patient and gaining informed consent. This may require the use of an interpreter to ensure patients understand the processes and implications of testing. This process is a valuable educational opportunity to help minimise HCV transmission in the community. The National HCV Testing Policy 2012, available at http://testingportal.ashm.org.au/hcv, provides full details of indications for testing and provides access to related resources, guidelines and policies. See Chart 2 for the HCV testing pathway.

Test results should always be given in person and again it may be necessary to use an interpreter to ensure results have been understood. Patients may benefit from the supply of culturally relevant written material and contact details for relevant support services.

If the result is negative, the discussion should reinforce harm reduction strategies, education and information messages about safe behaviours.

Gaining informed consent

This discussion should include:
- 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;
- possible need 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 and positive result means including basic printed information about HCV; and
- assessment of support mechanisms while waiting for the test result and/or if the result is positive.

Conveying a positive test result

If the test result is positive, discussion should include (at appropriate time intervals), issues such as:
- immediate needs and support for safe injecting behaviours – education, information and support including needle and syringe programs if appropriate;
- discussing results with family and friends;
- options in drug treatments and medical management and referral information where appropriate;
- ongoing counselling or therapy if required;
- ways to deal with loss and grief, depression, anger, anxiety, strong emotions and reactions to the infection;
- strategies for managing HCV which are flexible and appropriate to the person’s needs; and
- legislative requirements (notification, contact tracing, storage and coding).
Initial assessment

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. An HCV RNA test (usually HCV PCR test) documents viraemia, and thus active infection. HCV RNA tests can either be qualitative (result being positive or negative) or quantitative (result providing viral load).

<table>
<thead>
<tr>
<th>Test</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCV Ab test</td>
<td>If positive, shows evidence of previous exposure to the virus. Importantly, does NOT provide immunity against reinfection with the HCV virus. Remains positive following treatment.</td>
</tr>
<tr>
<td>HCV PCR test</td>
<td>If positive, shows active infection (i.e. viraemia, the presence of HCV RNA).</td>
</tr>
<tr>
<td>ALT</td>
<td>If elevated in the context of HCV Ab, generally shows some level of liver disease from HCV virus. High levels are associated with disease progression.</td>
</tr>
</tbody>
</table>

Table 3 provides a summary of baseline screening and further investigations which should be undertaken to exclude other forms of liver disease.

**Figure 2: HCV testing pathway**

- **Screen by HCV EIA**
  - **POSITIVE**
    - Confirm by alternate HCV EIA
      - **POSITIVE**
        - NAT for HCV RNA
          - **POSITIVE**
            - Active infection
              - Report to referring doctor who informs patient
          - **NEGATIVE**
            - Likely past infection with viral clearance OR if liver tests abnormal possible low V/L
              - Repeat HCV RNA in 6 months if infection still a concern
            - *Doctor refer for further evaluation genotype, viral load – notify relevant bodies*
  - **NEGATIVE**
    - Repeat at 1–2 months if acute infection Suspected

**Table 3: Baseline screening and further investigations**

**Baseline screening to exclude other conditions that may influence treatment:**
- Full Blood Count (FBC)
- Electrolytes, urea, creatinine
- Coagulation studies
- Fasting blood sugar level and lipids
- Thyroid function tests
- Liver ultrasound

**Detect other causes of liver disease:**
- Hepatitis A – check hep A IgG, vaccinate if -ve
- Hepatitis B – check anti-HBs, anti-HBc, HBsAg, vaccinate if all -ve
- HIV Ab
- Iron studies (haemochromatosis)
- Autoimmune screenscreen
- Alpha–1 – antitrypsin (deficiency)
- Copper, caeruloplasmin (Wilson’s disease)

**Determine hepatitis C genotype and quantitative PCR (viral load):**

Influences length of treatment and response to treatment

**Cleared infection**

Approximately 25% (20-45%) of people with acute HCV infection spontaneously clear the infection without treatment, generally within 3-6 months of infection. Qualitative HCV RNA (HCV PCR) testing should be a standard component of the diagnostic work-up of all individuals who are anti-HCV reactive.13

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

A qualitative HCV PCR test in these conditions is rebatable under Medicare. **Patients found to be HCV RNA negative should be reassured that while they have been exposed to HCV in the past, they have cleared the infection.**
It is recommended that patients with normal liver function and no detectable HCV RNA have repeat RNA (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 of patients, as their existing HCV antibody will remain positive, despite having cleared infection. Neither does their positive antibody confer any protection towards subsequent infection with hepatitis C. Although there are no specific guidelines for screening in this setting, an annual qualitative RNA test (PCR), regardless of ALT level, should be performed to detect any subsequent HCV infection.

**Chronic infection**

Approximately 75% of people exposed to HCV progress to a chronic 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 HCV RNA (PCR) 6 months or more after initial infection.

The outcomes for people with chronic HCV are variable as shown in Figure 1. Factors that will increase the risk of complications are highlighted in the section Identifying those most at risk below. 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 fibrosis.

After 20 years of infection, on average about 7% of people with chronic HCV infection may have developed liver cirrhosis with this figure increasing to 20% after 40 years. After 40 years of infection, about 5% may have developed liver failure or liver cancer.

**Monitoring someone with chronic HCV**

It is recommended that a patient with chronic HCV is seen every 6 to 12 months. The main aims for general practitioners seeing a patient in this setting are to:

- Reduce behaviours that risk re-infection or superinfection and transmission to others—this may involve referral for opioid substitution treatment;
- Identify and address any modifiable risk factors for liver disease (e.g. excessive alcohol consumption);
- Identify those most at risk of chronic HCV infection complications and who may be appropriate for antiviral therapy;
- Provide information about treatment and assess the patient’s 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) occurs where appropriate;
- Determine the person’s need for support services; consider a GPMP and TCA* including dental referral if appropriate; and
- Optimise general health—ensure appropriate health screening as per RACGP Guidelines.

* GPMP General Practice Management Plan (Medicare Item number 721), TCA Team care arrangement (Medicare Item number 723)

- see: www.ashm.org.au

**Identifying those most at risk**

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

**Alcohol intake**

This is discussed further in the section, ‘General management.’ Broadly speaking, increased alcohol intake is associated with increased risk of liver damage. Any patient with excessive alcohol consumption (more than 4 standard drinks per day) should be advised of their increased risk of disease progression and supported 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 in many patients. It is important not to assume date of first positive HCV Ab test is the date of infection. In those exposed through injecting drug use, assume likely infection in the first

**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
- Stage of fibrosis as shown on biopsy
- Obesity
- Insulin resistance
- Persistent elevation of ALT > 5x normal

**NB:** Most patients over 40 years of age with chronic HCV in Australia are likely to have been infected for more than 15 to 20 years. They should be considered more closely for HCV treatment assessment.
2-3 years of commencing IDU. Many patients, given the often asymptomatic nature of the disease, will not have been aware of their infection and so will have not been tested for some time following exposure. A patient’s age alone is often a very good indicator of duration of infection. Most patients who have acquired HCV through injecting drug use and are over the age of 40 years in Australia are likely to have been infected for more than 20 years. It is good practice to be thinking about HCV treatment assessment for any patient over the age of 40.

**Coinfection with HIV/HBV**

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

**Obesity/Insulin resistance**

There is a clear association between obesity and/or insulin resistance with or without diabetes and HCV liver disease progression. Patients with chronic HCV and obesity should be supported to lose weight and have regular exercise. This is discussed further in the section ‘General management’.

**ALT level**

ALT testing should no longer be the 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 fibrosis. In addition, among those with elevated ALT levels, the extent of elevation correlates poorly with disease progression risk. Despite these limitations, regular liver testing (every 6-12 months) is recommended to determine the extent of liver inflammation and assess synthetic function; albumin and bilirubin are important markers of liver function as opposed to inflammation (ALT). Normal ALT levels are now defined as <30 for males and <19 for females regardless of the stated laboratory normal range.

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

**Pathology tests**

Regular monitoring should include full blood count and liver tests.

**Liver (function) tests**

Liver (function) tests (every 6-12 months) can provide information about the extent of liver inflammation and stage of liver disease. A reduced albumin, particularly if combined with low platelet count (<100,000) suggests underlying cirrhosis. Other indicators of cirrhosis are prolonged prothrombin time (PT), elevated bilirubin (although if isolated may indicate Gilbert’s syndrome), an AST/ALT ratio of >1.0, and an AST/platelet ratio of >1.5. However, cirrhosis may (uncommonly) be present in the setting of normal albumin, bilirubin, platelet count and PT levels.

**HCV genotype**

HCV genotype determines the length, and soon the type, of treatment and likely response to current medications. Genotypes 2 and 3 require shorter (24 weeks) treatment and have a higher likelihood of success. Genotypes 1 and 4 require longer (48 weeks) treatment and have a lower likelihood of success. HCV genotype testing is Medicare funded for anyone considering treatment (see Table 3).

HCV genotype testing may assist both patients with HCV and their clinicians in relation to treatment decision-making and need not be delayed until specialist review. Patients with HCV genotype 2 or 3 should be advised that they have a high chance of eradicating the virus with just six months of standard treatment and that the new protease inhibitors will not be used for genotype 2 or 3 infections.

Patients with HCV genotype 1 infection should be informed of the coming availability of new medications which will Increase the success of treatment significantly. The HCV viral load also provides important information in relation to treatment success. In particular 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. The HCV viral load does not correlate with liver disease progression risk.

**IL 28B testing**

A recent addition to the assessment process is the measurement of a patient’s IL 28B genotype. In patients with genotype 1 infection this test can improve the prediction of treatment outcome by identifying the patient’s interferon responsiveness. Results are reported as a TT, TC or CC genotype and patients who have a CC genotype have a much higher response rate to standard therapy. Those with a TT genotype have a response of < 20% to interferon/ribavirin. While not funded by Medicare, this test is performed by specialist units managing genotype 1 patients.
Decision making about treatment
In determining whether a patient is appropriate for antiviral treatment, the general practitioner is in a good position to consider the patient's social situation, 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 patient may manage any HCV treatment. Of note, a number of studies now confirm that treating well selected patients on methadone or buprenorphine treatment results in outcomes equivalent to those achieved in non opioid dependent patients.

All patients with chronic HCV infection at risk of liver disease progression should be advised of the potential benefits of antiviral therapy and also of the changing nature of treatment. Where treatment is appropriate, much of the assessment should be related to identifying the opportune timing of therapy. Patients at highest risk of progression (based on associated factors listed) should be encouraged to consider therapy as soon as possible. For other patients, the timing of treatment can be based on other lifestyle issues such as work, social circumstance, control of substance use, desire for pregnancy and the changing nature of treatment, with interferon free regimens likely to be available in 5-7 years.

While most treatment is based in public hospitals at present, there is an important trend towards making treatment available in the community. This will involve primary care clinicians taking on a greater role in the support and monitoring of patients 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, Victoria, South Australia and Western Australia have been accredited to prescribe hepatitis C maintenance therapy following relevant State or Territory approval.

Liver clinics 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 or hepatologist, which can be made at any time, is necessary for the assessment of complex patients with comorbid mental health and medical illnesses, those with advanced liver disease, those who may need new drugs for therapy. Local Hepatitis Organisations or drug user groups can provide information and peer support for people considering treatment (Refer to the ‘Contacts’ section).

Antiviral treatment for HCV
Therapy with pegylated interferon and ribavirin has been available for several years to any previously untreated patient 18 years or older with chronic HCV infection and compensated liver disease, who agrees to effective contraception. The imminent arrival of two new protease inhibitor drugs for HCV is changing decision-making around treatment initiation at this time however.

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

Aims of treatment
The major aim of treatment is to achieve viral eradication. In HCV, viral eradication is defined as a negative HCV RNA (PCR) by a sensitive qualitative test six months after the completion of therapy (termed a sustained virological response or SVR).

Current therapy and predictors of response
Current therapy for HCV (2012) is a combination of once-weekly subcutaneously administered pegylated interferon plus twice-daily oral ribavirin. The likelihood of response is much higher in patients with HCV genotype 2 or 3 than genotype 1 or 4 (See table 5).

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) and in genotype 1(G1) a CC IL28B genotype. Treatment response is monitored at week 4 and 12 of therapy. A rapid virological response (RVR) is defined as a negative HCV RNA at week 4. This predicts a > 90% SVR in all
patients and it may allow a shorter course of therapy in G1 patients. An early virological response (EVR) may be defined as a >2 log fall in HCV RNA at week 12 or complete loss of HCV RNA at week 12. Both indicate a greater likelihood of an SVR and a failure to achieve a >2 log fall is an indication to cease treatment at week 12. Table 4 provides a summary of the terms and treatment response definitions.

With the introduction of new agents and more frequent viral load testing, patient treatment courses will be modified and shortened in many instances, but guidelines for these modifications are still being developed internationally.

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.

**Table 4: Treatment Response Definitions**

<table>
<thead>
<tr>
<th>Response</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non response</td>
<td>At no stage does the HCV RNA become negative (undetectable)</td>
</tr>
<tr>
<td>RVR (rapid virological response)</td>
<td>Undetectable HCV RNA at week 4</td>
</tr>
<tr>
<td>EVR (early virological response)</td>
<td>Complete EVR (cEVR) No RVR, but undetectable HCV RNA at week 12</td>
</tr>
<tr>
<td>EVR (partial EVR)</td>
<td>No RVR and detectable HCV RNA at week 12, but ≥2 log10 drop from baseline</td>
</tr>
<tr>
<td>Non-EVR</td>
<td>&lt;2 log10 drop from baseline at week 12</td>
</tr>
<tr>
<td>ETR (end of treatment response)</td>
<td>Undetectable HCV RNA at end of treatment</td>
</tr>
<tr>
<td>SVR (sustained virological response)</td>
<td>Undetectable HCV RNA 6 months post treatment</td>
</tr>
<tr>
<td>Relapse</td>
<td>Detectable HCV RNA post treatment</td>
</tr>
</tbody>
</table>

**Table 5: HCV genotype and treatment duration and outcomes with current s100 treatment (Pegylated Interferon & Ribavirin)**

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Duration of treatment</th>
<th>Likely success rate of treatment*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>48 weeks</td>
<td>40 – 54 %</td>
</tr>
<tr>
<td>2</td>
<td>24 weeks</td>
<td>65 – 82 %</td>
</tr>
<tr>
<td>3</td>
<td>24 weeks</td>
<td>65 – 82 %</td>
</tr>
<tr>
<td>4</td>
<td>48 weeks</td>
<td>43 – 70 %</td>
</tr>
</tbody>
</table>

* these outcomes are based on dual combination therapy only

People who have failed to respond to either interferon monotherapy or combination interferon plus ribavirin are eligible for further treatment under current Section 100 guidelines with pegylated interferon and ribavirin, and for those who have failed this form of treatment there is access to treatment with the new protease inhibitors through preregistration access programs. Access is restricted to major treatment units at the time of publication.

Retreatment of individuals who have relapsed after a course of pegylated interferon and ribavirin with the same two drugs can result in an SVR in a small percentage of cases, but in those with a G1 infection, it is better to seek access to the new protease inhibitors to optimise outcomes.

Because of the expectation that both Telaprevir and Boceprevir will be approved for use and funded by the Government in Australia in the next 12 months, patients with genotype 1 infections and mild or moderate but slowly progressing disease are being monitored and treatment-deferred until the more effective triple therapy combination becomes available. Table 5 provides the duration of treatment and treatment response for different genotypes using current combination Pegylated Interferon and Ribavirin treatment.


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

**Side effects**

Side effects are common but, importantly, do not usually require discontinuation of treatment. However, patients on treatment do require significant support and encouragement throughout treatment. 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 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, rarely, erythropoietin prescribed. Those who experience the greatest anaemia achieve the best results.
Interferon causes serotonin depletion which may result in depression and selective serotonin reuptake inhibitors (SSRIs) are effective in its management. 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 and white blood cell count.

Given the wide range and potential seriousness of side effects, patients must be closely monitored during therapy. Currently, most treatment is provided through public hospitals and patients have ready access to nurse specialists to advise and support them through therapy. In general, patients on therapy are seen twice in the first month, and then each month until the end of treatment, with blood counts and biochemistry evaluated at each visit. Dose modification guidelines are followed when side-effects or laboratory changes require intervention.

The majority of patients 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**

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

**Monitoring for complications, including cirrhosis**

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

Thrombocytopenia, prolonged PT or hypoalbuminaemia all suggest the presence of cirrhosis with some degree of hepatic decompensation and portal hypertension. However, patients with well-compensated cirrhosis due to chronic HCV 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. By specifically identifying features that may indicate cirrhosis in your ultrasound request, the reports can be made much more helpful.

All patients with HCV-associated cirrhosis should have an endoscopy to define the presence or absence of varices and they should all be monitored for deteriorating liver function and for the development of hepatocellular carcinoma (HCC). Where varices are identified, appropriate intervention, which may include banding and or pharmacological management, must be initiated. Often a specialist is involved in the care of a patient with cirrhosis but the patient may attend his or her general practitioner when new symptoms develop.

Patients with these features should be referred to a specialist hepatologist. Hepatocellular carcinoma is becoming a major clinical problem in patients with HCV-associated cirrhosis.

Controversy does exist as to the cost effectiveness of this strategy but the recommended approach ensures patients are reviewed regularly. Suspicion of an HCC should lead to referral to a specialist centre for further investigation and treatment.

**General management**

**Vaccination**

Coinfection with more than one hepatitis virus may be associated with more severe liver disease. Super infection with hepatitis A infection in a patient with chronic HBV or HCV, or acute HBV in a patient with chronic HCV may precipitate the development of acute liver failure. In the long term, patients with HBV and HCV coinfection tend to be more likely to progress to cirrhosis and to develop hepatocellular carcinoma. Vaccination against hepatitis A is recommended in all HCV infected people at risk of coinfection (travellers, those with multiple sexual partners, men who have sex with men). Hepatitis B vaccination is recommended for all those with chronic HCV.

**The major contraindications to therapy include:**

- Decompensated liver disease;
- Major (untreated or non-responsive) 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).

**Markers of cirrhosis include:**

- Prolonged prothrombin time (PT) or international normalised ratio (INR);
- Low albumin;
- Low platelet count (thrombocytopenia);
- AST/ALT ratio > 1;
- AST/platelet ratio (APRI) >1.5.

**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).

**The current recommendations regarding screening hepatocellular carcinoma (HCC) include:**

- Ultrasound; and
- AFP levels every six months for those patients with chronic HCV infection and determined or suspected underlying cirrhosis, to detect small lesions that may be amenable to curative treatment.
Lifestyle issues

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

Alcohol intake ideally should be minimal. Excessive alcohol consumption (>40 g/day) is associated with a higher risk of disease progression and a poorer response to treatment. Advice to your patient about alcohol intake should be tailored to your assessment of 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 patient with significant fibrosis will have an increased need for moderation of alcohol intake. People with cirrhosis should be certainly be encouraged to stop drinking alcohol altogether.

Advice to your patient about alcohol intake should be tailored to your assessment of their stage of disease and risk of progression and should be guided by the NHMRC Australian Guidelines to Reduce Health Risks from Drinking Alcohol.

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 little evidence that herbal medicines have a significant antiviral effect in HCV but evidence for an effect on oxidative stress and thus hepatic inflammation is increasing. This may explain why ALT levels may fall and many patients report some symptomatic improvement when taking specific therapies (especially silymarin containing products).

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

HCV and HIV

HCV is found in 10% of people living with HIV/AIDS, which means hepatitis C is a significant cause of co-morbidity in HIV. On the other hand, only about 1% of people living with hepatitis C have HIV. The viruses are very different. Hepatitis C is an RNA virus, while HIV is a retrovirus, which affects reverse transcriptase. In Australia, the majority of HIV infections are among men who have sex with men (MSM), while the majority of hepatitis C is among current and past IDUs. It is important for general practitioners to understand these differences so they can advise their patients appropriately.

HIV/HCV co-infection is associated with higher HCV viral load and an accelerated rate of liver disease progression. There is no fundamental difference in the management of HCV in the presence of HIV. Patients with HIV/HCV co-infection who have stable CD4 cell counts on antiretroviral therapy with ongoing evidence of active HCV may be considered for combination pegylated interferon plus ribavirin. Such management is difficult, particularly in patients already taking multiple medications, as side-effects, drug interactions, toxicity and poor tolerability are common.
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. In addition, 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.23

<table>
<thead>
<tr>
<th>Discriminatory behaviours in this setting may include:</th>
</tr>
</thead>
<tbody>
<tr>
<td>■ Refusal of care or treatment;</td>
</tr>
<tr>
<td>■ Lack of pre- and post-test discussion, gaining of informed consent and providing results in an appropriate manner;</td>
</tr>
<tr>
<td>■ Giving a lower standard of treatment.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>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 and should be avoided. Such behaviours include:</th>
</tr>
</thead>
<tbody>
<tr>
<td>■ Breaches of confidentiality and disclosure related to hepatitis C, even among health care workers;</td>
</tr>
<tr>
<td>■ Assumptions about how people acquired hepatitis C;</td>
</tr>
<tr>
<td>■ Assumptions about people’s past or present drug use.</td>
</tr>
</tbody>
</table>

Avoiding discrimination

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 injecting drug use).

<table>
<thead>
<tr>
<th>Discrimination and stigmatizing behaviours can be avoided by:</th>
</tr>
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<tbody>
<tr>
<td>■ Ongoing health care worker education and continuing medical education;</td>
</tr>
<tr>
<td>■ Ensuring standard infection control procedures are followed, thus reducing the need for disclosure or differential treatment;</td>
</tr>
<tr>
<td>■ Ensuring people’s privacy and confidentiality are protected.</td>
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</table>

Needlestick injury and health care workers with HCV

See supplementary section at the end of this document for further information.

Glossary of Terms

<table>
<thead>
<tr>
<th>Antibody test</th>
<th>an initial screening blood test that looks for antibodies to the virus and not for the virus itself.</th>
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<tbody>
<tr>
<td>Fibrosis</td>
<td>formation of scar tissue on the surface of the liver to replace normal tissue lost through injury or infection.</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>extensive and usually permanent scarring of the liver. Cirrhosis interferes with the normal functioning of the liver.</td>
</tr>
<tr>
<td>Combination therapy</td>
<td>the use of two or more types of antiviral and antiretroviral drugs in combination to achieve optimum results.</td>
</tr>
<tr>
<td>Exposure-prone procedure</td>
<td>any situation where there is a potentially high risk of blood-borne virus transmission from a health care worker to a patient during a medical or dental procedure. Any submucosal invasion with sharp hand-held instruments, or procedure dealing with sharp pathology/bone spicules, usually in a confined space or where visibility is poor.</td>
</tr>
<tr>
<td>Non occupational post-exposure prophylaxis (NPEP)</td>
<td>PEP (see below) given to a person following an exposure outside of an occupational setting, e.g. sexual exposure, sexual assault or reuse of injecting equipment.</td>
</tr>
<tr>
<td>Post-exposure prophylaxis (PEP)</td>
<td>drugs and/or vaccination given as soon as possible within 72 hours of exposure to HIV or HBV as an attempt to prevent infection.</td>
</tr>
<tr>
<td>Polymerase chain reaction (PCR)</td>
<td>a laboratory technique that amplifies the genetic material of a virus to a level that can be detected. The presence or absence of the virus can then be determined.</td>
</tr>
<tr>
<td>Window period</td>
<td>the period immediately after a person is infected with an agent, during which the infection is not detectable by laboratory tests, although the person may be infectious.</td>
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</table>
## ASHM resources

Other ASHM resources, including the following hepatitis C related publications, are available from the ASHM website: [www.ashm.org.au](http://www.ashm.org.au)

### Profession Based Booklets
- An Overview of Hepatitis C: Clinical management in opiate pharmacotherapy settings
- Antenatal Testing and Blood-Borne Viruses
- Correctional Officers and Hepatitis C
- Dental and Orofacial Health and Hepatitis C
- Dentists and HIV
- Emergency Service Providers and Blood-Borne Viruses
- General Practitioners and HIV
- Hepatitis B and Primary Care Providers
- Nurses and Hepatitis C
- Pharmacy and Hepatitis C
- Police and Blood-Borne Viruses

### Factsheets
- Decision Making in HBV
- Decision Making in HCV
- Hepatitis B Factsheet: for people newly diagnosed
- Hepatitis C in Brief – patient factsheet
- Hepatitis C Management and Treatment for Clients of Pharmacotherapy Services
- HIV Patient Fact Sheet

### Monographs
- B Positive: all you wanted to know about hepatitis B – a guide for primary care
- Co-infection: HIV & viral hepatitis – a guide for clinical management
- Hepatitis C: clinical management in opiate pharmacotherapy settings
- HIV and Viral Hepatitis C: policy, discrimination, legal and ethical issues
- HIV Management in Australia: a guide for clinical care
- HIV, Viral Hepatitis and STIs: a guide for primary care

### Distance-learning Kit
- Clinical Science of HIV Medicine CD

### Manuals
- Australasian Contact Tracing Manual

### Online Resources
- ASHM Directory of HIV, Viral Hepatitis and Sexual Health Services
- Guide to Australian HIV Laws and Policies for Healthcare Professionals
- DVD
  - C Me, Hear Me. Hepatitis C in our own words

### Online Learning Module

*Hepatitis C management - we can do more* is a case-based online module for clinicians available at [www.ashm.org.au/e-learning](http://www.ashm.org.au/e-learning)

### Further resources and support information are available from the following organisations:

<table>
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<tr>
<th>Australia – Hepatitis organisations</th>
<th>New Zealand – Hepatitis organisations</th>
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<tbody>
<tr>
<td><strong>Hepatitis Australia (Provides links to State and Territory Hepatitis Councils)</strong> Tel: 1300 437 222 (or 1300 HEP ABC) Web: <a href="http://www.hepatitisaustralia.com">www.hepatitisaustralia.com</a></td>
<td><strong>Hepatitis C Support Group (NZ)</strong> Tel: 64 9 377 8500 Web: <a href="http://www.hcvsupport.org">www.hcvsupport.org</a></td>
</tr>
<tr>
<td><strong>The Hepatitis Foundation</strong> Tel: 0800 332 010 (Freecall in NZ) Email: <a href="mailto:hepteam@hepfoundation.org.nz">hepteam@hepfoundation.org.nz</a> Web: <a href="http://www.hepfoundation.org.nz">www.hepfoundation.org.nz</a></td>
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### Acknowledgements

Updated and reviewed by: Prof. Robert Batey, Dr David Baker, Sonja Hill

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**Disclaimer:**

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**FUNDED BY:**

The Australian Government, Department of Health and Ageing

**ENDORSED BY:**

- Australian Liver Association (ALA), ASID Viral Hepatitis Special Interest Group and Australasian Hepatology Association (AHA)
- Australian Drug Information Network
  - Tel: 03 9278 8100 Web: [www.adrn.com.au](http://www.adrn.com.au)
- Australian Drug Foundation
  - Tel: 03 9278 8100 or 1300 858 584 (Infoline) Web: [www.adf.asn.au](http://www.adf.asn.au)
- Australian Government Department of Health and Ageing
- Australian Liver Association, Gastroenterological Society of Australia
  - Tel: 1300 766 176 Web: [www.gesa.org.au](http://www.gesa.org.au)
- Australian Hepatology Association
- Australian Society for Infectious Diseases (ASID)
  - Web [www.asid.net.au](http://www.asid.net.au)
- Australian Injecting and Illicit Drug Users League (AILV)
  - Tel: 02 6279 1600 Web: [www.ailv.org.au](http://www.ailv.org.au)
- Australian Drug Information Network
  - Tel: 1300 000 64672
- Haemophilia Foundation Australia (HFA)
  - Tel: 03 9885 7800 Web: [www.haemophilia.org.au](http://www.haemophilia.org.au)
- National Centre for Education and Training on Addictions
  - Web [www.nceta.flinders.edu.au](http://www.nceta.flinders.edu.au)
- National Health and Medical Research Council
  - Tel: 13 000 64672
- Hepatitis Foundation
  - Tel: 64 9 377 8500
  - Hepatitis C Support Group (NZ)
  - Tel: 0800 332 010 (Freecall in NZ)
  - Email: hepteam@hepfoundation.org.nz
  - Web: [www.hepfoundation.org.nz](http://www.hepfoundation.org.nz)

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ASHM offers training in HIV, viral hepatitis and sexually transmissible infections for general practitioners, nurses and allied health care workers around Australia.

Needlestick injury
The risk of HCV transmission through a needlestick injury depends on the viral load of the source patient, the first aid administered and the nature of the instrument responsible (higher risk with hollow bore needle). In the event of a needlestick or other blood accident, the source (if known) should be approached regarding consent for HBV, HCV or HIV antibody testing.

All general practitioners and other health care workers should have access to infection control guidelines that advise about the management of an occupational injury, including clear written instructions on the appropriate action to take in the event of a needlestick injury and other blood or body substance exposure. They should indicate the need to report occupational exposures immediately and all testing procedures and follow-up treatment should be fully documented. Confidentiality should be maintained.

In general, if an injury or incident occurs where blood or body substances come into contact with non-intact skin or membranes, the following action should be taken:

• Wash exposed membrane or injury with soap and water (an antiseptic could also be used on the skin)
• If eyes have been exposed, thoroughly rinse the eyes with tap water or saline while open
• If mouth has been exposed, thoroughly rinse the mouth with water and spit out
• Seek medical advice immediately for medical evaluation and assessment of the nature of the exposure, the risk of transmission of blood-borne viruses and the need for HIV or HBV post-exposure prophylaxis (PEP) – not available for HCV and other testing
• If the exposure is significant and the source patient is known, his or her consent for HIV antibody, HCV antibody and HCV RNA, and HBsAg testing should be sought
• The staff member should be tested for HCV antibodies at the time of reporting the incident and HCV RNA should be measured at 4 weeks to determine if infection has occurred where the source is known or suspected to be HCV positive.

Health care workers with HCV
All health care workers who perform exposure-prone procedures have an ongoing responsibility to know their HBV, HCV and HIV status, and should not perform exposure-prone procedures if there is evidence of current/active HBV, HCV or HIV infection, as there is a risk of transmission of infection.

An exposure-prone procedure is any in which there is a potentially high risk of BBV transmission from a health care worker to a patient during a medical procedure, such as any procedure with sharp hand-held instruments beneath the mucous membrane, or any procedure dealing with sharp pathology or bone spicules in a confined space or where visibility is poor. Exposure-prone procedures do not include non-invasive examinations or procedures, intact skin palpation, injections or venepuncture.

For more information regarding the rights and responsibilities of health care workers with HBV, HCV or HIV, contact your state or territory’s health department, your local Hepatitis C Council or AIDS Council, or your state or territory’s Anti-Discrimination Board or Equal Opportunity Commission (refer to Contacts).
Detailed References

Detailed references are available at the ASHM website at www.ashm.org.au/publications

1 The Kirby Institute. HIV, viral hepatitis and sexually transmissible infections in Australia Annual Surveillance Report 2011. The Kirby Institute, the University of New South Wales, Sydney, NSW.


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


19 ASHM. HIV/Viral Hepatitis and STIs: a guide for primary care, 2008 Edition 16


