

Eliminating hepatitis C

Part 4. Ongoing care after hepatitis C treatment

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Most patients who receive direct-acting antiviral treatment for hepatitis C are cured. The need for and nature of ongoing clinical care after treatment depends on whether cure has been achieved, the presence of cirrhosis or persistently abnormal liver function test results and ongoing risk of reinfection with hepatitis C virus.

In Australia, over 70,000 people living with hepatitis C have received direct-acting antiviral (DAA) treatment, and GPs are writing an increasing proportion of all DAA prescriptions.^{1,2} Primary care is crucial to management of people after they have received DAA treatment for hepatitis C.

This is the fourth article in a series about treatment of patients with hepatitis C in general practice. Previous articles outlined how to identify patients with hepatitis C, their assessment and treatment with DAAs.³⁻⁵ This article focuses on general practice care of patients after DAA treatment. This includes

recommended care of those who have been cured of hepatitis C, the small proportion who are not cured, those with cirrhosis and those with ongoing risk factors for reinfection.

Determining treatment outcome

Over 95% of patients with chronic hepatitis C are cured after a full course of DAA treatment. Hepatitis C virus (HCV) RNA testing is required to determine treatment success or failure (or subsequent reinfection).

A patient is defined as cured of hepatitis C if HCV RNA is no longer detected by a PCR test on a blood sample taken at least 12 weeks after completing the DAA treatment course.⁶ Cure is also referred to as a sustained virological response at 12 weeks (SVR12).

Advice for patients who are cured

After successful treatment, it is important to inform patients of the following:

- Antibodies against HCV will remain detectable long term. These antibodies represent the body's immune response to the virus and reflect exposure, not active infection.
- Past infection does not result in immunity and the presence of HCV antibodies does not prevent

Medicine Today 2019; 20(9): 36-42

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reinfection. People who continue to engage in behaviours that put them at risk can be reinfected with HCV.

People who inject drugs should be reminded that practising harm reduction will help minimise the risk of reinfection (see below). Men who have sex with men should be reminded about safe sexual practices to minimise the risk of reinfection. It is also worth mentioning that HIV pre-exposure prophylaxis with tenofovir-emtricitabine does not protect against HCV infection.

For people who continue to be at risk of HCV reinfection, HCV RNA testing by PCR should be offered at least annually (note that the MBS funds only one HCV RNA PCR test per 12-month period).⁷ This is also an opportunity to discuss harm reduction measures. There is no indication for repeat hepatitis C antibody testing, as the result will continue to be positive. It is important to let people know that they can be retreated if they are reinfected.

Clinical follow up

The recommended follow up for patients after hepatitis C DAA treatment is shown in the Flowchart.⁸ The need for ongoing clinical follow up is determined by several factors:⁶

- whether hepatitis C has been cured

- the degree of liver fibrosis present before DAA treatment
- liver function test results 12 weeks after treatment is completed
- ongoing exposure to risk factors.

Follow up of a patient who is cured is described in Box 1.

Patients who are cured *Patients without cirrhosis and with normal liver function*

Most people currently living with hepatitis C in Australia do not have cirrhosis.⁹ No further clinical follow up of hepatitis C is needed for those without cirrhosis who:

- achieve a cure
- have normal liver function test results after treatment, and
- are not at risk of reinfection.

Other comorbidities and risk factors may contribute to the development of liver disease, such as excessive alcohol use and fatty liver disease/metabolic syndrome. These people should be encouraged to maintain a healthy lifestyle, including smoking cessation, safe alcohol consumption, maintaining a healthy weight, healthy diet and exercise. They should also be encouraged to avoid reinfection through harm reduction practices. Patients who have not received hepatitis A and hepatitis B vaccinations should be offered them.¹⁰

KEY POINTS

- Over 95% of patients are cured after a full course of DAA treatment.
- Patients with persistent liver function test abnormalities after DAA treatment need specialist referral for further investigation.
- Patients with cirrhosis need specialist referral and lifelong monitoring for complications such as hepatocellular carcinoma.
- Past infection does not result in immunity to hepatitis C, so patients should be counselled about the risk of reinfection and importance of harm reduction.
- Harm reduction is an effective approach to reduce hepatitis C risk, including access to clean needles, syringes and other injecting equipment, and opioid substitution therapy.
- Patients at risk of reinfection should be offered at least annual hepatitis C virus RNA PCR testing in the knowledge that they are eligible for retreatment if reinfected.

Patients without cirrhosis but with abnormal liver function results

Patients without cirrhosis who have abnormal liver function test results after treatment (alanine aminotransferase [ALT] ≥ 30 U/L [men] or ALT ≥ 19 U/L [women]) may have comorbid liver disease. Routine investigations for liver disease can be initiated by the GP. These patients should be referred to a gastroenterologist for further investigation and management.

Patients with cirrhosis

Patients who were diagnosed with cirrhosis before DAA treatment would usually have been referred to a specialist at that time. After DAA treatment, they will require ongoing management of their liver disease by a gastroenterologist and should be referred if not already receiving specialist care.

Patients who are not cured

About 5% of patients will not achieve cure of hepatitis C with initial DAA treatment. Possible reasons include:

- resistance of the virus to the

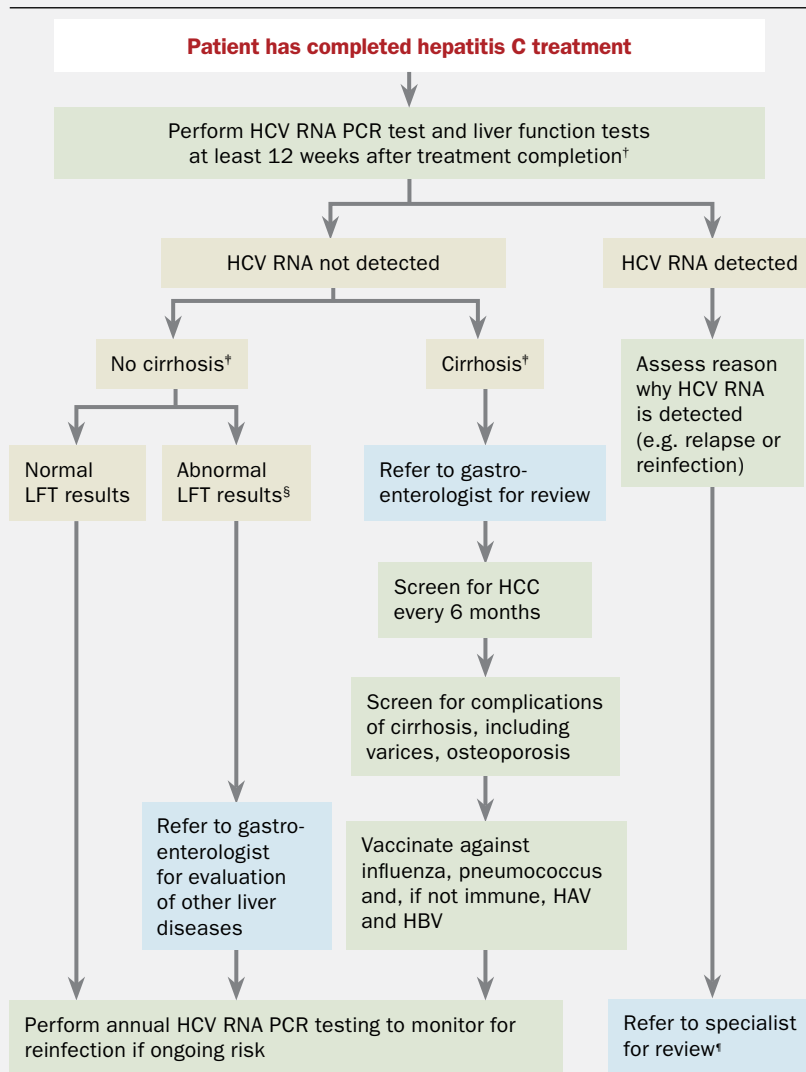
DAA's used

- nonadherence with medication
- presence of advanced liver disease.

Patients who are not cured should be referred to a gastroenterologist or

infectious disease specialist who is experienced in the management of hepatitis C for further assessment and potential retreatment. Retreatment of a patient after DAA treatment failure may require a

FOLLOW-UP CARE OF PATIENTS AFTER HEPATITIS C TREATMENT WITH DIRECT-ACTING ANTIVIRALS^{§*}



Abbreviations: HAV = hepatitis A virus; HBV = hepatitis B virus; HCC = hepatocellular carcinoma; HCV = hepatitis C virus; LFT = liver function test; PCR = polymerase chain reaction.

* Adapted from Burnet Institute Eliminate Hepatitis C Partnership. Eliminate hepatitis C partnership practice support toolkit. Melbourne: Burnet Institute; 2018 (<https://ecpartnership.org.au/toolkit>).[§]

† HCV RNA PCR determines whether the patient is currently infected with HCV.

‡ Liver fibrosis assessment should be completed before commencing treatment to determine whether patient has cirrhosis.

§ Abnormal LFT results: alanine aminotransferase ≥ 30 U/L (men) or ≥ 19 U/L (women).

¶ Suitable specialists include gastroenterologists, hepatologists and infectious disease physicians. Patients will need to see a gastroenterologist for any liver-related follow up (persistent abnormal LFTs, HCC screening, oesophageal varices monitoring) and can see another specialist for relapse and reinfection assessment.

1. CASE STUDY: FOLLOW UP AFTER DAA TREATMENT

Presentation

Michelle is a fit and active 49-year-old woman. About six months ago, you diagnosed her with chronic hepatitis C and prescribed a pangenotypic direct-acting antiviral (DAA) regimen (see part 3 in this series).[§] It is now 12 weeks since the scheduled completion of her DAA course and you send her a text message reminder to see you.

Michelle attends and reports that she completed the DAA treatment. She experienced mild headaches and nausea in the first few weeks of treatment but was able to cope. She forgot the tablets on only two days during the whole course.

Management

You order a PCR test for hepatitis C virus (HCV) RNA (qualitative) and liver function tests. Michelle returns a week later to receive her results, which show:

- HCV RNA PCR – not detected
- liver function tests – normal range.

These results indicate that Michelle is cured of hepatitis C. Because she had no evidence of cirrhosis before DAA treatment and her liver function results are within the normal range after treatment, she does not require any follow up related to hepatitis C.

You take the opportunity to remind Michelle that being cured of hepatitis C does not mean she is immune to reinfection. She is no longer injecting drugs and is currently using methadone opioid substitution therapy. However, you remind her to have an HCV RNA PCR test if she is exposed to new risks in the future.

You also explain to Michelle that even though her hepatitis C is cured, her HCV antibody results will remain positive. This does not mean she has a current HCV infection. Finally, you explain there are other causes of liver disease, such as excessive alcohol use and excess weight, and it is important to maintain a healthy lifestyle.

2. USEFUL RESOURCES FOR GPs AND PATIENTS AFTER HEPATITIS C TREATMENT

- Hepatitis C treatment resources for healthcare providers are available from Gastroenterological Society of Australia (GESA; www.gesa.org.au/resources/hepatitis-c-treatment). These include:
 - *Australian recommendations for the management of Hepatitis C virus infection: a consensus statement* September 2018
 - Wallchart for GPs: *Clinical guidance for treating hepatitis C virus infection: a summary*
- Resources for patients and healthcare providers are available from Hepatitis Australia, including downloadable information for patients (<https://www.hepatitisaustralia.com>)
- *Eliminate hepatitis C (EC) practice support toolkit*: developed for primary care practitioners, the toolkit contains resources to promote hepatitis C testing and treatment and to encourage people to remain engaged in high-quality hepatitis C care (<https://ecpartnership.org.au/toolkit>)
- *Safer using tips*: two resources from Harm Reduction Victoria provide information on safer use of drugs, with specific reference to reducing hepatitis C transmission (https://docs.wixstatic.com/ugd/ebb8bf_61a57e28de614e4dea74585d8951275fb.pdf, https://docs.wixstatic.com/ugd/ebb8bf_f26901243d6f4c4295d46010e8d90088.pdf)
- *Removing barriers: it's easy as 1, 2, 3* webpage from Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine (ASHM) includes steps to reduce stigma and discrimination in your practice (<http://removingbarriers.ashm.org.au>)

specific salvage regimen but generally has a good outcome.¹¹

Hepatitis C virus reinfection

People with ongoing risk factors for infection are at risk of reinfection with HCV.

TABLE. RECOMMENDED SURVEILLANCE FOR CIRRHOSIS COMPLICATIONS^{6,15}

Condition	Test	Frequency
Hepatocellular carcinoma	Liver ultrasound examination	Six-monthly
Oesophageal varices	Gastroscopy	Individualised by gastroenterologist according to Baveno VI criteria ¹⁶
Osteoporosis	DXA Vitamin D level	Two-yearly Six-monthly
Other monitoring	Liver function tests, full blood count, urea, electrolytes, creatinine, INR/prothrombin time, others as required	Based on individual circumstances and gastroenterologist's opinion

Abbreviation: DXA = dual emission x-ray absorptiometry.

The main risk groups in Australia are:

- people who inject drugs – most new HCV infections occur in this group⁶
- men who have sex with men, particularly those who are HIV-positive
- people in custodial settings
- people who have received a tattoo or body piercing in an unsterile setting.

Treatment of HCV reinfection

Patients with HCV reinfection should be retreated to prevent both progression of liver disease and transmission of HCV to others. Importantly, people with reinfection are eligible for PBS-subsidised DAA therapy. Those with clear reinfection – for example, HCV RNA detected after confirmed SVR12 or a different HCV genotype detected – can be treated as if they are treatment-naïve.⁶

Further, patients with HCV reinfection should be invited to bring in or refer their sexual or injecting partners (who may have been the reinfection source) for treatment. They should also be offered advice and support to reduce their infection risk.

Reducing risk of reinfection for people who inject drugs

People who inject drugs are at ongoing risk of HCV infection. Three simple hepatitis C harm reduction messages are:

- Use sterile injecting equipment and

do not share any injecting equipment

- Encourage injecting partners to be tested and treated
- Remind people they can be retreated if they are reinfected.

Harm reduction is an effective approach to reduce hepatitis C risk. It includes providing access to clean needles, syringes and other injecting equipment and opioid substitution therapy (OST). Informative harm reduction resources for people who inject drugs are readily available on the internet and provide easily accessible information on topics such as safe injecting practices and OST (Box 2). GPs can play an active role in harm reduction by:

- offering OST within their practice or discussing pathways to access
- discussing safer injecting behaviours.

GPs are also recommended to offer HCV RNA PCR testing at least annually to people who inject drugs to screen for HCV reinfection, as previously discussed.

People who inject drugs may have other comorbidities requiring long-term care. A trusting and lasting relationship with a GP is very important for this patient group.¹² People who inject drugs often report experiencing stigma and discrimination from healthcare providers, which can be a significant barrier to seeking health advice and treatment.¹³ Resources for primary care staff to help raise awareness about stigma

and discrimination are available from the Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine (Box 2).¹⁴

Hepatitis C-related cirrhosis

Liver cirrhosis is a significant complication that occurs in about two to three of every 10 people with chronic hepatitis C, generally after longstanding (20 to 30 years) infection.⁶ People with cirrhosis remain at risk of complications of liver disease such as hepatocellular carcinoma (HCC), even after being cured of hepatitis C.

Follow up for patients with cirrhosis

Patients with cirrhosis require lifelong follow up (Table).^{6,15,16} They should be referred to a gastroenterologist for specialist care. In particular, all patients with cirrhosis require HCC surveillance with six-monthly targeted liver ultrasound examinations. The GP should also provide hepatitis A and B, influenza and pneumococcal vaccinations to all patients with cirrhosis in accordance with Australian immunisation guidelines.¹⁰

Shared models of care with open lines of communication between the GP and specialist can facilitate safe and effective management of patients with cirrhosis. This includes timely adherence to screening programs, safe prescribing of medications when liver dysfunction is present and early identification of decompensating liver function. Shared models of care can be supported through initiation of chronic disease care plans, team care arrangements and case conferencing.

Rural and remote GPs

Patients in a rural or remote area may not always be able to access a gastroenterologist. In this situation, the GP may need to take greater responsibility for co-ordinating care and may organise screening and monitor the patient's liver function in collaboration with the specialist (Table).^{6,15,16} Co-ordination of care can be facilitated through a good relationship with a specialist in the regional centre, use of telemedicine and case conferencing.

Conclusion

After hepatitis C treatment with DAAs, all patients need follow up by their GPs. Over 95% of patients are cured after a full course of DAA treatment and will not need further hepatitis C treatment. A small proportion of patients will require further management, and GPs can play a valuable role in their ongoing care in partnership with specialists. Patients at risk of reinfection will also need support to reduce their risk as well as regular HCV RNA testing by PCR. **MI**

Acknowledgement

The authors gratefully acknowledge the contribution to this work of the Victorian Operational Infrastructure Support Program received by the Burnet Institute.

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COMPETING INTERESTS: Ms Chan, Dr Gooley, Dr Greenwood-Smith, Dr Chaney, Dr Howell: None. Professor Hellard receives funding support from Gilead Sciences, AbbVie and Bristol-Myers Squibb for investigator-initiated research.

Dr Baker has received clinical trial funding and conference sponsorship and serves on the advisory Board for AbbVie, Gilead and MSD. Dr Pedrana receives funding for investigator-initiated research from AbbVie, Gilead and MSD. Dr Doyle receives funding for investigator-initiated research or consulting from AbbVie, Bristol-Myers Squibb, Gilead and MSD.