



Hepatitis C: you can't treat it if you don't test for it

Approximately half of people with hepatitis C virus (HCV) infection in New Zealand are unaware they have it. New medicines, known as directly-acting antivirals (DAA), have much greater effectiveness than previously used interferon-based treatment regimens, and result in cure in the vast majority of patients. DAA are associated with fewer adverse effects and shorter treatment courses than interferon regimens, and they can be prescribed in primary care. This has the potential to change the implications of an HCV diagnosis, altering it from a life-long to a largely treatable condition. In New Zealand, fully subsidised DAA treatment is currently available for over half of patients with HCV infection, however, these people cannot benefit from early intervention if they remain undiagnosed.

KEY PRACTICE POINTS:

- The treatment of hepatitis C virus (HCV) infection is a changing area of medicine and it is likely that patients will increasingly be managed in primary care
- Newer direct-acting antiviral (DAA) medicines result in high rates of cure (>95%) with fewer adverse effects than previous treatment regimens. This has the potential to substantially reduce the incidence of long-term complications, reduce transmission and decrease the stigma of HCV infection.
- More testing in primary care is required for people with HCV infection to benefit from DAA treatments: it is estimated that 50,000 people are infected with HCV in New Zealand and approximately half are undiagnosed.
- Patients with risk factors for HCV should undergo testing; a blood sample for HCV serology is the first step for most patients.

In 2016, bpac^{nz} published a comprehensive article on the management of HCV infection after newly subsidised direct-acting antiviral (DAA) medicines became available. This represented a major change in practice, with many patients with HCV infection now able to be managed in primary care. Targeted testing for HCV infection is now required in order for people in New Zealand to gain the maximum possible benefit from these medicines, and other treatments which may become available in the future.

👁 Further information on testing and managing treatment in patients with HCV is available from: "Treatment of hepatitis C (HCV) has changed" www.bpac.org.nz/2016/hepc/default.aspx

Symptoms and signs of HCV infection

The majority of patients with HCV infection are asymptomatic or have non-specific symptoms.^{6,7} Diagnosis of HCV infection is based on laboratory testing.

Acute HCV infection

Acute infection generally refers to the first six months after acquisition of the virus.² Up to 80% of people are asymptomatic at this stage.² As a result, few people have cause to seek medical attention and acute HCV infection is an uncommon diagnosis. In New Zealand, acute HCV infection is a notifiable disease and approximately 30–40 cases are reported per year.⁸ Patients who seek medical attention during acute infection may have symptoms of acute hepatitis, such as jaundice, dyspepsia, a loss of appetite and lack of energy.⁹ Marked elevations of alanine aminotransferase (ALT) levels, to over five to ten times the upper limit of normal, occur during acute infection.² Patients with clinical findings suggestive of acute HCV infection should undergo testing.

Chronic HCV infection

Approximately three-quarters of people who acquire HCV infection develop a chronic infection, which can also go undetected as many remain asymptomatic.² Fatigue is a non-specific symptom of chronic HCV infection, reported by approximately 50% of patients.⁷ Approximately 16% of people with chronic HCV infection develop cirrhosis after 20 years, increasing to 41% after 30 years.¹⁰ Patients with chronic HCV infection may have symptoms and signs consistent with liver disease, such as a spider naevi, oedema, ascites or bruising.² Patients with non-specific symptoms such as unexplained fatigue can be asked about risk factors to assess whether testing is appropriate.

Why we need more testing

Approximately 50,000 people in New Zealand are infected with hepatitis C virus (HCV).¹ Only a minority of patients are symptomatic when they first acquire the virus and most progress to a chronic infection which can go undetected for many years (see: "Symptoms and signs of HCV infection").² The majority of HCV diagnoses in New Zealand are in people aged in their 40s and 50s who are likely to have been infected earlier in their life.^{1,3} The prevalence of chronic HCV infection is higher in males than females; in a pilot programme in the Bay of Plenty and Wellington which aimed to increase rates of testing, two-thirds of those diagnosed were male, and the average age of diagnosis was 52 years.^{1,3}

It is estimated that approximately half of people with HCV in New Zealand are undiagnosed.¹ Many patients in New Zealand have their HCV infection first identified only after they present with complications from long-term infection. For example, from 2003 to 2013, only half of patients with HCV-related hepatocellular carcinoma had their HCV infection detected prior to developing cancer.¹

Many patients with HCV infection can now be treated in primary care. The DAA medicines Viekira Pak and Viekira Pak with ribavirin (Viekira Pak-RBV)* were subsidised in July, 2016 and can be prescribed by general practitioners. These have fewer adverse effects than previous HCV treatments and patients can now be responsible for self-administering their medicines in the community, with monitoring by their general practitioner. Another DAA medicine, Harvoni,* can also be prescribed by general practitioners, but patients eligible for this medicine are likely to be treated in secondary care.

A diagnosis of HCV infection no longer carries the same prognosis for patients. Previously, infection with HCV was largely a life-long and difficult to treat condition. The high success rates of newer medicines has important ramifications which can change the way HCV infection is managed and perceived by both clinicians and patients.

Treatment can reduce the risk of long-term complications and improve a patient's quality of life. Chronic HCV infection increases the risk of liver disease and can cause other symptoms such as fatigue and depression, as well as increase the risk developing type 2 diabetes and cardiovascular disease.⁴ Earlier diagnosis and treatment may help prevent cancer and other HCV complications, as well as reduce transmission.⁵

* Viekira-Pak contains four medicines: dasabuvir sodium & paritaprevir + ritonavir + ombitasvir. Viekira-Pak-RBV contains the same medicines with the addition of ribavirin. Harvoni contains two medicines: ledipasvir and sofosbuvir. For simplicity, the brand names are used in this article.



Who should be tested for HCV infection?

Injectable drug use is the most common risk factor for HCV infection (based on people diagnosed during acute infection).¹¹ The risk of sexual transmission of HCV is low and occurs mainly in people who are infected with HIV.^{2,6}

It is recommended that all patients with risk factors for chronic HCV infection undergo testing.² This includes people who:^{2,6,12}

- Have used injectable drugs
- Received a blood transfusion or organ transplant in New Zealand, or another developed country, prior to July, 1992*
- Have migrated from or received a medical or dental intervention in a region with high HCV prevalence. This includes Eastern Europe, the Middle East, North Africa, Western and Central Sub-Saharan Africa, Central Asia and the Indian subcontinent.
- Have spent time in prison, which can be associated with injectable drug use and unsafe tattooing practices
- Have a tattoo, body piercing or alteration, e.g. scarification, which was performed in an unsafe environment, e.g. in prison or in a country with a high prevalence of HCV (see above)
- Have a history of acute hepatitis, jaundice or persistently elevated ALT level
- Were born to an HCV infected mother; mother to infant transmission occurs in approximately 5% of cases¹³

It may be possible to use the practice's patient management system to identify patients who should be tested for HCV, but it is likely that in many cases risk factors will not be recorded in the patient's clinical record, e.g. injectable drug use or unsafe tattooing.

* Screening for HCV in blood transfusions and organ transplants began in July 1992 in New Zealand and at approximately the same time in other developed countries; screening in less developed countries may have occurred at a later date.

Strategies for discussing risk factors and testing

Ideally, patients should feel comfortable discussing HCV and disclosing any risk factors, however, this will not always be the case. Some patients may need more time and additional consultations to allow them to develop sufficient confidence and trust to discuss risk factors, and therefore allow the clinician to assess whether testing is appropriate.

Understanding the reasons why people may be reluctant to discuss HCV can help clinicians to frame discussion. This may include:^{14,15}

- Lack of awareness about HCV:
 - The low level of publicity about HCV; people who use injectable drugs may be more concerned about contracting HIV although HCV prevalence is much higher
 - Believing HCV is not a concern, since it is a long-term condition which develops over many years
 - Not understanding that HCV can cause serious complications
- Lack of obvious symptoms:
 - People may believe that since they are asymptomatic and their potential exposure was some time in the past that they did not contract the virus or it did not have any consequences.
 - Knowing other people who are infected who appear well
- Lack of awareness of the new treatments available and high chance of cure
- Confusing hepatitis C with hepatitis A or B and believing they have been vaccinated
- Embarrassment and perceived stigma of:
 - Having HCV
 - Risk factors for HCV such as drug use (drug users may also have associated fears such as difficulty having blood samples taken)
- Concerns from anecdotes about other hepatitis C treatments and procedures, such as:
 - Undergoing liver biopsy and the associated risks of bleeding and death
 - Having interferon treatment and the associated adverse effects and poor chance of cure
- Preferring not to know if they are infected

Create a safe space for patients to open up about risk behaviours

Establish open communication. Risky behaviours can be difficult for patients to disclose. Reiterate confidentiality; people using injectable drugs may fear repercussions such as problems with the police, employment or removal of children from their care.¹⁶

Try asking the same question in different ways. For example, patients may reply with a "no" when asked if they have used injectable drugs, but may respond differently to a follow-up question of "not even once?"¹⁷

Minimise questioning if the patient is reluctant to reveal details. In order to decide whether testing for HCV is necessary, it just needs to be established whether a risk behaviour occurred; further details about the incident do not have to be revealed. N.B. In some cases, clinicians will want to ascertain if the risk is ongoing in order to provide appropriate advice, e.g. using a needle exchange facility for current drug use.

Give people time to consider. Some patients may require time to process the information discussed before revealing risk behaviours or agreeing to undergo testing. Make a note in the patient's record to revisit the discussion at their next appointment.

Instead of asking about risk behaviours, ask if patients would like to undergo a hepatitis C test

An alternative approach to asking patients directly about topics such as injectable drug use is to discuss risk factors for HCV infection and then let them decide if they should undergo testing, without them having to reveal why. This may also be achieved with the use of posters or handouts in the clinic waiting room which explain risk factors for HCV infection and encourage patients to discuss testing when they see the doctor.

 Printable handouts are available from: www.hepatitisfoundation.org.nz/resources-new/hepatitis-c-resources/

How to test for HCV infection

A positive diagnosis and initiation of treatment for HCV requires three laboratory tests: HCV serology, an HCV RNA assay and HCV genotyping (Figure 1).

In the first instance, a blood sample should be taken for HCV serology, which is ordered as per standard practice on a community laboratory testing form. If this test is positive, an HCV RNA assay should be ordered, and if this is positive, HCV genotyping should follow. Some laboratories will do these tests automatically if initial serology is positive in a previously undiagnosed patient.

HCV serology

HCV serology detects the presence of anti-HCV antibodies:

- A positive result indicates current infection, previous infection or a false positive; further testing is required
- A negative result indicates a patient is unlikely to have an HCV infection unless their exposure occurred within the last six months

Antibodies to HCV can take up to six months to develop and only 50% of patients are likely to have positive serology during the acute stage of infection.¹⁸ If patients have negative HCV

serology within the first six months of an exposure, a repeat test should be performed after the six month period.

It is estimated that one-quarter of people who contract HCV infection are able to clear the virus without medical intervention, and these people are likely to test positive for anti-HCV antibodies for a number of years following the infection.^{2,19} A positive result could therefore indicate previous infection which has now resolved.

HCV serology is highly specific; false positives do, however, occur. The rate of false positives to true positives depends on the background prevalence of HCV; in populations with a low prevalence of HCV, such as New Zealand, up to 35% of positive serology results may be false positives.²⁰

HCV RNA assay

Positive serology should be followed by an HCV RNA assay:

- A negative result indicates the patient does not have an active infection and does not require treatment.¹⁸
- A positive result indicates the patient has an active infection

Patients found to have active infection can then be assessed for suitability of different treatment options. If the patient's exposure to HCV was recent, a conservative watch and wait approach is generally recommended before commencing treatment, as one-quarter of patients spontaneously clear the virus without intervention.²

HCV genotyping

After current infection is confirmed, HCV genotyping is required to identify the type of HCV and therefore the most suitable treatment option. Viekira-Pak regimens can be used for the treatment of patients infected with genotype 1 (approved indication) or genotype 4 (unapproved indication), with expected cure rates of over 95%.^{2,21} Harvoni can be initiated, with subsidy subject to Special Authority approval, for patients with decompensated cirrhosis or extra-hepatic complications of HCV infection who are infected with any HCV genotype.

If patients are not currently eligible for subsidised treatment with the above medicines, guidelines from the New Zealand Society of Gastroenterology recommend they should wait until they can access a DAA regimen rather than undergo treatment with a pegylated interferon regimen (the previous standard treatment for HCV).²² Some patients may wish to import unapproved generic DAA medicines.

 For further information on importing generic medicines, see: www.medsafe.govt.nz/consumers/miet/importmedicines.asp

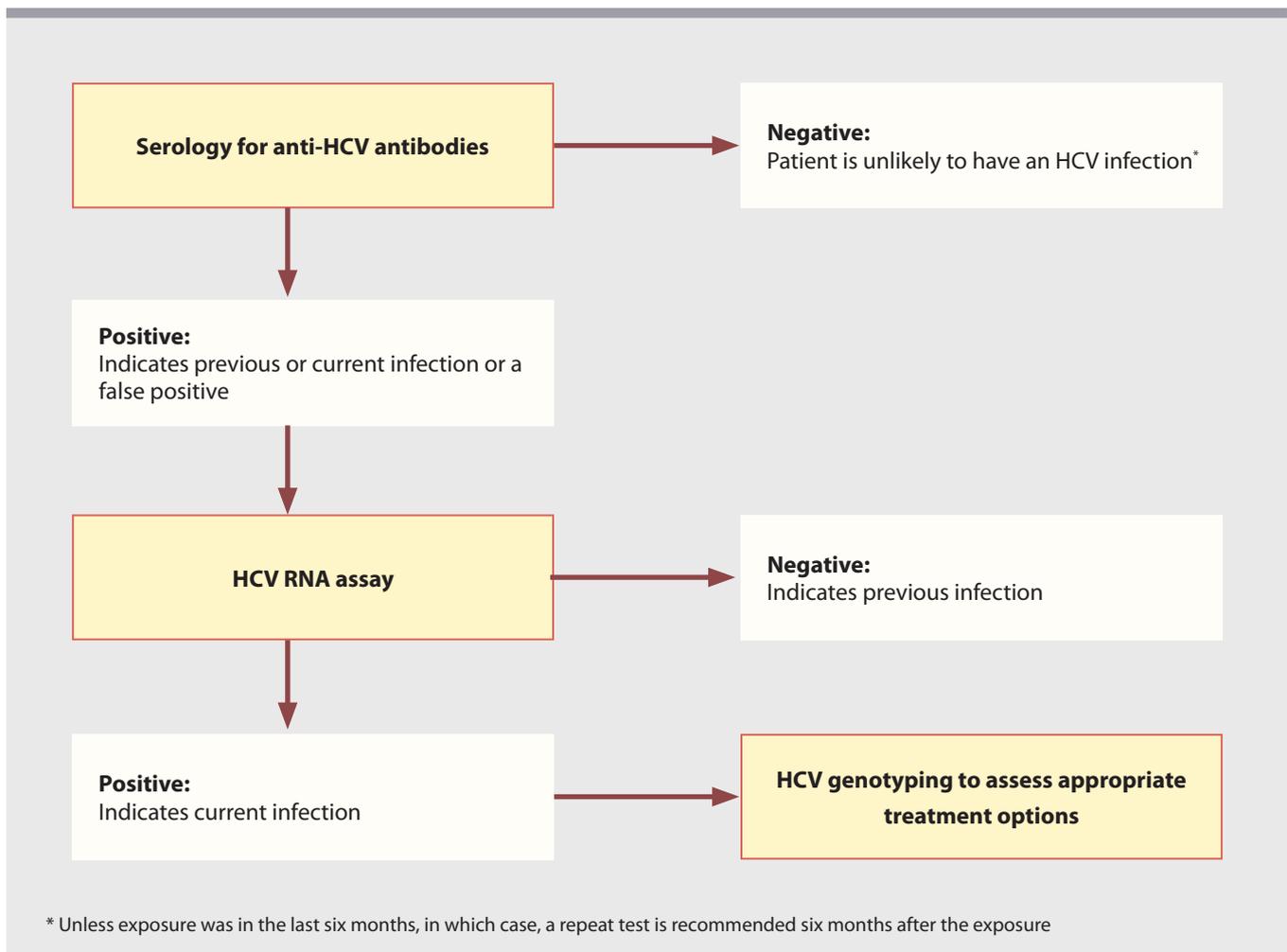


Figure 1: Testing for active HCV infection.

This is a developing area of medicine and things may change

The development, testing and approval of DAA medicines for the treatment of HCV infection is a rapidly evolving area of medicine. Viekira-Pak and Harvoni treatment regimens were subsidised in July, 2016, with Special Authority criteria for Harvoni altered in June, 2017.^{23,24} In 2016, four additional DAA medicines were approved for use in New Zealand by Medsafe.²⁵ Additional subsidised DAA medicines may become available in the future.

Further information for patients and clinicians:

“Treatment of hepatitis C (HCV) has changed”, available from: www.bpac.org.nz/2016/hepc/default.aspx

Goodfellow Unit webinar with Dr Ed Gane, available from: www.goodfellowunit.org/events/curing-hepatitis-c

Further information for clinicians:

- Ministry of Health hepatitis C learning programme: <http://learnonline.health.nz/course/category.php?id=9>
- PHARMAC information on Viekira-Pak regimens for prescribers and pharmacists: www.pharmac.govt.nz/medicines/my-medicine-has-changed/hepatitis-c-treatments/
- Hepatitis Foundation information on referrals to secondary care: www.hepatitisfoundation.org.nz/health-professionals/hepatitis-c-for-health-professionals/

Information for patients:

- www.health.govt.nz/your-health/conditions-and-treatments/diseases-and-illnesses/hepatitis-c

Acknowledgement: Thank you to **Professor Ed Gane**, Professor of Medicine, University of Auckland, Chief Hepatologist and Deputy Director of the New Zealand Liver Transplant Unit for expert review of this article.

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