**Information Sheet** | Canberra Health Services

# Hepatitis C Testing Guidelines

## Background

Hepatitis C virus (HCV) infection remains a major public health problem in Australia. Cirrhosis develops in 5-10% of those with chronic HCV within 20 years, and hepatocellular carcinoma will develop in 3-5% of people per annum who develop cirrhosis.

Direct acting antiviral (DAA) therapy, subsidised by the Pharmaceutical Benefits Scheme (PBS) since 2016, has greatly improved HCV sustained viral responses (SVR).

Appropriate HCV testing can indicate whether an individual has:

- No evidence of HCV infection
- Past HCV infection with clearance of virus
- Current HCV infection
- Chronic HCV infection

Benefits of timely testing include reduction in onwards transmission and modification of disease progression through earlier advice and treatment. PBS eligibility for treatment requires evidence of chronic HCV infection, meaning detectable HCV antibody and HCV RNA (qualitative or quantitative HCV RNA test) for longer than 6 months.

Testing for HCV includes serology, nucleic acid testing and genotyping.

## Indications for HCV testing

An individual's risk of HCV infection should inform the decision to perform HCV testing. It is recommended that informed consent be obtained for HCV testing.

Populations in which HCV testing should be undertaken:

- People who inject drugs or who have ever injected drugs.
- People in custodial settings
- People with tattoos or body piercing
- People who received a blood transfusion or organ transplant before 1990

- People with coagulation disorders who received blood products or plasma-derived clotting factor treatment products before 1993.
- Children born to mothers with HCV infection.
- Sexual partners of a person with HCV infection (higher risk of transmission include MSM, HCV-HIV coinfection)
- People with liver disease e.g. persistently abnormal liver function tests, acute hepatitis, chronic liver disease or cirrhosis, hepatocellular cancer
- People who have had a needle-stick injury.
- Migrants from high-HCV prevalence regions e.g. Egypt, Pakistan, Mediterranean and Eastern Europe, Africa and Asia

Other situations where HCV testing may be indicated include:

- Healthcare workers who perform exposure prone procedures
- Contact tracing where exposure to blood of a person with a potential infection is documented.
- Diagnosis of another infection with shared mode of acquisition e.g. HBV, HIV
- The report of a reactive result on a HCV test not approved for supply in Australia
- A person who requests a HCV test in the absence of declared risk factors – a small number of people may request a HCV test but choose not to disclose risk factors. A person's choice not to declare risk factors should be respected and HCV testing should be offered.

## Specimen type, laboratory frequency of testing & MBS Indications

| **Test** | **Alternative Test Request Terms** | **Preferred Sample** | **Alternative Sample** | **Laboratory Testing Frequency** | **Medicare Benefits Scheme Indications (Jan 2021)*** |
|---|---|---|---|---|---|
| HCV serology | HCV antibody<br><br>Anti-HCV | Serum | Lithium heparin | Daily,<br><br>Mon-Fri | i. antenatal screening OR<br><br>ii. investigation of acute or chronic hepatitis OR |

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|---|---|---|---|---|---|
| | | | | | iii. investigation following exposure |
| HCV qualitative PCR | HCV PCR | EDTA plasma | Serum | Twice per week | i. patient undertaking antiviral therapy for chronic HCV (max 4 per 12 months) OR<br><br>ii. patient is HCV antibody positive OR<br><br>iii. serological status is uncertain after testing OR<br><br>iv. determining HCV status in immunocompromised OR<br><br>v. detection of acute HCV infection prior to seroconversion if necessary for patient management<br><br>(ii.-v. max 1 per 12 months) |
| HCV quantitative PCR | HCV viral load | EDTA plasma | Serum | Twice per week | i. pre-treatment evaluation of a patient with chronic hepatitis C or<br><br>ii. assessment of efficacy of antiviral therapy |

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|---|---|---|---|---|---|
| | | | | | (i.-ii. max 2 per 12 months) |
| HCV genotype | N/A | EDTA plasma | Serum | Weekly | i. patient HCV RNA positive and is being evaluated for antiviral therapy for chronic HCV<br><br>(max 1 per 12 months) |

* please ensure appropriate clinical history is provided on the request form

## Hepatitis C serology

Serology testing for HCV involves the use of immunoassays to detect total antibody (IgG and IgM) in serum. Serology is used to diagnose HCV infection; however, the detection of HCV antibody does not differentiate between current infection versus past infection with clearance of virus (spontaneously resolved or antiviral-treated).

To minimise the risk of false positive results, samples that are reactive (HCV antibody detected) in the initial immunoassay are subjected to a second immunoassay, that includes different HCV antigens, to confirm true reactivity. A sample that is reactive in both HCV immunoassays is reported as HCV antibody detected.

The seroconversion window period for HCV infection can be lengthy, on average 8 weeks but can be up to 12 weeks, and so repeat testing is recommended if very recent infection is suspected.

Consider annual HCV serology for seronegative individuals with ongoing risk factors for HCV transmission.

*Individuals with prior positive HCV serology do not require repeated serological testing as most people will have detectable HCV antibodies for life. If chronic infection or re-infection is suspected, then Hepatitis C RNA testing is recommended.*

# Hepatitis C RNA

### Qualitative HCV RNA nucleic acid test:

Qualitative HCV RNA testing is a nucleic acid amplification test to detect HCV RNA (genotypes 1-6) in plasma (EDTA) or serum. Testing is recommended for all individuals shown to have detectable HCV antibody to determine whether they have current or past HCV infection. It is also sometimes used to aid in diagnosing current HCV infection if the serological results are uncertain.

### Interpretation of results

- HCV RNA NOT detected – HCV antibody detected samples which are negative for HCV RNA most likely represent past infection with clearance (spontaneously resolved or antiviral treated).
    - Repeat HCV RNA in 6 months if *current* HCV infection is still a concern.
    - Repeat HCV RNA in 1-2 months if *acute* HCV infection is suspected.
    - Remember that reinfection can occur. Consider annual testing in those with ongoing risk factors for HCV transmission.
- HCV RNA DETECTED – the presence of HCV RNA indicates active viral replication and therefore current HCV infection.

Qualitative HCV RNA is also used to monitor treatment response. For example, a qualitative HCV PCR test is required to confirm SVR, which is defined as an undetectable HCV RNA at 12 weeks after the completion of DAA therapy.

### Quantitative HCV RNA nucleic acid test (also known as HCV viral load):

The HCV viral load is a nucleic acid amplification test performed on plasma (EDTA) or serum. The assay includes RNA quantitation standards so that HCV RNA concentration, expressed as IU/mL and IU/mL(Log10), can be reported.

With most DAA treatments, the baseline HCV viral load has little impact on the likelihood of achieving a SVR. Some preliminary reports show that monitoring of the viral load may help identify people who are eligible for shorter duration with some DAA regimens, but this requires further evaluation.

# Hepatitis C genotyping

HCV genotyping uses nucleic acid amplification and sequencing to differentiate between HCV genotypes 1-6.

HCV genotype is no longer a strong predictor of achieving a SVR in response to antiviral therapy. Despite this it is recommended that, where possible, the HCV genotype be documented. It can be useful to help determine whether a recurrence of active infection in an individual represents a relapse (e.g. failure of antiviral therapy) or reinfection.

For further information, please contact one of our clinical microbiologists or registrars via the Canberra Hospital switch on 02 5124 0000.

## References

Australasian Society for HIV Medicine, Viral Hepatitis and Sexual Health Medicine (ASHM). Management and Treatment of Hepatitis C.

Available at https://ashm.org.au/HCV/management-hepc/

Hepatitis C Virus Infection Consensus Statement Working Group. Australian recommendations for the management of hepatitis C virus infection: a consensus statement (June 2020). Melbourne: Gastroenterological Society of Australia, 2020.

Available at https://www.hepcguidelines.org.au/

**Acknowledgement of Country**

Canberra Health Services acknowledges the Ngunnawal people as traditional custodians of the ACT and recognises any other people or families with connection to the lands of the ACT and region. We acknowledge and respect their continuing culture and contribution to the life of this region.

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