Hepatitis C infection and its management in primary care

Introduction

Hepatitis C virus (HCV) is a blood-borne, single-stranded RNA virus that causes liver infection in humans. HCV is subdivided into six genotypes, with genotypes 1,2 and 3 being more common in the northern hemisphere, genotype 4 in the Middle East, genotype 5 in Southern Africa and genotype 6 in South Asia.

After an acute infection, approximately 15 - 45% clear spontaneously and 55 - 85% progress to chronic infection, while around 80% progress to chronic HCV infection.

As of 2018, around 143 000 people in the UK were living with chronic hepatitis C infection in the UK, an overall prevalence of 0.3% (NICE 2012). The large majority of patients with chronic HCV infection in the UK (around 90%) have contracted the condition through injecting drug use (NICE 2012).

The majority of patients with chronic HCV infection are unaware they have the infection, and though those in current contact with drug treatment services are likely to be tested, for those whose drug use is historic, access to testing is more problematic.

Each person with chronic hepatitis C infection is at significant risk of developing life-threatening liver disease. Around 10-30% of those with chronic infection will develop cirrhosis over a 20 year period and of those with cirrhosis around 2% will develop hepatocellular carcinoma each year.

Because hepatitis C infection is concentrated in marginalised populations, even when individuals are diagnosed, some may fail to access effective treatment, and some experience barriers to accessing specialist treatment.

However, for most who are infected, chronic hepatitis C is curable, particularly since the development of newer direct acting antiviral (DAA) medication. This has led the World Health Organisation (WHO) to set the target of 'eliminating hepatitis C as a major public health threat by 2030' (WHO 2016).

Hepatitis C virus

Core

RNA

E protein
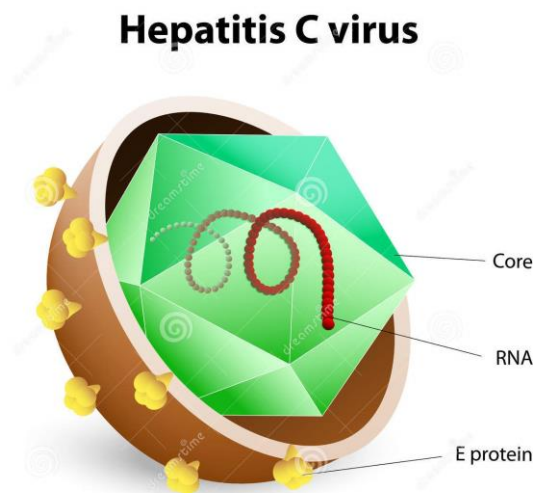
HCV transmission

HCV is primarily transmitted through practices that allow exchange of blood, though the virus has been identified in other body fluids such as saliva and breast milk.

The primary transmission route in the UK is injecting drug use where there is sharing of needles or other injecting equipment. Use of 'traditional' illicit drugs such as heroin and amphetamine is not the only vector; the virus may equally be transmitted through use of steroid and other performance and image enhancing drugs. HCV may also be transmitted through sharing crack pipes where there is no injecting. For those injecting users attending drug services the prevalence of HCV infection is between 40 and 55% depending on geographical area.

Transmission of HCV infection can also occur as a result of medical interventions such as the use of unscreened or non-heat treated blood transfusion or blood products. In the UK, this risk has been minimal since the introduction of donor screening. However, those who received a blood transfusion pre 1991 or a blood product pre 1986 in the UK may have contracted HCV infection as a result, and there still may be some risk in developing countries.

Re-use of un-sterilised injecting equipment or surgical instruments may also transmit infection and HCV infection is associated with haemodialysis treatment. Infection can occur through needle-stick or sharps injury where the risk of transmission in a single incident is thought to be between 2% and 3%. Direct contact with the blood of an infected person in the healthcare environment or occasionally through fights may transmit the virus, as may use of unsterilized or shared needles in other environments for example in acupuncture, tattooing or body piercing in unregulated settings. Sexual transmission of HCV can occur but is uncommon.

Vertical transmission from mother to baby at the time of birth is uncommon. The risk of perinatal transmission is estimated at 3-5% in mothers with HCV infection but is higher at around 15 - 45% where human immunodeficiency virus is present as a co-infection. Though the virus has been found in milk, there is no evidence to suggest that HCV infection can be transmitted through breast feeding.

For some with HCV infection, the source may not be identified. Whenever a liver function test is returned with an unexplained raised transaminase levels, the GP should consider testing for HCV as part of further investigation, even when there are no over risk factors.

The natural history of HCV infection

Acute HCV infection is usually symptomless, though for some there may be a short illness with fatigue, fever and right upper quadrant discomfort. **While approximately 15 - 45% of those with acute infection clear the virus, up to 15 - 45% progress to chronic infection.** Resolution of HCV infection does not give protection against re-infection.

Chronic infection is identified by the persistence of HCV RNA in the blood for six months or longer. Among patients with chronic infection, liver disease progression is variable and takes place over a timescale which may be decades. Progression of liver disease is faster in the presence of co-factors for liver damage including excess alcohol consumption; age over 40 years; male gender; and co-infection with HIV or hepatitis B virus (HBV). The development of cirrhosis is associated with related complications including portal hypertension, oesophageal varices, ascites, hepatic encephalopathy and hepatocellular carcinoma.

Screening for HCV infection.

NICE guidance recommends screening for HCV infection in the following situations (NICE 2013):

- Current and past injecting drug use;
- Blood transfusion pre-1991;
- Treatment with a blood product pre-1986;
- Born or brought up in a high prevalence country (includes all of Africa, Asia, the Caribbean, Central and South America, Eastern and Southern Europe, the Middle East, the pacific islands);
- Babies whose mothers have HCV infection;
- Prisoners including young offenders;
- Looked after children;
- Those living in hostels or who are homeless;

- HIV positive men who have sex with men;
- Close contacts of someone with HCV infection.

Initial screening for HCV infection is with anti-HCV serology. **Hepatitis C antibody can first be detected somewhere between 5 and 12 weeks after an acute infection**, though for some patients it is longer, and typically is positive lifelong, including when the virus is cleared spontaneously or following anti-viral treatment.

Where patients are found to be anti-HCV positive they should be tested for HCV RNA (PCR test) to demonstrate the presence of the virus and demonstrate whether an infection is active or not. Many laboratories perform automatic RNA (PCR) testing once HCV antibody is detected, and this both reduces the time it takes to confirm the diagnosis and reduces the risk of the patient being 'lost to follow up' through not attending for further blood samples.

Typically blood samples are obtained by venepuncture. For many injecting drug users venous access is difficult, and sampling options include dry blood spot testing (DBST) using dried blood spots on filter paper from a finger prick sample of blood and oral fluid testing. However, tests based on oral fluid may have a lower sensitivity than blood-based tests.

Further tests of particular value in secondary care to support planning and monitoring of treatment include HCV genotype and viral load.

Summary of hepatitis C test results

HCV antibody test (anti-HCV): If positive, this demonstrates antibody production following an HCV infection, but not necessarily current infection. The antibody normally stays positive for life following acute infection. It can be positive as little as 5 weeks after initial infection, but in some may take up to 6 months for a patient to seroconvert.

HCV PCR: This detects HCV RNA. If positive a PCR test denotes current infection. The PCR test becomes positive between 7 and 21 days after acute infection. If the virus is cleared the PCR test is negative.

HCV genotype: This identifies the genotype of the primary HCV infection. This can be useful in assessing prognosis and planning treatment.

HCV viral load test: This estimates the number of viral particles per ml of blood. It is useful in assessing prognosis and planning and monitoring treatment.

Hepatitis C pre- and post-test discussion

Preparation, giving clear information and offering support are all important parts of discussions surrounding HCV testing. These rely on generalist skills and some specific knowledge, but do not require the skills of a specialist counsellor.

Areas to discuss before a patient has an HCV test include:
- Ensure the patient is aware why the test is being considered;
- Discuss the benefits of the test for the individual, including details of the natural history and treatment opportunities for HCV infection;
- Reassure the patient that results will be managed confidentiality;
- Advise that the person may need to disclose having an HCV infection when applying for insurance or a mortgage;
- Discuss alternatives to venepuncture testing, especially if venous access may be a problem;
- The HCV antibody test is a screening test and if positive will need to be followed up with a second test to see if infection is active;
- Discuss the implications of a positive result: the benefits of referral to secondary care for management: harm reduction for the individual: and prevention of transmission;
- Discuss the implications of a negative test: any risk activities the patient has been involved in: and ongoing harm reduction;

- Make sure the patient is aware of the relevant 'window' periods for seroconversion;
- Allow time for the patient to ask questions and address any concerns the person might have;
- Check what support resources the patient has;
- Record that there is verbal informed consent for testing;
- Agree plans for how the result will be given. Results should preferably be given in person and by the clinician who arranged the test.

When giving a negative result:
- Remind about 'window' periods and arrange retesting if necessary
- Remind about at-risk behaviour and reinforce harm reduction advice

When giving a positive anti-HCV result:
- Ensure the patient has a good understanding of what the result means; discuss the need for confirmatory testing to check if the infection is still active
- Give the patient the opportunity to ask questions and for you to address any mistaken beliefs about HCV infection
- Check what support the patient has, and offer follow up support
- Reinforce harm reduction advice and discuss ways to prevent transmission if this is appropriate

When giving a positive HCV PCR result:
- Ensure the patient has a good understanding of what the result means
- Give the patient the opportunity to ask questions and for you to address any mistaken beliefs about HCV infection
- Check what support the patient has, and offer follow up support
- Encourage the patient to share the result with family members and other relevant contacts so they can be tested whenever this is appropriate
- Discuss the next steps, which should include the offer of specialist referral, and make sure the patient has grasped fully what is going to happen. Answer any questions the patient has about treatment
- Ask for consent to refer the patient for secondary care review, or if the patient isn't ready for this, ensure there is a clear entry in the case notes about the diagnosis and a clear plan for further discussion of referral with the patient.
- Offer patient information - leaflets, useful websites, local specialist groups

Harm-reduction information in HCV infection
- Reducing personal risk:

The patient with HCV infection can reduce the risk of liver harm by avoiding excess alcohol, co-infection with HBV or HIV viruses and avoiding obesity.

It is recommended that all patients with HCV infection should be offered vaccination against both HBV and hepatitis A infection (Green book, 2022). They also fall within the eligibility criteria for annual flu vaccination.

- Reducing risk to others:

The patient can reduce the risk of transmission of the virus to others by not sharing any drug-injecting equipment with other people including needles, syringes, spoons and filters and not sharing razors or toothbrushes that might be contaminated with blood. The risk of getting hepatitis C through sex is very low, however, it may be higher if exposure to blood is more likely, such as menstrual blood or from bleeding during anal sex and in these cases condoms should be worn. Patients should be asked to discuss their infection with contacts who can be offered testing as needed.

Treatment of chronic HCV infection

The aim of HCV treatment is to achieve a 'sustained virological response' (SVR) which means clearance of the virus and potential 'cure'. The decision when to start treatment and the treatment regimen of choice depend on a number of complex factors, including the presence of progressive liver disease, the viral load, HCV genotype, the patient's readiness for treatment, and the presence of complicating factors such as unstable mental health problems or advanced liver disease.

'Traditional' antiviral treatment for hepatitis C consisted of weekly subcutaneous injections of pegylated interferon alpha, which has virucidal activity, in combination with daily oral ribavirin, a drug which interferes with viral replication.

Newer direct acting antiviral (DAA) agents have now been approved by NICE and are becoming first line treatment for the majority of patients. They are the most expensive drugs ever recommended by NICE and treatment is being co-ordinated through a number of centralised 'operational delivery networks' countrywide. They have fewer unwanted effects than the more traditional medications and usually a significantly shorter treatment course duration. Just under 80% of those who are start treatment attain SVR.

The effectiveness of treatment

The probability of achieving SVR depends on multiple factors including patient factors, the HCV genotype causing the infection and the viral load.

Return to the toolkit for useful further links:

- SIGN 133 management of hepatitis C guidance (2013)

- NICE PH43 hepatitis B and C testing guidance (2013)

- WHO Hepatitis C fact sheet.

- 'Shooting Up: Infections among people who inject drugs in the UK'.

- Hepatitis C in England 2017 report.

- HCV Action educational film: Detecting & managing hepatitis C in primary care.

- Clinical audit ideas: managing hepatitis C in primary care

- Personal learning reflection template

- Information for patients Web Link

- Hepatitis C Patient leaflet (free download)

- Hepatitis C Trust

References

NICE (2013) NICE PH 43 Hepatitis B and C testing: people at risk of infection. NICE 2012

Hepatitis A, in The Green Book, chapter 17 (2022). GOV.UK website

Hepatitis A, in The Green Book, chapter 18 (2022), GOV.UK website

WHO (2017) Action plan for the health sector response to viral hepatitis in the WHO European Region

PHE (2022) Hepatitis C in England, full report. PHE 2022