Hepatitis C

1. Hepatitis C

This article was written in December 2023. It's based on a Lancet Seminar (2023;402:1085), the HepCULater GP Toolkit and training module produced by the NHS Hepatitis C Elimination Programme, and other sources where specified.

1.1. What's new?

Over the past decade, the development of direct-acting antiviral treatments (DAAs) has revolutionised care in hepatitis C. It is now **curable in >95% of people**, usually with a single course of safe and well-tolerated oral treatment, given for as little as 8 weeks. The use of these treatments in the UK, alongside other successful strategies, means that England is on track to

eliminate the virus by 2025.

Let's put these new treatments into context with a recap of hepatitis C, and look at what we can do in primary care to help elimination happen.

You may also be interested in our articles on HIV (there are some parallels with hepatitis C in terms of highly-effective treatments, with the goal of eliminating transmission on the horizon) and hepatitis B.

1.2. Presentation and natural course: a reminder

Hepatitis C (shortened to 'hep C' from here) is an RNA virus that can cause acute and chronic hepatitis, which, left untreated, can cause progressive liver damage, cirrhosis, decompensated liver disease and hepatocellular cancer. Transmission is bloodborne. There is currently no effective vaccine against it.

Acute infection

For **>70% of people, acute infection is asymptomatic**. In a minority, we *may* see:

- Jaundice.
- Fever, headache, malaise.
- Anorexia, nausea.
- Vomiting, diarrhoea, abdominal pain.
- Abnormal LFTs, e.g. ALT >5–10 times the upper limit of normal.

If we suspect acute hep C infection, we should refer for same-day assessment.

Outcome after acute infection

Most develop chronic hep C infection, but around 20% of people spontaneously clear the virus without treatment, usually within 6 months. Those who clear the virus **do not** gain lifelong immunity.

Chronic infection

Chronic hep C infection causes:

- Liver inflammation and fibrosis in *most* people.
- Cirrhosis in *5–10% of people* by 20 years of infection.

Among people with cirrhosis caused by hep C infection, there's a yearly risk of:

- Decompensated liver failure of about 3%.
- Hepatocellular cancer of about 2%.

Chronic hep C infection is also associated with extrahepatic disease, including:

- Mixed cryoglobulinaemic vasculitis, which can cause purpura, arthralgia, glomerulonephritis and peripheral neuropathy.
- Porphyria cutanea tarda (painful blisters that appear on sun-exposed areas).
- Lichen planus.
- Non-Hodgkin's lymphoma.
- Type 2 diabetes.

Genotypes

Of the 6 main numbered genotypes, 1 and 3 are the most common in the UK. Genotyping sometimes affects what treatment a person is offered; however, there are 'pan-genotypic' treatments available which are effective against all strains of hep C virus.

1.3. How is it usually transmitted, and who is at risk?

Injecting drug use

In the UK, the most important risk factor is injecting drug use**.** In 2021, it was estimated that just over half of people who inject drugs had ever hep C infection, and about 14% had active infection – although, thankfully, the numbers with active infection are rapidly falling; more on this later (Hepatitis C in the UK 2023, UKHSA).

Unsafe healthcare practices

Globally, unsafe healthcare practices – such as reusing needles and unscreened blood transfusions – are the major route of transmission in many low and middle-income countries. This is particularly relevant to those of us who care for refugees and other immigrant populations, or for anyone who has had healthcare or other procedures abroad. Examples of areas with high prevalence of active hep C infection are listed below, with estimated prevalence figures for 2020 in brackets. For comparison, UK prevalence in this period was 0.2% (Lancet Gastroenterol Hepatol

2022;7:396):

- Pakistan (3.3%).
- Russia (2.9%).
- Ukraine (3.1%).
- Central Asia, e.g. Mongolia (4.2%), Uzbekistan (3%).
- Some central and Eastern European countries, e.g. Romania (3%), Latvia (2%).
- Some African countries, e.g. Gabon (4.7%), Burundi (3.5%).

Within the UK, having had certain medical procedures before the introduction of proper screening is also a risk factor:

- Being given blood products before 1986.
- Being given a blood transfusion before 1991.
- Being given an organ transplant before 1992.

Sexual transmission

This is the second most important route of transmission in the UK, commonest in men who have sex with men, with risk factors including:

- Sexual behaviours, including anal sex without condoms, a high number of sexual partners and group sex.
- HIV infection.
- Ulcerative sexually transmitted infections.
- Exposure to menstrual blood during sex.

Vertical transmission

About 5% of babies born to mothers with active hep C infection acquire the virus.

Other modes

Less commonly, transmission can occur through sharing toothbrushes or razors in the presence of open wounds, or through sharing items used to take drugs through routes other than injecting, such as bank notes for snorting cocaine.

1.4. When should I test for hepatitis C?

Acute infection is usually asymptomatic, and people can be well with chronic infection for many years. It's estimated that in the UK, about three-quarters of people with active hep C infection are undiagnosed. Early diagnosis and treatment are crucial both for the individual's health outcomes and for reducing transmission. A key message, therefore, is:

HAVE A LOW THRESHOLD TO OFFER TESTING, AND NORMALISE TESTING AS A ROUTINE PART OF HEALTHCARE.

Testing based on abnormal LFTs

We should screen **everyone** with raised transaminases (ALT or AST) for hep C; see our GEMS on abnormal liver function tests for more detail. Note, though, that normal LFTs *do not* exclude hep C infection.

Testing based on risk factors

Based on risk factors, the most important groups for us to offer testing to are (Lancet 2023;402:1085 and Hep CU Later training module):

1. People who have ever injected drugs, including gym drugs.
2. Men who have sex with men.
3. People who were born in, or who have had medical treatment or skin-breaching procedures (tattoos, cosmetics, etc.) in, high-prevalence countries – see above section for examples of these areas.

After a one-off test in these groups, primary care should offer annual testing for hep C if the person tests negative and remains at increased risk of infection (NICE 2013, PH43).

The table below shows the other groups who should be offered hep C testing (PHE 2019; Hepatitis C: interventions for case-finding and linkage to care):

Drug and alcohol related	• All people who inject drugs, including steroids or other gym drugs (currently or ever). • People who snort drugs. • People with alcohol dependence.
Sex related	• Men who have sex with men. • People who engage in 'chem-sex'. • Sexual partners of people with known hepatitis C infection (but note that sexual hep C transmission is rare in straight people).

	• Anyone involved with sex work.
Origin related	• People born in a country with intermediate/high prevalence (the 2019 PHE reference above says this includes Eastern Europe, Asia, Africa and Central America; see previous section for more on high-prevalence countries).
Social/environment related	• Homeless people. • People who are in or have been in prison. • Young offenders. • Looked-after children and young people, including those living in care homes. • Close contacts of people with known hep C infection, including household members, family and close friends (because of the small risk of transmission via shared items such as razors, etc.).
Others	• All people with HIV infection. • People with haemophilia. • People who received blood before 1991 or blood products before 1986 and have not already been tested. • Needle-stick injuries – follow UKHSA advice. • People who have had acupuncture, piercings, tattoos, or medical, dental or cosmetic procedures such as semi-permanent makeup and electrolysis abroad and/or in unsterile conditions (not all mentioned by PHE, but highlighted by HepCULater's toolkit). • Babies born to mothers with hepatitis C infection.

Testing in other settings

The NHS Hepatitis C Elimination Programme (more on this later in the article) means that patients are increasingly being offered hep C testing across a variety of settings, including:

- Drug treatment services and prison settings (some have already achieved 'micro-elimination' of hep C in their populations through enhanced testing and engagement with treatment).
- Pharmacies offering testing for people who access opioid substitution therapy and/or needle and syringe programmes.
- 'Opt-out' hepatitis B, C and HIV screening in many emergency departments.

Some of these services use types of testing that we will be less familiar with, including antibody and RNA tests that give results within 60 minutes, sometimes with an option to use saliva rather than blood.

Note that pregnant women are *not* screened for hep C routinely on their booking bloods as they are for hepatitis B, HIV and syphilis – hep C testing is *only* done if there are risk factors.

1.5. Testing and interpreting tests

Before testing

In depth pre-test counselling is not needed, but we should let the patient know what we're testing for, get verbal consent, and explain the availability of safe and effective treatment. A useful phrase might be:

"In this situation, we routinely screen for hepatitis C, a liver virus which is curable with a short course of tablets. Is that ok?"

If a person declines hep C screening, we might want to let them know about the availability of free home-test kits (more below).

Types of test

In primary care, there are two tests we need to think about:

- **Hep C antibody**: tests whether a person has *ever* come into contact with the hep C virus.
- **Hep C RNA**: tests whether a person has *active* hep C infection.

Our usual first line-screening test for all the scenarios above will be **hep C antibody testing**.

If someone believes they've been at risk of infection, it's important to consider hep C's incubation period. If they initially test negative for hep C antibody, we should retest at 3 and 6 months after the exposure.

As we said earlier, in someone who remains at risk, we should continue to offer hep C antibody testing every 12 months.

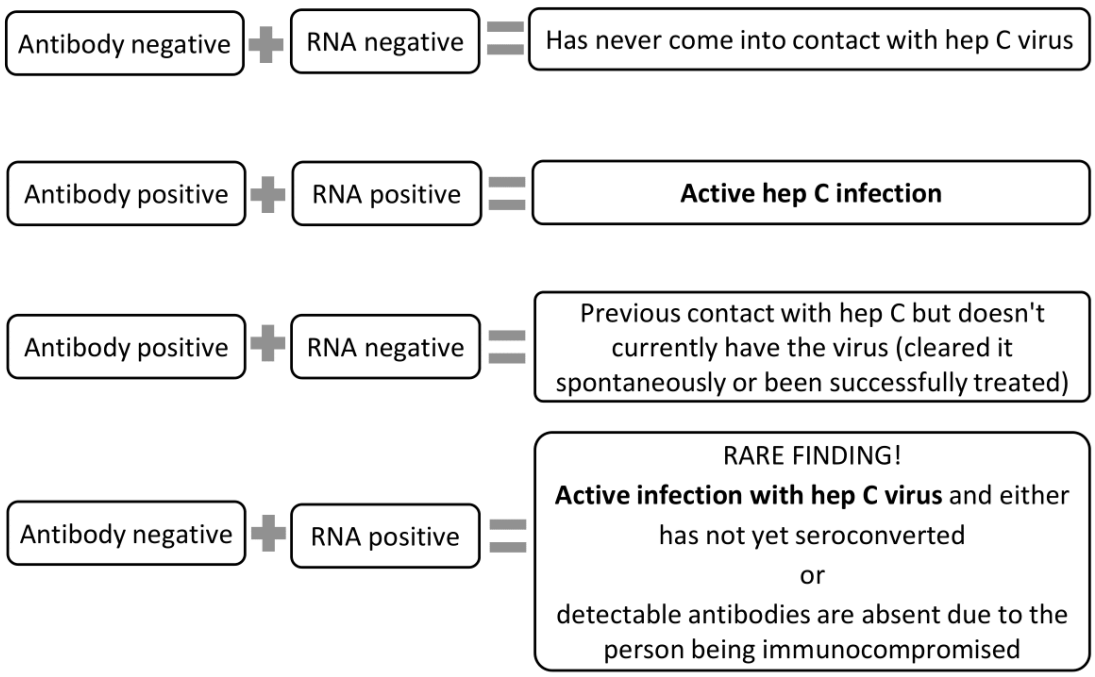
There are three scenarios in which we should request hep C RNA (although note that some of us may not have access to request this test separately and your local lab may just add on if needed; speak to your lab if in doubt):

1. After a positive hep C antibody test (may be done automatically by lab).
2. In an immunocompromised person (antibodies may not be produced in active infection).

3. In someone who has previously cleared or been successfully treated for hep C who is at risk of reinfection (antibodies aren't helpful here as they'll be positive for life).

Interpreting test results

Possible outcomes are:



What to do with a positive result

If we find active hepatitis C, we should (taken from Hep CU Later):

- Inform the person, let them know treatment with a 95% chance of cure is available, and offer support through the Hepatitis C Trust.
- Refer urgently to hepatology (or some areas have a specific viral hepatitis pathway – use this if you have it!).
- If possible, support hepatology by requesting viral genotype, FBC, U&E

and LFTs.

- Give harm-reduction advice, e.g. accessing needle exchange and condoms.

If we're unsure about how to interpret results, we should discuss urgently with secondary care.

1.6. Treatment

Everyone with active infection will be considered for treatment by hepatology. The goal is cure, defined as viral RNA being undetectable, and this is achievable in over 95% of people.

Before DAAs, the main treatment was interferon, which was given for up to a year by injection and caused severe side-effects. When speaking with patients who experienced the 'old' treatment, we need to be clear that things are now *extremely* different. Read on for more…

Direct-acting antivirals (DAAs)

- DAAs are now first line in almost everyone, and can be used in either acute or chronic infection, regardless of duration of infection or comorbidity.
- There are DAA options effective against all genotypes of hep C.
- They work by inhibiting viral replication.
- They are given orally, usually as either an 8 or 12-week course.
- They are described in the Lancet Seminar as being 'exceptionally' safe and well tolerated.

- There are 3 types:
    - NS3/4A protease inhibitors (e.g. glecaprevir).
    - Non-nucleoside and nucleotide analogue NS5B RNA-dependent RNA-polymerase inhibitors (e.g. sofosbuvir).
    - NS5A inhibitors (e.g. pibrentasvir).
- Most regimens use a combination of two drugs.
- Hep C RNA is retested 12 weeks after starting treatment. At this point, the vast majority will be RNA negative, but those who have not responded can be retreated. People who fail to respond to a first course still have an excellent prognosis, with >90% being successfully treated after a second course (falling to 80–90% in people with cirrhosis and genotype 3 infection).

If we need to make **any changes** to the person's normal medications during their 8–12-week course of DAAs, we should **discuss this with hepatology** due to the risk of interactions. There is an online interaction checker for these drugs – link in resources below – which may also be helpful.

1.7. Hepatitis C elimination

The WHO has a global aim to eliminate hepatitis C by 2030, and NHS England aims to eliminate it 5 years ahead of the 2030 target. England may be the first country in the world to reach hepatitis C elimination. Since the NHS Hepatitis C Elimination Programme began in 2015:

- The number of people living with active hepatitis C has fallen dramatically.
- Liver transplants have reduced by 52%.
- Deaths from hep C have reduced by 37%.

- The number of people accessing treatment for hep C has more than doubled.

Primary care has a key role to play in the final stages of the programme by:

- Identifying those who are unaware of their hep C infection through testing. As we said above, that means offering testing to *everyone* with raised transaminases and *everyone* in an at-risk group, with ongoing testing if they remain at risk.
- Coding risk factors and hep C infection correctly so people in need of screening or other outreach can be easily identified.
- Supporting anyone with known hep C who has been lost to follow-up or disengaged with treatment – perhaps in the era of poorly-tolerated interferon therapy – and encouraging them back into treatment.
- Improving awareness by sharing information with colleagues and patients: Hep CU Later has resources you can display in your practice.

The Hepatitis C Elimination Programme can support you with using a search tool called PSIT (patient search identification tool), now built into most clinical systems, to search for those who may have undiagnosed or known hep C and are in need of treatment. To discuss this, or if you're interested in becoming a GP champion for Hep C, email connect.HepCULater@mpft.nhs or england.hepc-enquiries@nhs.net.

1.8. Free NHS home-testing kits

Anyone in England can request a free, self-sampled finger-prick bloodspot test kit for hep C to use at home and return by post. Order online at hepctest.nhs.uk. People with a negative result are informed via text, and those with a positive result are linked directly to their local viral hepatitis

team.

1.9. Stigma

Stigma around hep C is one of the major barriers to treatment. The HepCU Later training tool has some suggestions as to how we can help tackle it within healthcare (much of this can apply to other stigmatised conditions too!):

- Share knowledge with others. A key message for hep C is that it's easily curable, and those who have been cured cannot transmit the virus.
- Inform people that they don't legally have to declare their hep C status to anyone.
- Use person-first language: 'a person living with hep C' not 'a hep C carrier'.
- Link people to appropriate support networks. The support helps the person, and the visibility the groups promote helps reduce stigma.
- Make access to testing and treatment easy and non-judgemental. Think about how rigid pathways and protocols might deter someone from engaging.

Hepatitis C

- Thanks to DAAs, hep C is now curable in >95% of people with a single, short course of oral treatment.
- Acute infection is usually asymptomatic. 20% of people spontaneously clear the virus within 6 months of infection. The rest develop chronic hep C infection, which, untreated, can lead to cirrhosis, liver failure and hepatocellular cancer.

- The commonest routes of transmission globally are:
    - Injecting drug use.
    - Unsterile healthcare practices (or other skin-penetrating practices such as tattoos, cosmetic treatments).
- Some areas of the world have extremely high prevalence of hep C; being born in or having had treatment in these regions is an important risk factor.
- Other less common routes include sexual (most common in men who have sex with men) and vertical transmission.
- Have a low threshold for testing. Test everyone with raised transaminases and everyone at risk, and continue to test every 12 months in those who remain at risk.
- Hep C antibodies tell us whether a person has *ever* been infected; hep C RNA tells us if they have *active* infection.
- Refer all active infection to hepatology, support the person and provide harm-reduction advice.
- DAAs are usually given for 8–12 weeks, are effective in acute and chronic infection, against all genotypes, and are extremely safe and well tolerated. Make sure patients with experience of interferon, which was very different, know this.
- People who have been successfully treated can be reinfected and should have ongoing screening if needed.
- Anyone can order a free home hep C testing kit online.

- Are you routinely testing those at risk in your practice?
- Do you have a system for retesting those who remain at risk every 12 months?
- If you have capacity for a 'meatier' QI project, could you, with support from the Hepatitis C Elimination Programme, look at who in your practice population needs testing and treating? GPs who have done this report getting multiple people on appropriate treatment!

Useful resources:

Websites (all resources are hyperlinked for ease of use in Red Whale Knowledge)

- HepCULater (educational resources for patients and professionals)
- The Hepatitis C Trust
- HEP Drug Interactions (interaction checker for DAAs)
- NHS - hep C test (order a free home hep C test kit online)