Management of Hepatitis C

Background

Hepatitis C (HCV) is contracted by blood to blood contact. Sexual transmission is reported but is rare and probably by anal intercourse. Between 5 and 10% of patients develop an acute hepatitis, usually unnoticed, about six weeks from HCV exposure. Around 20% clear HCV RNA, but remain susceptible to reinfection (despite developing HCV antibody). 80% evolve to a chronic hepatitis, which is progressive rather than relapsing and remitting. 20% of the patients with chronic HCV develop cirrhosis within 1 to 3 decades. Risk factors for rapid progression are smoking, older age at the time of infection, high BMI, concomitant alcohol abuse, being male and HIV co-infection. Cirrhotic patients have a 25% risk of death in 5 to 10 years. The annual risk of HCC in HCV with cirrhosis is 3 to 5% and is rare in the absence of cirrhosis.

Who to test

The following groups should be tested for HCV:

- Blood/tissue donors
- Patients on haemodialysis
- Healthcare professionals who intend to pursue a career in a specialty that requires them to perform exposure prone procedures.

The following groups should be offered an HCV test:

- Patients with a persistently elevated alanine aminotransferase
- People with a history of injecting or snorting drug use
- People who are human immunodeficiency virus (HIV) or hepatitis B positive
- Recipients of blood clotting factor concentrates prior to 1987
- Recipients of blood, blood components and organ/tissue transplants in the UK before the end of 1996
- Children whose mother is known to be infected with HCV
- Healthcare professionals following percutaneous or mucous membrane exposure to blood which is, or is suspected to be, infected with HCV
- Prisoners
- People who originate from high prevalence populations, including Africa, Asia, the Caribbean, Central and South America, Eastern and Southern Europe, the Middle East, and the Pacific islands
- People who have received medical or dental treatment in countries where HCV is common and infection control may be poor
- People who have had tattoos, body piercing or Botox in circumstances where infection control procedure is, or is suspected to be, suboptimal
- People who have had a sexual partner or household contact who is HCV infected
- Looked-after children and young people, including those living in care homes
- People living in hostels for the homeless or sleeping on the streets
- HIV-positive men who have sex with men
- Pregnant women with any of the above risk factors

Timing of testing

Patients without ongoing infection risk

Single screening test (anti-HCV)

Patients with ongoing risk

Testing every six to twelve months (HCV RNA and anti-HCV [unless known seropositive])

Patients with an acute risk

At baseline, anti-HCV and HCV RNA

At 6 weeks, HCV RNA

At 12 weeks, anti-HCV and HCV RNA

At 24 weeks, anti-HCV

How to test and interpretation/management of results

1) *Screening*. A serum sample should be tested for anti-HCV antibody. A positive result demonstrates previous exposure or active infection.
2) *Testing for active infection*. If a screening test returns positive, a large EDTA sample should be sent to test for HCV RNA (unless reflex testing has already been undertaken). A positive result indicates active infection. A negative result indicates clearance, which should be confirmed by repeat testing and no further action taken. Repeat testing is recommended for those in high risk groups.
3) *Workup for patients positive for HCV RNA*. A full liver screen, HCV genotyping (no longer mandatory), HIV testing, HAV/HBV immunity assessment and an ultrasound scan to stage liver disease should be undertaken preferably before referral to secondary care. The liver screen includes: hepatitis BsAg and anti-HBc, liver autoantibodies, immunoglobulin profile, alpha-1 antitrypsin level, caeruloplasmin (if < 50 y o), ferritin, HBA1c, random glucose, LFT, AST, INR, UE and FBC.

Point of care testing and dry blood spot testing (DBST)

In general, these assays test for HCV RNA. Point of care testing offers rapid results. Neither require venous phlebotomy. It is important to recognize that no test is 100% accurate. When there is a disparity in results (for example between point of care and DBST) then venous blood laboratory testing is recommended as an arbiter.

Hepatitis C treatment centres

Usually, patients should be referred to their nearest treatment centre. These are:

- Addenbrooke's Hospital
- Basildon Hospital
- Bedford Hospital
- Ipswich Hospital
- Luton and Dunstable Hospital
- Norfolk and Norwich Hospital
- Peterborough Hospital

The other regional hospitals will be able to offer advice and workup for patients if they would like to be seen locally initially.

Management of acute and chronic infection

Management of patients includes focus on viral eradication, staging of liver disease, addressing other risk factors for chronic liver disease (particularly alcohol and obesity), screening for blood borne viruses, contact tracing and vaccination recommendations. A treatment pathway follows.

Treatment pathway

Pre-treatment investigations

Minimum: recent HCV RNA positive or historical HCV RNA positive x 2 at least 12/52 apart

Desirable: UE, LFT, FBC, PT, staging by FIB4 or FibroScan, BBV screen, HAV/HBV vaccination requirements

Optional: chronic liver screen, liver ultrasound scan, genotype

Before retreatment: genotype and resistance analysis profile

Treatment monitoring

See below regarding treatment regimens. Medication should be started by an appropriately trained health care professional and dispensed at a volume appropriate to individual circumstance.

Weeks 2-4:
Contact (usually by telephone) to assess for compliance and complications

Weeks 4-end of treatment:
Contact depending on case complexity and support requirements

End of treatment:
HCV RNA

SVR12, SVR24 and SVR48 (see below for discharge recommendations in relation to SVR):
HCV RNA, LFT

FibroScan if either not already undertaken or > 7 kPa at initial assessment

Discharge

Following SVR assessment (SVR12 acceptable, SVR24 desirable but not essential), patients should be discharged if the following criteria are met:

- FibroScan score < 7 kPa
- Normal LFT, plt and PT (if blood tests had been taken)

Advice should be given regarding blood borne virus prevention, vaccination recommendations and liver disease risk factor avoidance. Those with risk factors for reinfection should have HCV RNA testing undertaken every 6 to 12 months through their drug and alcohol service or general practice.

Follow up

If liver tests do not normalise with treatment or FibroScan score is between 7 and 12.5 kPa then a liver disease screen and ultrasound scan should be undertaken and an appropriate management plan made with the results. A repeat FibroScan six months following treatment for those with a 7 to 12.5 kPa score, as the reading may have partially reflected hepatitis C associated inflammation.

If FibroScan is suggestive of cirrhosis at any stage on the treatment pathway then cirrhosis surveillance should be considered. For indeterminate cases, a plan should be made in conjunction with the local MDT which could include a repeat FibroScan, liver imaging and/or liver biopsy for disease staging.

Discharge of patients covered by either of the paragraphs above should be made in conjunction with the local MDT.

Surveillance/prevention

- 6-monthly ultrasound scanning for HCC is recommended for patients with significant fibrosis or cirrhosis (≥ F3 fibrosis). AFP can be assessed, but has a low specificity in active HCV.
- A variceal surveillance programme is indicated for cirrhotic patients (but can reasonably be delayed until the development of thrombocytopenia and splenomegaly).
- Cirrhotic patients should receive osteoporosis surveillance.
- Vaccination against HAV and HBV in unexposed individuals is reasonable.

Adult treatment

Available treatment regimens are dictated centrally by NHS England and NICE. Regional prioritisation for therapy follows.

Regional selection and prioritisation

Patients are discussed at a multidisciplinary team meeting and if it felt that they are appropriate for therapy, will be treated as soon as possible.

Blueteq, data collection and regional run rates

For all patients being treated with direct acting antiviral therapies (DAAs), the following processes apply. Blueteq forms require completing, minimum datasets entered and treatment kept within the “rate card” stipulated by NHS England.

Treatment regimens

There are several treatment regimens that are available through NHS England and NICE. Given budgetary constraints, NHS England stipulates that specific regimens are used. The treatment proportions should be allocated according to the NHS England procurement deal, which is available for ODN members on request.

Retrospective ratification process

To avoid treatment delay for patients with uncomplicated hepatitis C and no significant drug interactions, it is reasonable practice to start patients on hepatitis C treatment with the following regimens and ratify that decision retrospectively at MDT.