Hepatitis C virus (HCV) infection is a leading cause of chronic liver disease worldwide. Over the past decade significant advances have been made in the understanding and treatment of HCV. The advent of peginterferon alfa and ribavirin combination therapy has led to a “cure” for approximately 55 per cent of patients treated.

However, despite the availability of National Institute for Health and Clinical Excellence-endorsed treatment, awareness of and access to treatment still remains low. This is likely to be because most of those infected are unaware of their condition. This article discusses the aetiology and diagnosis of HCV infection, and disease progression.

**Background**

Hepatitis C is a viral infection predominantly affecting the liver, first identified in 1989. Before this it was recognised as the major cause of “non-A, non-B hepatitis”. HCV is a significant health problem and the World Health Organization estimates that around 170 million people worldwide are chronically infected with the virus. According to figures from the Health Protection Agency, it is estimated that between 200,000 and 500,000 people in England and Wales could be infected, with the vast majority of these people unaware they carry the virus. In the UK, the prevalence of hepatitis C is estimated to be 1.1 per cent of the population.

Figures show that, of the 47,000 people diagnosed with HCV in England and Wales in 2005, only 7,000 people actually received treatment, so work is being done to try to raise awareness of HCV among the public and healthcare professionals.

**Transmission**

HCV is a blood-borne virus and is primarily transmitted via blood and blood products. Panel 1 lists the common routes of transmission.

According to the WHO, around 90 per cent of people with chronic HCV infection living in developed countries are current or former injecting drug users, or people with a history of transfusion of unscreened blood or blood products before September 1991. This is likely to be because most of those infected are unaware of their condition. This article discusses the aetiology and diagnosis of HCV infection, and disease progression.

**Disease progression**

There are two stages of infection: acute and chronic.

The severity of the acute illness will vary and it is uncommon to encounter acute HCV infection in clinical practice; most people with HCV present with chronic disease. After exposure to the virus, it usually takes several weeks for serum alanine aminotransferase and aspartate transferase levels to rise.

**Panel 1: Routes of transmission of hepatitis C**

- Blood transfusion, especially with unscreened blood products
- Reuse of needles and syringes not adequately sterilised, eg, by intravenous drug users
- Needle-stick injuries
- Tattooing
- Acupuncture
- Intranasal cocaine use
- Perinatal (mother to baby)
- Sexual (exposure to an infected partner or multiple partners)
become elevated. Approximately 70 per cent of patients will be asymptomatic in the acute phase.

In patients who do develop symptoms these are usually non-specific, including decreased appetite, fatigue, abdominal pain, jaundice and flu-like symptoms. Rarely, acute HCV infection may lead to acute liver disease or liver failure. Patients who become symptomatic in the acute phase are more likely to clear the virus spontaneously. Patients who spontaneously recover should not suffer any long-term complications or require any pharmacological treatment. They will also have developed antibodies to HCV.

Some patients may spontaneously clear the virus but approximately 85 per cent of those infected with HCV will subsequently develop chronic infection. Hepatitis C is often referred to as the “silent killer” as it may take from 20 to 50 years for the disease to progress. The progression of HCV is variable and each person has a different response to the virus. Not every infected individual will go on to develop serious complications and the severity of liver damage varies greatly. For many years most people infected with HCV will be asymptomatic or exhibit minor symptoms such as fever or malaise.

Cirrhosis will develop in approximately 20 per cent of patients over a period of 20 to 25 years. This can further progress to end-stage liver disease, which may require liver transplantation or result in death. Hepatocellular carcinoma (a primary liver cancer) may also develop. HCV is thought to be responsible for 50–76 per cent of all liver cancers and is the most common reason for liver transplantation in Europe and North America.

Almost all the mortality associated with chronic HCV infection is due to the complications of cirrhosis. Once the functional capacity of the liver is affected, patients will experience signs and symptoms of end-stage liver disease, including jaundice, ascites, gastrointestinal varices (which may haemorrhage), encephalopathy, coagulopathy and pruritus. Certain factors associated with increased fibrosis, or rate of progression to cirrhosis, have been identified for patients with HCV. These include high alcohol intake, immunosuppression, age at time of infection, HCV viraemia, obesity and co-infection with other viruses such as hepatitis B or HIV.

Figure 1 provides a pictorial summary of progression of HCV infection.

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**Diagnosis**

HCV is a single-stranded RNA virus belonging to the Flaviviridae family. Patients in whom HCV infection is suspected should undergo a serological test that detects antibodies to HCV (known as anti-HCV). It can take up to three months for antibodies to become detectable following infection with HCV. A positive antibody test does not necessarily mean that the patient has chronic HCV infection since they may have spontaneously cleared the virus, as explained above.

If a patient tests positive for anti-HCV then the next step is to test for the presence of HCV RNA, which indicates the presence of viraemia. Various qualitative and quantitative assays for HCV RNA are available. The level of HCV RNA in the blood can be a useful predictor of response to treatment. HCV RNA can also be monitored during treatment to assess response to therapy. There is ongoing debate around the frequency of HCV RNA monitoring during treatment and the usefulness of this. For those patients who have a rapid fall in their HCV RNA, a shorter duration of treatment may be appropriate. This will be discussed in further detail in the next article (p413).

HCV genotyping must also be performed before starting treatment. There have been six main HCV genotypes identified to date (numbered 1 to 6). Genotype 1 is the most prevalent type in the western world and accounts for approximately half of the cases of HCV in the UK. Genotype is important in predicting the response rate to treatment and also treatment duration. Patients infected with genotype 2 or 3 have a far better chance of responding to treatment than those infected with the other genotypes.

Liver biopsy is traditionally performed before starting treatment, although this is not mandatory for good patient care. A biopsy can provide useful information on disease severity (by describing the degree of hepatic inflammation and fibrosis) and the natural history of the infection, guiding decisions on when to start treatment and prognosis. Nonetheless, biopsy is not without risks, and these risks must be weighed against the potential benefits of the information obtained.

Non-invasive techniques to assess liver fibrosis, such as Fibroscan, are still under evaluation, although their use in this setting is now widespread. Fibroscan uses a mechanical pulse generated at the skin surface, which is propagated through the liver. The velocity of this pulse is measured by ultrasound and is directly correlated to the stiffness of the liver, which in turn reflects the degree of fibrosis. The use of this technique for assessment of hepatitis C patients is growing, as it provides useful, non-invasive information on the degree of liver damage.

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**Summary**

Hepatitis C has been identified by the WHO as a global health problem and it is believed that 1.1 per cent of the UK population has chronic infection. Its long-term consequences include cirrhosis, end-stage liver disease and primary liver cancer. It is the most common reason for liver transplantation in Europe and North America and thus represents a huge burden on resources.

A small proportion of patients may spontaneously clear the virus but the majority will become infected chronically. An antibody test is used to confirm exposure to HCV, with chronic infection confirmed using a HCV RNA assay. HCV genotyping is critical in the consideration of antiviral therapy and predicts response rate to treatment and treatment duration. A liver biopsy was traditionally performed but is now not mandatory for initiation of treatment, with new, non-invasive techniques such as Fibroscan being used.

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**References**