

Hepatitis B infection and immunisation in primary care

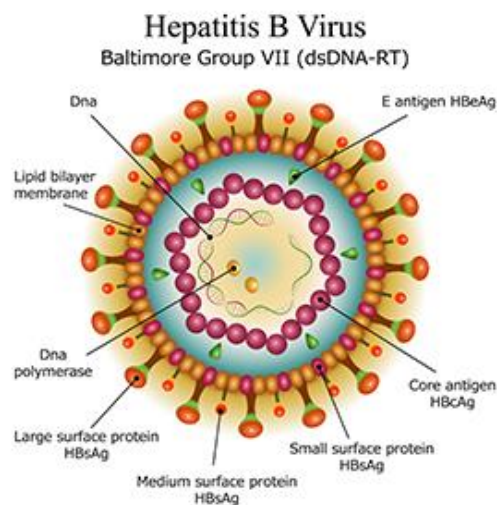
Introduction

Hepatitis B virus (HBV) is a blood-borne, double-stranded DNA virus that causes liver infection in humans. **The most recent estimates suggest that around 180,000 individuals are thought to have chronic hepatitis B infection in the UK, an overall prevalence of 0.3% (NICE CKS 2022).** The large majority of people with chronic HBV in the UK (around 95%) have contracted the condition in countries outside the UK where HBV infection is endemic, and are members of migrant communities (NICE CKS 2022). In these groups transmission is predominantly vertical from mother to baby, though there is also horizontal transmission from close contacts particularly during childhood.

Most of those with chronic HBV infection are not aware that they have the infection. However, they are at risk of developing life-threatening liver disease, including cirrhosis and its complications including hepatocellular carcinoma.

Because hepatitis B infection is concentrated in marginalised populations, even when individuals are diagnosed, some may fail to access effective specialist care.

However, for most who are infected, chronic hepatitis B infection is manageable, and monitoring, and anti-viral treatment when indicated, can reduce in large part the impact of long-term liver disease and improve health outcomes.



HBV transmission

HBV is transmitted through activities that involve percutaneous or mucosal contact with infectious blood or body fluids containing the virus. Although HBV may be present in bodily fluids such as semen, vaginal exudate, sweat, tears and saliva, it is most readily spread through blood to blood contact and through unprotected sex.

In many countries, HBV infection is endemic. In high prevalence countries children typically contract the infection at the time of birth through vertical transmission from their mother. Horizontal transmission during early childhood through close contact with family members and other children with the virus is another mode of transmission.

In contrast, in countries like the UK where the overall prevalence of HBV infection is low, new cases of infection are typically acquired in adulthood, and the principal routes are injecting drug use with sharing of needles or other equipment and via sexual transmission.

Other transmission routes in both high and low prevalence areas include iatrogenic transmission in healthcare settings, including re-use of hypodermic needles, use of unscreened blood transfusion or blood products, organ transplant and haemodialysis, and needle-stick and sharps injuries. Other environments where needles may be re-used such as tattooing, acupuncture and body piercing may be associated with HBV transmission. Direct contact with the blood of an infected person in the healthcare setting, or even in fights, may also be associated with transmission of the disease.

Occasionally HBV infection may be transmitted as a result of a household or casual contact including direct contact between young children in the home or nursery, sharing a toothbrush or razor with an HBV infected person or through a human bite.

Although the overall prevalence of HBV infection is low in the UK, vertical transmission of infection from a mother infected with HBV remains a risk. All pregnant women are offered screening for HBV in order to identify infection prior to delivery so that newborn infants can be protected by immunisation immediately after birth. This may be active immunisation through vaccination or a combination of active and passive immunisation.

Although HBV has been shown to be present in breast milk, transmission during breastfeeding is very unlikely. There is no need to delay breastfeeding until a baby is fully immunised, but if a baby has not received prophylaxis through active and passive immunisation then any mother with HBV infection should consider abstaining from breastfeeding if she has bleeding nipples. There is no reason not to breast feed a baby who has received prophylaxis.

HBV infection is *not* spread through food or water, sharing eating utensils, breastfeeding (unless nipples are cracked or bleeding), hugging, kissing, hand holding, coughing, or sneezing.

The natural History of HBV infection

The natural history of HBV infection varies from person to person and depends on the patient's age at infection.

Chronic HBV infection has been classified into five phases:

- HBeAg-positive chronic infection
- HBeAg-positive chronic hepatitis
- HBeAg-negative chronic infection
- HBeAg-negative chronic hepatitis
- HBsAg-negative phase

All patients with chronic HBV infection are at increased risk of progression to cirrhosis and hepatocellular carcinoma (HCC), depending on host and viral factors.

Vertical transmission of infection from mother to baby results in infection in up to 90% of cases if the mother is HBsAg and HBeAg positive (See 'Interpreting HBV panel test results' later in this document). **Around 70-90% of infected infants become chronic carriers of the hepatitis B virus.**

In adults, the incubation period from the time of exposure to onset of acute HBV infection symptoms varies between 6 weeks to 6 months. For most, acute infection is asymptomatic, though some may have general symptoms including tiredness, fever, aches and pains, loss of appetite, nausea, vomiting and diarrhoea and some may become jaundiced. A small proportion with acute infection (1%) will develop fulminant hepatitis which in some cases is fatal.

Following acute infection, the large majority of adult patients will recover from the infection fully and uneventfully. **Around 5-10% will be unable to mount an immune response to the virus and will develop chronic hepatitis B infection.** Chronic infection is identified by persistence of HBsAg in the serum for six months or longer. Of those patients who show chronic infection, around 20% (10-30%) will have active infection characterised by high viral turnover and inflammation in the liver. These patients are at high risk of developing cirrhosis of the liver and hepatocellular carcinoma (Fig.1).

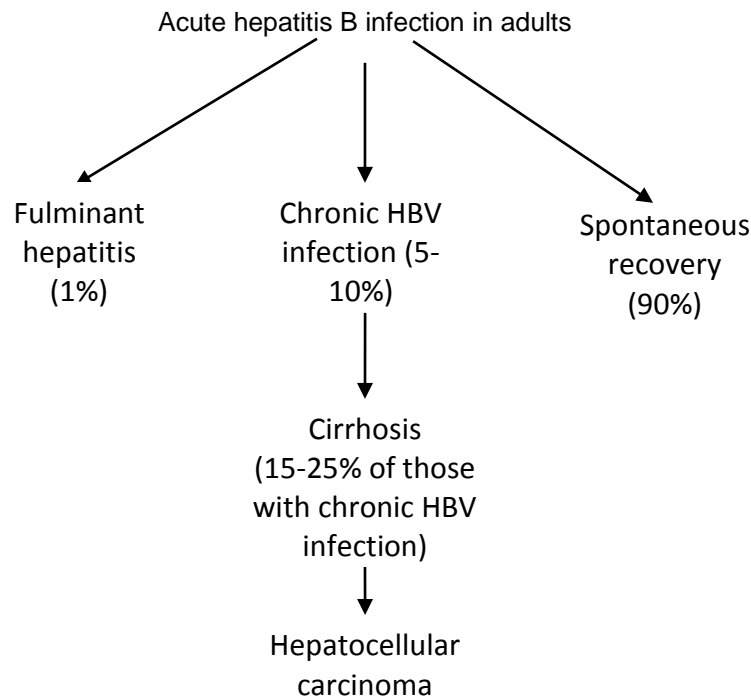


Figure 1. The natural history of HBV infection in adults

Screening for hepatitis B infection

NICE guidance (NICE 2013) recommends screening of members of the following groups for HBV infection:

- People born in a high-risk country (includes Africa, Asia, the Caribbean, Central and South America, Eastern and Southern Europe, the Middle East);;
- Babies born to mothers with HBV infection;
- People who are historical or current drug injectors;
- Men who have sex with men;
- People with multiple sexual partners;
- Individuals with hepatitis C or HIV;
- Looked after children;
- Prisoners;
- Close contacts of someone with HBV infection.

Typically blood samples for testing are obtained by venepuncture, and requests for hepatitis B serology leads to a panel of test results which may differ from laboratory to laboratory.

Sampling options where venous access is difficult include dry blood spot testing (DBST) where dried blood spots from a finger prick sample of blood on filter paper or card can be used.

Hepatitis B pre- and post-test discussion

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

Specific areas to consider before a patient has an HBV test may include:

- Ensure the patient is fully 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 HBV infection;
- Reassure the patient that results will be managed confidentially;

- Discuss alternatives for testing, especially if venous access may be a problem;
- Discuss the implications of a positive result: the need for 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, answer them 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 patient about 'window' periods and arrange retesting if necessary;
- Remind patient about at-risk behaviour and reinforce harm reduction advice.

When giving a positive 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 HBV 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;
- Encourage the patient to share the result with family members and other relevant contacts so they can be tested and immunised whenever this is appropriate;
- Discuss the next steps, which might include 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.

Interpreting HBV panel test results

If a sample of blood is sent for hepatitis B serology, the panel of tests that is reported may vary from laboratory to laboratory. Typical results will include:

HBsAg Hepatitis B surface antigen. The surface antigen is part of the virus particle itself and demonstrates presence of the virus in the blood. A positive HBsAg result means current acute or chronic infection that can be transmitted to others.

Anti-HBs or HBsAb Hepatitis B surface antibody. This is an antibody to the surface antigen. A positive result means someone has received hepatitis B vaccine or has recovered from hepatitis B infection. The person generally has lifelong immunity to HBV infection and cannot infect others.

Anti-HBc or HBcAb Hepatitis B core antibody. This is an antibody to the core antigen, part of the HBV virus particle. HBcAb becomes detectable early in an acute infection and generally remains positive lifelong. If positive it indicates past or current hepatitis B infection. Despite the fact that it is an antibody to the virus, the presence of HBcAb does not indicate immunity and the person may be infective to others.

Harm-reduction information in HBV infection

- Reducing the risk to self

The patient with HBV infection can reduce the risk of liver harm by avoiding excess alcohol, co-infection with HCV or HIV viruses and avoiding obesity. Those with HBV infection should be offered immunised against hepatitis A infection (PHE 2013) and fall within current eligibility criteria for an annual flu jab.

- Reducing the risk of transmission to others

The patient can reduce the risk of transmission of the virus to others by not sharing drug-injecting equipment including needles, syringes, spoons and filters, and not sharing razors or toothbrushes that might be contaminated with blood. Condoms should be worn to prevent sexual transmission.

The patient should be asked to discuss their infection with relevant contacts who can be offered testing and immunisation as needed.

Immunisation against hepatitis B

The Green Book recommends that the following groups of people be immunised against hepatitis B.

- Infants, as part of the routine childhood immunisation programme
- Individuals at high risk of exposure to the virus or complications of the virus (pre-exposure immunisation)
 - People who inject drugs
 - Individuals who change sexual partners frequently
 - Close family contacts of an individual with chronic hepatitis B infection
 - Families adopting children from countries with a high or intermediate prevalence of hepatitis B
 - Foster carers
 - Individuals receiving regular blood or blood products and their carers
 - Patients with chronic renal failure
 - People with chronic liver disease
 - Inmates of custodial institutions
 - Individuals in residential accommodation for those with learning difficulties
 - People travelling to or going to reside in areas of high or intermediate prevalence
 - Individuals at occupational risk
- Individuals who have already been exposed to the virus (post exposure immunisation)
 - Infants born to Hepatitis B infected mothers who should have their first vaccine within 24 hours of birth
 - Individuals exposed to hepatitis B infected blood or body fluids e.g. sexual partners of those with acute hepatitis B or those contaminated via needlestick injury, bite or contact with hepatitis B contaminated fluids to the eyes or mouth.

Primary immunisation typically consists of three doses of vaccine and for some regimens, a fourth booster dose is recommended.

The current childhood vaccination programme in England includes the pentavalent vaccine which protects against diphtheria, tetanus, pertussis, polio, and haemophilus influenza type b. Since autumn 2017 this has **been replaced by a six in one (hexavalent) vaccine which also protects against hepatitis B, and from this time all infants will routinely be offered hepatitis B vaccination.**

HBV treatment

After diagnosing current hepatitis B infection in a patient, primary care practitioners should encourage the patient to be referred to a hepatology specialist for further assessment. Monitoring of patients with hepatitis B is covered in NICE CG165 hepatitis B (chronic): diagnosis and management (2013).

The primary aim of antiviral treatment in chronic HBV infection is to contain the condition by preventing or reducing viral replication. This may delay or prevent disease progression and the development of liver complications including cirrhosis and hepatocellular carcinoma, improve survival and the quality of life, and may reduce the risk of transmission. It is possible that curative treatments become available with time.

Antiviral treatment is not indicated for all those with chronic HBV infection, and those who do not start treatment will be monitored regularly in specialist care for disease activity and for the early signs of progression of liver disease.

For those who are treated, response to therapy is monitored by virological testing and monitoring of liver function tests.

Available treatment agents include:

Interferon: pegylated interferon alfa-2a

Antiviral medicines: These include lamivudine, entecavir, and telbivudine (nucleoside analogues) and adefovir and tenofovir (nucleotide analogues).

Combinations of anti-viral therapy are not generally used in hepatitis B treatment.

Unwanted effects with these medicines can occur including gastrointestinal, mental health, haematological and thyroid disorders.

Hepatitis D

Hepatitis D virus (HDV) is a small, spherical viroid particle that can cause liver infection only when there is current hepatitis B infection. Infection with HDV occurs either at the same time as infection with HBV or it can be transmitted later to those who already have HBV infection. The modes of transmission for HDV are similar to those for HBV infection.

Super-added HDV infection can result in more severe liver disease than infection with HBV alone, and this includes fulminant liver failure in acute infections and faster progression to cirrhosis for those with chronic HBV infection.

More useful links can be found in the toolkit:

- NICE PH43 hepatitis B and C testing guidance (2013)
- NICE CG165 hepatitis B (chronic): diagnosis and management (2013)
- Hepatitis B: the Green Book chapter 18.
- WHO Hepatitis B fact sheet.
- 'Shooting Up: Infections among people who inject drugs in the UK'.
- EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection
- Clinical audit ideas: managing hepatitis B in primary care
- Personal learning reflection template
- Hepatitis B Patient leaflet (free download)
- Hepatitis B – web link for patients
- Hepatitis B positive

References

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

Guidance: Hepatitis B, in The Green Book, chapter 18. Gov.uk website