Executive summary of recommendations

Details of recommendations can be found in the main text at the pages indicated.

Epidemiology and natural history

C Patients with chronic hepatitis B virus infection and who are HBeAg negative should be checked for presence of hepatitis B virus DNA if their serum alanine aminotransferase is repeatedly or persistently above normal limits (pg 13).

Grade C, Level 2+

B Patients with chronic hepatitis B virus infection who are above 40 years of age should be followed up closely if they are still HBeAg positive or have chronic HBe-negative-hepatitis B. These patients should be actively evaluated for cirrhosis and be more readily considered for treatment of hepatitis B virus infection. Regular and frequent surveillance of hepatocellular carcinoma should be carried out in these patients (pg 14).

Grade B, Level 2++
Screening and vaccination of those at risk

C Hepatitis B vaccine should be given to protect children at birth or as soon as possible thereafter in regions where the prevalence of hepatitis B virus infection is high. Babies born to HBsAg-positive mothers are at high risk of developing chronic infection (pg 17).

Grade C, Level 2+

D Other high risk groups, including persons who come into contact with blood or blood products (e.g. laboratory staff, surgeons and dentists, hospital personnel, drug abusers) and individuals requiring repeated transfusions of blood or blood products, should also be vaccinated for hepatitis B (pg 17).

Grade D, Level 4

D The following individuals should be vaccinated for Hepatitis B:
- Sexually active individuals, especially those with multiple partners
- Close family and sexual contacts of subjects with chronic hepatitis B virus infection
- Individuals infected with human immunodeficiency virus (HIV)
- Travellers to hepatitis B endemic areas.

Grade D, Level 4

Screening prior to Hepatitis B vaccination

D The following groups of people should be screened prior to hepatitis B vaccination:
- Persons born in intermediate and high endemic areas (see Fig. 1 in pg 19 of main text)
- Young adults
- Health care workers
- Pregnant women
- Contacts of subjects with chronic hepatitis B virus infection (family, household and sexual contacts)
- Persons with multiple sexual partners/ history of sexually transmitted diseases
- Individuals with chronically elevated alanine aminotransferase (ALT) or aspartate aminotransferase (AST)
- Individuals infected with hepatitis C virus or human immunodeficiency virus (HIV)
• Men who have sex with men
• Subjects with high risk behaviours (IV drug users, sex workers)
• Immunocompromised subjects (dialysis patients, HIV-infected patients)
• Immigrants
• Prisoners

The following blood tests should be done as part of serologic screening before hepatitis B vaccination:

• HBsAg
• Anti-HBs
• Anti-HBc

Serological screening for hepatitis B surface antigen and antibody should be done within 6 months pre-vaccination for all except newborn babies.
Based on the results of an individual’s serological screening for HBs antigen and antibody, clinicians should then act according to the table below:

<table>
<thead>
<tr>
<th>HBsAg</th>
<th>Anti-HBs</th>
<th>Interpretation</th>
<th>Action to take</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non reactive</td>
<td>&lt; 10 IU/L</td>
<td>i) If an individual did not have hepatitis B vaccination before,</td>
<td>i) Administer hepatitis B vaccination</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Not immune to hepatitis B virus.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>ii) If an individual had hepatitis B vaccinations before</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>either:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>a) the antibody level has waned to less than 10 IU/L,</td>
<td>ii) Offer a booster dose of hepatitis B vaccination and check anti-HBs within 3 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>but the individual is still immune to the hepatitis B virus.</td>
<td>OR</td>
</tr>
<tr>
<td></td>
<td></td>
<td>b) the individual did not develop immunity against hepatitis B virus after the</td>
<td>Give them another course (3 injections) of hepatitis B vaccination &amp; recheck anti-HBs within 3 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>primary course of hepatitis B vaccination.</td>
<td>(to discuss options with patient)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NB *</td>
<td></td>
</tr>
</tbody>
</table>

| Non reactive | > 10 IU/L | Immune to hepatitis B.                                                        | Immunisation is not required.                                                 |

| Reactive    | < 10 IU/L | Presence of hepatitis B virus infection.                                       | Clinically assess the patient for liver disease.                             |
|            |          |                                                                                | To repeat the HBsAg test 6 months later.                                     |
|            |          |                                                                                | If HBsAg positive 2 times, 6 months apart, chronic hepatitis B infection confirmed. |

*Under rare circumstances, the emergence of hepatitis B surface mutant (‘s’ mutant) virus can be associated with the absence of HBsAg and a negative or low titre of anti-HBs antibody.

(Grande B, Level 2++)
D Babies born to HBsAg-positive mothers should be tested for seroconversion following the hepatitis B vaccination, preferably 3 months after completion of course (pg 22).

Grade D, Level 4

C For children not born to HBsAg-positive mothers, as well as adults, three doses of hepatitis B vaccine should be given at months 0, 1 and 6. After the primary 3-dose vaccine series, check anti-HBs within 3 months after the booster dose at month 6 (pg 22).

Grade C, Level 2+

If anti-HBs > 10 IU/L, the individual has developed immunity against hepatitis B virus.

C For individuals previously vaccinated for hepatitis B and with anti-HBs levels < 10 IU/L, consider repeat booster of hepatitis B vaccination or give a second course of hepatitis B vaccination before rechecking the anti-HBs antibody titre (pg 23).

Grade C, Level 2+

C For immuno-competent people:
• with low risk of acquiring hepatitis B and
• who have completed their hepatitis B vaccination and
• who had previously demonstrated immunity to hepatitis B virus after their vaccination, there is no need to check for immunity again or receive booster injections if their anti-HBs is < 10 IU/L later on. (pg 23)

Grade C, Level 2+

D Anti-HBc total should be checked if an otherwise Immunocompetent individual fails to seroconvert after 2 courses of hepatitis B vaccinations.

1) HBsAg negative, anti-HBs < 10 IU/L, anti-HBc positive

These individuals may have hepatitis B virus infection with low viral load and an undetectable level of HBsAg. Those who are tested positive for anti-HBc alone may be in the ‘window’ phase of acute hepatitis B infection or they may have chronic hepatitis B virus infection with low level viraemia. Refer them to gastroenterologists/hepatologists for further workup.
2) **HBsAg negative, anti-HBs < 10 IU/L, anti-HBc negative**
Consider repeat vaccination with pre-S vaccine or other 3rd generation vaccine, if available, especially if the individuals belong to the high-risk group. They should be advised against high risk behaviour, which may expose them to hepatitis B virus infections.

(pg 24) Grade D, Level 3

**GPP** Patients whose HBsAg is positive for the first time should be evaluated as they may be patients with undiagnosed chronic hepatitis B virus infection even if the clinical criteria may not have been met yet. The appropriate follow-up actions should then be taken:

1) **History taking**
   Ask for symptoms of liver disease, family history of chronic hepatitis B virus infection, any recent travel or high risk activity.

2) **Physical Examination**
   Examine the patients. Look for signs of liver disease e.g. stigmata of chronic liver disease, ascites, jaundice, etc.

3) **Investigation**
   Check blood for liver function test and alpha-fetoprotein level.

If either the physical examination or the blood test results are abnormal, refer to the gastroenterologist. Consider admitting the patient to the hospital through A&E or direct access, if acute hepatitis B infection is suspected (pg 26).

**GPP**

**Management of Chronic Hepatitis B Virus Infection**

**D** The following advice should be given to patients with chronic hepatitis B virus infection:
- Ensure that their sexual partners are vaccinated
- No sharing of toothbrushes and razors
- Cover open wounds
- No donation of body parts
- Clean blood spills with bleach/detergents
**Note: Hepatitis B virus transmission is not transmissible through:**
- Sharing of utensils, food or kissing as part of social greetings
- Participating in all activities including contact sports
- Social interaction with others (e.g. in schools, day care centres)

(1) For patients with HBsAg positive > 6 months and well-compensated liver disease, in association with:

(A) **HBeAg-positive Hepatitis B virus infection and:**
   
   i) Alanine aminotransferase (ALT) < Upper limit of normal (ULN): no pharmacotherapy needed. Monitor ALT at least 6 monthly and HBeAg at least 12 monthly.
   
   ii) ALT 1-2 X ULN: monitor ALT 3 to 6 monthly and HBeAg 6 monthly. Refer to specialist if persistent evidence of early deterioration of liver function or age > 40. Consider liver biopsy and treat if biopsy shows significant liver damage.
   
   iii) ALT > 2X ULN: repeat ALT and HBeAg within 1 to 3 months. Refer to specialist if persistent. Treat immediately upon evidence of hepatic decompensation.

(B) **HBeAg-negative Hepatitis B virus infection and:**
   
   i) ALT < ULN: Monitor ALT 3 months later. If still normal, monitor ALT every 6 to 12 monthly.
   
   ii) ALT 1-2X ULN: Monitor ALT 3 to 6 monthly. Refer to specialist if persistent, evidence of early deterioration of liver function or age > 40. If HBV DNA is > 2000 IU/ml, consider liver biopsy and treat if biopsy shows significant liver damage.
iii) ALT > 2X ULN: repeat ALT within 1 to 3 months. Refer to specialist if persistent. If HBV DNA > 2000 IU/ml, consider treatment if persistent.

2) For patients with decompensated hepatitis B virus–related cirrhosis:
Refer to gastroenterologist or hepatologist for management.

Grade D, Level 4

Surveillance of patients with chronic hepatitis B should be carried out regularly. The required frequency of surveillance for an individual will depend on his/her risk profile, which should be determined before the start of the surveillance programme (see below):

(A) Baseline assessment to stratify risk
- check serum ALT, AST, bilirubin, albumin, prothrombin time, alpha-fetoprotein, HBsAg, HBeAg, anti-HBe and hepatitis B virus DNA
- liver imaging

(B) Periodic reassessment is necessary
Frequency of surveillance is dependent on patients’ risk profile:

i) Low-risk group
6 monthly serum ALT and bilirubin assessment - if abnormal, hepatitis B virus DNA should be checked.

ii) Medium-risk group
4-6 monthly serum ALT and bilirubin assessment - if abnormal, hepatitis B virus DNA should be checked.

iii) High-risk group
2-4 monthly serum ALT, bilirubin assessment, hepatitis B virus DNA assessment, appropriate to each set of circumstances. If abnormal the specialist will have to decide on further appropriate management

GPP
Most patients in medium risk group and all patients in high risk group should be referred for management by a specialist (pg 33).

For patients who have average risk of developing hepatocellular carcinoma (HCC), six-monthly blood tests for alpha-fetoprotein level and annual ultrasonographic examination of the liver is recommended.

For patients with increased risk of HCC, such as patients with cirrhosis, frequency of blood tests and ultrasonographic examination can be increased (pg 34).

Grade B, Level 2++

Patients who have undergone treatment for hepatitis B within the last 6 months and developed serum ALT > ULN or patients who display evidence of hepatic decompensation should be referred to a specialist for further management immediately (pg 35).

Grade B, Level 2++

Patients can be considered for alternative class of therapeutic agents after they fail to respond to one class of drug.

• Patients should be actively screened for contraindications for use of interferon-alpha before they are considered for treatment with interferon-alpha as an alternative therapeutic agent

• Treatment with nucleoside/tide analogue indefinitely may be considered in patients who have persistently elevated serum ALT and evidence of active cirrhosis histologically when he/she has failed to respond to treatment with interferon-alpha previously.

These patients, however, should only be managed by specialists (pg 35).

Grade B, Level 2++

Patients with HIV or hepatitis C virus co-infection should be referred for management by specialists (pg 36).
Patients with chronic hepatitis B virus infection post-organ transplantation should be managed by specialists, even if the liver function test appears normal (pg 36).

Pregnant women with replicative hepatitis B virus infection should be monitored closely after the mid-trimester and immediately postpartum for acute exacerbation of chronic hepatitis B (pg 36).

Grade C, Level 2+