UK Standards for Microbiology Investigations

Hepatitis B Diagnostic Serology in the Immunocompetent (including Hepatitis B in Pregnancy)
Acknowledgments

UK Standards for Microbiology Investigations (SMIs) are developed under the auspices of Public Health England (PHE) working in partnership with the National Health Service (NHS), Public Health Wales and with the professional organisations whose logos are displayed below and listed on the website https://www.gov.uk/uk-standards-for-microbiology-investigations-smi-quality-and-consistency-in-clinical-laboratories. SMIs are developed, reviewed and revised by various working groups which are overseen by a steering committee (see https://www.gov.uk/government/groups/standards-for-microbiology-investigation-steering-committee).

The contributions of many individuals in clinical, specialist and reference laboratories who have provided information and comments during the development of this document are acknowledged. We are grateful to the Medical Editors for editing the medical content.

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Logos correct at time of publishing.
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Amendment table

Each SMI method has an individual record of amendments. The current amendments are listed on this page. The amendment history is available from standards@phe.gov.uk.

New or revised documents should be controlled within the laboratory in accordance with the local quality management system.

<table>
<thead>
<tr>
<th>Amendment No/Date.</th>
<th>10/dd.mm.yy &lt;tab+enter&gt;</th>
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</thead>
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</table>

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DRAFT - THIS DOCUMENT WAS CONSULTED ON BETWEEN 20 AUGUST - 17 SEPTEMBER 2015
UK Standards for Microbiology Investigations#: scope and purpose

Users of SMIs

- SMIs are primarily intended as a general resource for practising professionals operating in the field of laboratory medicine and infection specialties in the UK.
- SMIs provide clinicians with information about the available test repertoire and the standard of laboratory services they should expect for the investigation of infection in their patients, as well as providing information that aids the electronic ordering of appropriate tests.
- SMIs provide commissioners of healthcare services with the appropriateness and standard of microbiology investigations they should be seeking as part of the clinical and public health care package for their population.

Background to SMIs

SMIs comprise a collection of recommended algorithms and procedures covering all stages of the investigative process in microbiology from the pre-analytical (clinical syndrome) stage to the analytical (laboratory testing) and post analytical (result interpretation and reporting) stages.

Syndromic algorithms are supported by more detailed documents containing advice on the investigation of specific diseases and infections. Guidance notes cover the clinical background, differential diagnosis, and appropriate investigation of particular clinical conditions. Quality guidance notes describe laboratory processes which underpin quality, for example assay validation.

Standardisation of the diagnostic process through the application of SMIs helps to assure the equivalence of investigation strategies in different laboratories across the UK and is essential for public health surveillance, research and development activities.

Equal partnership working

SMIs are developed in equal partnership with PHE, NHS, Royal College of Pathologists and professional societies.

The list of participating societies may be found at https://www.gov.uk/uk-standards-for-microbiology-investigations-smi-quality-and-consistency-in-clinical-laboratories.

Inclusion of a logo in an SMI indicates participation of the society in equal partnership and support for the objectives and process of preparing SMIs. Nominees of professional societies are members of the Steering Committee and Working Groups which develop SMIs. The views of nominees cannot be rigorously representative of the members of their nominating organisations nor the corporate views of their organisations. Nominees act as a conduit for two way reporting and dialogue. Representative views are sought through the consultation process.

SMIs are developed, reviewed and updated through a wide consultation process.

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Microbiology is used as a generic term to include the two GMC-recognised specialties of Medical Microbiology (which includes Bacteriology, Mycology and Parasitology) and Medical Virology.

Virology | V 4 | Issue no: dzf+ | Issue date: dd.mm.yy <tab+enter> | Page: 5 of 25

UK Standards for Microbiology Investigations | Issued by the Standards Unit, Public Health England
Quality assurance

NICE has accredited the process used by the SMI Working Groups to produce SMIs. The accreditation is applicable to all guidance produced since October 2009. The process for the development of SMIs is certified to ISO 9001:2008.

SMIs represent a good standard of practice to which all clinical and public health microbiology laboratories in the UK are expected to work. SMIs are NICE accredited and represent neither minimum standards of practice nor the highest level of complex laboratory investigation possible. In using SMIs, laboratories should take account of local requirements and undertake additional investigations where appropriate. SMIs help laboratories to meet accreditation requirements by promoting high quality practices which are auditable. SMIs also provide a reference point for method development.

The performance of SMIs depends on competent staff and appropriate quality reagents and equipment. Laboratories should ensure that all commercial and in-house tests have been validated and shown to be fit for purpose. Laboratories should participate in external quality assessment schemes and undertake relevant internal quality control procedures.

Patient and public involvement

The SMI Working Groups are committed to patient and public involvement in the development of SMIs. By involving the public, health professionals, scientists and voluntary organisations the resulting SMI will be robust and meet the needs of the user. An opportunity is given to members of the public to contribute to consultations through our open access website.

Information governance and equality

PHE is a Caldicott compliant organisation. It seeks to take every possible precaution to prevent unauthorised disclosure of patient details and to ensure that patient-related records are kept under secure conditions.

The development of SMIs are subject to PHE Equality objectives https://www.gov.uk/government/organisations/public-health-england/about/equality-and-diversity. The SMI Working Groups are committed to achieving the equality objectives by effective consultation with members of the public, partners, stakeholders and specialist interest groups.

Legal statement

Whilst every care has been taken in the preparation of SMIs, PHE and any supporting organisation, shall, to the greatest extent possible under any applicable law, exclude liability for all losses, costs, claims, damages or expenses arising out of or connected with the use of an SMI or any information contained therein. If alterations are made to an SMI, it must be made clear where and by whom such changes have been made.

The evidence base and microbial taxonomy for the SMI is as complete as possible at the time of issue. Any omissions and new material will be considered at the next review. These standards can only be superseded by revisions of the standard, legislative action, or by NICE accredited guidance.

SMIs are Crown copyright which should be acknowledged where appropriate.
Scope of document

Type of specimen
Blood

Scope
This virology algorithm outlines laboratory testing for hepatitis B virus (HBV) infection, for diagnosis of acute infection and chronic infection, including in pregnant women.

Refer to S 1 - Acute infective hepatitis for further information regarding clinical presentations of acute infective hepatitis, and associated tests.

This SMI should be used in conjunction with other SMIs.

Introduction

Laboratory diagnosis
Testing for hepatitis B infection is based on detection of HBsAg in the first instance. HBsAg will be detectable in the blood if there is current hepatitis B infection. For many years very sensitive immunoassays have been available for this purpose including radioimmunoassay (RIA) and a range of enzyme immunoassays (EIA). Many tests now are carried out using EIA tests on automated analysers, for example where HBsAg bound by anti-HBs antibody on microparticles is detected by a chemiluminescent reaction. Mutations in the 'S' gene can lead to reduced sensitivity or failure to detect HBsAg, especially if monoclonal anti-HBs is used for both capture and probe in the immunoassay. Although the published specification for the minimum level of sensitivity for HBsAg detection in the UK National Blood Service is at present 0.2 IU/mL there is general acceptance that assays should detect 0.05 IU/mL HBsAg or less. Assays should be CE marked. Because of the important implications of a positive finding the initial HBsAg reactivity should be confirmed by a neutralisation test or by repeat HBsAg reactivity in a second assay, and a second sample tested as well. HBsAg appears about 2-4 weeks before the ALT rises. However, HBV DNA can be detected about 3-4 weeks earlier than surface antigen.

A reactive anti-HBc IgM is consistent with recent HBV infection. However, interpretation should take into consideration results of other assays and the clinical picture. It must be clearly identified that this is not a “flare” during a chronic infection. Anti IgG core avidity is often used to differentiate between the two.

Negative results should be interpreted in light of the anti-hepatitis B core antibody (anti-HBc) result and the onset date of illness.

Detection of HBsAg by immunoassay at a single time point does not give information on the duration of infection. Its presence in samples 6 months or more apart defines chronic hepatitis B infection. Presence of detectable IgM antibody to hepatitis B core antigen (anti-HBc IgM) is used to help determine whether the HBsAg is associated with an acute or a chronic infection. In acute hepatitis B anti-HBc IgM appears in high levels in both symptomatic and asymptomatic individuals and is commonly said to be detectable for about 3-6 months. However, this antibody is a marker of HBV activity and its appearance and disappearance are quite variable. In a study using RIA anti-HBc IgM appeared in most within a week of symptoms, but was delayed to 2 weeks in
about 8%\textsuperscript{5}. Median duration of anti-HBc IgM was 32 weeks, with a range from two weeks to over two years; 14% had detectable IgM for over one year\textsuperscript{3}. Thus anti-HBc IgM results need to be interpreted with caution and with the clinical and biochemical information. Because it can be found in chronic hepatitis B with active viral replication, quantitation of anti-HBc IgM is also important in differentiating acute and chronic hepatitis B with high levels of anti-HBc IgM correlating with acute infection rather than chronic infection with exacerbation of symptoms\textsuperscript{6,7}. HBsAg levels tend to be higher in acute infection, and in early infection determination of anti-HBc avidity might also be a useful test\textsuperscript{7,8}.

Antibody to hepatitis B core antigen (anti-HBc) was recognised as persisting after hepatitis B infection by counterimmunoelectrophoresis and, as it persists generally for life is used as a marker of infection with HBV at some time\textsuperscript{9,10}. Most commercial tests are total antibody tests detecting both IgG and IgM, most are competitive assays. It is a useful test for validating a positive HBsAg result, and is found together with anti-HBs antibody in past resolved infections. Isolated anti-HBc found in the absence of HBsAg or any other serological markers of hepatitis B infection is difficult to interpret.

Detection of circulating HBeAg, a soluble derivative of the core ORF product, occurs when virus is actively replicating in the liver, so it is associated with high levels of HBV DNA in the blood and high potential infectivity. Its association with progressive liver disease varies with the stage in the natural history, so both HBeAg and anti-HBe antibody are monitored to follow the stage of infection and response to treatment. Both HBeAg and anti-HBe antibody are detected using enzyme immunoasays, with anti-HBe tests usually in a competitive format\textsuperscript{4}. Both HBeAg and anti-HBe may coexist\textsuperscript{11}.

Anti-HBs assays use HBsAg bound to solid phase to capture the antibody. Automated assays usually use recombinant antigens as capture antigen and for the labelled probe\textsuperscript{4}. In immunocompromised patients anti-HBs may be used to monitor post-vaccination immunity. An initial level of 10 IU/mL is recognised as conferring protection against HBV\textsuperscript{12}. Contacts who are HBAg negative, but that are high risk and who are anti-HBc positive should not be vaccinated. Anti-HBs is also used as a marker of resolution of infection (absent HBsAg, positive anti-HBc) but HBsAg and anti-HBs can coexist, particularly where the subtype specificities are different, so the presence of anti-HBs cannot exclude chronic hepatitis B infection\textsuperscript{11,13}.

Hepatitis B DNA is measured by PCR (both in house and commercial assays are available) or by other amplification assays such as branched chain DNA. Assays may not be directly comparable and vary in performance and dynamic range. Detection of HBV DNA is useful in early diagnosis in at risk individuals before HBsAg appears, and for monitoring viral load during therapy. HBV DNA should also be tested for in those not yet on therapy, and following therapy, yearly to monitor. The best endpoint for management is to reach a level of HBV DNA which is undetectable by current methods with a sensitivity of 10-15 IU/mL\textsuperscript{14,15}. HBV DNA is also a significant prognostic marker for cirrhosis.

In the UK, guidance for hepatitis B infected health care workers (HCW) is available\textsuperscript{16-18}. HCWs who are HBsAg positive and HBeAg negative must be tested for levels of HBV DNA before carrying out blood exposure prone procedures. A level below 10\textsuperscript{3} genome equivalents/mL is acceptable\textsuperscript{16,18}. If the pre-treatment viral load is between 10\textsuperscript{3} and 10\textsuperscript{5} geq/mL, the HCW may work whilst taking antiviral therapy provided the HBV DNA level is supressed to below 10\textsuperscript{3} geq/mL. If baseline viral load is above 10\textsuperscript{5}
geng/mL the HCW should be ineligible to perform exposure procedures\(^{18}\). All infected HCWs performing exposure prone procedures while on therapy should have their HBV DNA levels monitored regularly at 3-monthly intervals (on two blood samples, one month apart), followed by yearly monitoring\(^{18}\).

Assays for detecting ccc DNA in blood have been developed but as yet their clinical relevance is uncertain\(^{19}\).

**Public health management**

Positive anti-HBc IgM results consistent with recent HBV should be reported urgently (eg by telephone) to the local public health team to facilitate timely public health interventions.

For information regarding notification to PHE (or equivalent in the devolved administrations) refer to page 23.


**Definitions**

For all antigen, antibody and NAAT results the following definitions apply:

- **Reactive** – Initial internal-stage positive result pending confirmation.
- **Not reactive** - Initial internal-stage negative result.
- **Detected** – Report-stage confirmed reactive result.
- **Not detected** – Report-stage not reactive result.
Hepatitis B Surface Antigen (HBsAg) confirmation by neutralisation

HBsAg assay
HBsAg minimum target sensitivity level of 0.05iu/mL

Not reactive

REPORT: “HBsAg not detected”

Reactive

Consider Repeat if weakly reactive

Neutralisation from original sample

Reactive

REPORT: “HBsAg detected. Confirmed by neutralisation. Please send a further sample for confirmation”

Not reactive

REPORT: “HBsAg not detected. Repeat or investigate discrepancy”

Test other markers

Not confirmed

REPORT: “HBsAg reactive, but not confirmed by neutralisation. Further tests to follow. Please repeat.”

Confirmed

Test other markers
Footnotes relating to Hepatitis B Surface Antigen (HBsAg) confirmation by neutralisation

a) It is recommended that only those assays which are able to detect immune / vaccine escape variants should be used.

b) Low level HBsAg might not neutralise. Very high HBsAg also might not neutralise unless diluted. Haemolysed samples (eg cadaver samples) are prone to give non-neutralisable false reactive results. An alternative surface antigen is recommended.
Hepatitis B Virus Serology – HBsAg confirmation by alternative assay

HBsAg assay \(^{a,b}\)

- HBsAg minimum target sensitivity level of 0.05 IU/mL

**Not reactive**

- REPORT: HBsAg not detected

**Reactive**

-Confirmatory HBsAg test from original sample using alternative assay of at least equivalent sensitivity

**Not reactive**

- Repeat 1st assay from original sample \(^{c}\) (if available)

**Both tests not reactive**

- REPORT: HBsAg not detected

**1st test reactive, 2nd test not reactive**

- Anti-HBc (IgG/total) test

**Anti-HBc not reactive**

- REPORT: HBsAg equivocal, Anti-HBc negative. Likely to be non specific surface antigen reactivity. Request another sample.

**Anti-HBc reactive**

- REPORT: HBsAg equivocal, Anti-HBc reactive. Further test results to follow. Please send another sample.

Consider testing other markers
Footnotes relating to Hepatitis B Virus Serology – HBsAg confirmation by alternative assay

a) It is recommended that only those assays which are able to detect immune/vaccine escape variants should be used.
b) Haemolysed samples (eg cadaver samples) are prone to give false reactive results.
c) Consider carrying out HBV DNA PCR if early hepatitis B is likely due to risk factors and raised LFTs with an appropriate pattern are observed. Consider anti-HBe antigen test.
**Hepatitis B Surface Antigen confirmed reactive**

- **Anti-HBc total**
  - Reactive
    - Core IgM
      - Reactive
        - Consider report: Consistent with recent Hepatitis B infection. See Table
        - Perform HBeAg/Anti HBe
          - For interpretation: see Table
          - Report urgently to the public health team
      - Not reactive
        - Core IgM
          - Reactive
            - Consider report: Consistent with early Hepatitis B infection.
            - Perform HBeAg/Anti HBe
              - For interpretation: see Table
            - Refer to hepatitis service. Report with comment footnote e
        - Not reactive
          - Consider HBV DNA on this or another sample and investigate vaccination history
          - Perform HBeAg/Anti HBe
            - For interpretation: see Table
            - Report urgently to the public health team and consider NAAT test

- Not reactive
  - Core IgM
    - Not reactive
Footnotes relating to Hepatitis B Surface Antigen confirmed reactive

a) All newly diagnosed patients with chronic hepatitis should be referred to a hepatologist. Quantitative hepatitis B surface antigen may be useful for identifying recent infection.

b) When interpreting anti-HBc reactivity consider the possibility of false reactivity, especially if low level reactivity is observed. Response to HBV vaccine may also help to differentiate true from false reactivity\textsuperscript{20}.

c) Hepatitis delta virus (HDV) testing should be done in all HBsAg positives at presentation of chronic HBV infection and during any clinical flares or during acute infection, especially if complicated by acute liver failure\textsuperscript{21}.

d) HIV and hepatitis C testing should be carried out if hepatitis testing is positive\textsuperscript{21}. It is good practice to test for HIV\textsuperscript{21}.

e) Refer to hepatitis service. Test and vaccinate sexual and household contacts as per guidelines www.dh.gov.uk/greenbook.
Hepatitis B reporting for immunocompetent individuals

There are other combinations of results (equivocal HBsAg reactive HBeAg is one) which have not been tabled but which do occur and require individual comments based upon profile and clinical setting, along with a further sample.

<table>
<thead>
<tr>
<th>HBs Ag</th>
<th>Anti HBc (total)</th>
<th>HBc IgM</th>
<th>HBe Ag</th>
<th>Anti HBe</th>
<th>Anti HBs</th>
<th>Hep B DNA</th>
<th>Suggested wording of report comment (see footnotes for further information and actions)</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Not reactive</td>
<td>Not reactive</td>
<td>Not tested</td>
<td>Not tested</td>
<td>Not reactive or Not tested</td>
<td>Not tested</td>
<td>No evidence of current or past hepatitis B infection. iv</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Not reactive</td>
<td>Reactive</td>
<td>Not tested</td>
<td>Not tested</td>
<td>Reactive</td>
<td>Not tested</td>
<td>Consistent with past hepatitis B infection. v</td>
<td></td>
</tr>
<tr>
<td>3 iv, vi, vii</td>
<td>Not reactive</td>
<td>Reactive</td>
<td>Not tested</td>
<td>Not tested</td>
<td>Not reactive</td>
<td>Not tested</td>
<td>Consistent with probable past hepatitis B infection. v</td>
<td>Consider the possibility of false anti-HBc. Consider anti-HBc IgM testing to exclude relatively recent resolving infection.</td>
</tr>
<tr>
<td>4</td>
<td>Not reactive</td>
<td>Not reactive</td>
<td>Not tested</td>
<td>Not tested</td>
<td>Reactive</td>
<td>Not tested</td>
<td>No evidence of current or past infection with hepatitis B. Anti HBs is compatible with a vaccine response.</td>
<td></td>
</tr>
<tr>
<td>5 iv, vii</td>
<td>Not reactive</td>
<td>Reactive</td>
<td>Reactive</td>
<td>Not reactive or Reactive</td>
<td>Not reactive or Low Reactive</td>
<td>Not tested</td>
<td>Suggests relatively recent resolving infection with hepatitis B. Please send a repeat sample to confirm.</td>
<td>Is there a history of infection or recent jaundice?</td>
</tr>
<tr>
<td></td>
<td>HBs Ag</td>
<td>Anti HBc (total)</td>
<td>HBc IgM</td>
<td>HBe Ag</td>
<td>Anti HBe</td>
<td>Anti HBs</td>
<td>Hep B DNA</td>
<td>Suggested wording of report comment (see footnotes for further information and actions)</td>
</tr>
<tr>
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</tr>
<tr>
<td>6(^{viii})</td>
<td>Reactive</td>
<td>Not reactive</td>
<td>Not reactive</td>
<td>Not reactive</td>
<td>Not reactive</td>
<td>Not reactive</td>
<td>Detected</td>
<td>Indicates early acute infection with hepatitis B. Please repeat testing to confirm and notify public health team urgently(^{ix}).</td>
</tr>
<tr>
<td>7</td>
<td>Reactive</td>
<td>Not reactive</td>
<td>Not tested</td>
<td>Not tested</td>
<td>Not reactive</td>
<td>Not tested</td>
<td></td>
<td>Has this patient been recently immunised? The HBsAg in vaccine can be detectable for about one week after vaccination(^{22}).</td>
</tr>
<tr>
<td>8</td>
<td>Reactive</td>
<td>Not reactive</td>
<td>Not reactive</td>
<td>Reactive</td>
<td>Not reactive</td>
<td>Not reactive</td>
<td>Detected</td>
<td>Indicates early acute infection with hepatitis B. Send an immediate repeat to confirm and send another sample in 6 months to determine whether the chronic state has been reached or resolution has occurred. Notify Public Health team urgently.</td>
</tr>
<tr>
<td>9</td>
<td>Reactive</td>
<td>Reactive</td>
<td>Reactive</td>
<td>Reactive</td>
<td>Not reactive</td>
<td>Not reactive</td>
<td>Not tested</td>
<td>Indicates recent infection with hepatitis B(^{ix}). Immediate repeat and send another sample in 3-6 months to check for resolution.</td>
</tr>
</tbody>
</table>
## Hepatitis B Diagnostic Serology in the Immunocompetent (including Hepatitis B in Pregnancy)

<table>
<thead>
<tr>
<th>HBs Ag</th>
<th>Anti HBc (total)</th>
<th>HBe Ag</th>
<th>Anti HBe</th>
<th>Anti HBs</th>
<th>Hep B DNA</th>
<th>Suggested wording of report comment (see footnotes for further information and actions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reactive</td>
<td>Reactive</td>
<td>Reactive</td>
<td>Reactive or Not reactive</td>
<td>Not reactive or Reactive</td>
<td>Detected</td>
<td>Suggests active chronic hepatitis B or a flare of hepatitis in chronic hepatitis B, but recent acute infection cannot be excluded. Immediate repeat and send another sample in 3-6 months to check for resolution. Interpretation depends on anti-HBc IgM level.</td>
</tr>
<tr>
<td>Reactive</td>
<td>Reactive</td>
<td>Reactive</td>
<td>Not reactive</td>
<td>Not reactive or Low Reactive</td>
<td>Detected</td>
<td>Consistent with chronic HBeAg positive hepatitis B. Immediate repeat and send another sample in 3-6 months to confirm chronic infection. Refer to hepatitis service. Test and vaccinate sexual and household contacts as per guidelines <a href="http://www.dh.gov.uk/greenbook">www.dh.gov.uk/greenbook</a>.</td>
</tr>
<tr>
<td>Reactive</td>
<td>Reactive</td>
<td>Reactive</td>
<td>Not reactive</td>
<td>Not reactive or Low Reactive</td>
<td>Not detected or Detected</td>
<td>Consistent with anti-HBe positive chronic hepatitis B. Please send another sample in 3-6 months to confirm chronic infection. Refer to hepatitis service. Test and vaccinate sexual and household contacts as per guidelines <a href="http://www.dh.gov.uk/greenbook">www.dh.gov.uk/greenbook</a>.</td>
</tr>
<tr>
<td>Reactive</td>
<td>Reactive</td>
<td>Reactive</td>
<td>Not reactive</td>
<td>Not reactive or Low Reactive</td>
<td>Detected</td>
<td>Indicates chronic hepatitis B, at present without detectable HBe markers. Please send another sample in 3-6 months to confirm chronic infection. Refer to hepatitis service. Test and vaccinate sexual and household contacts as per guidelines <a href="http://www.dh.gov.uk/greenbook">www.dh.gov.uk/greenbook</a>.</td>
</tr>
</tbody>
</table>
### Hepatitis B Diagnostic Serology in the Immunocompetent (including Hepatitis B in Pregnancy)

<table>
<thead>
<tr>
<th></th>
<th>HBs Ag</th>
<th>Anti HBc (total)</th>
<th>HBc IgM</th>
<th>HBe Ag</th>
<th>Anti HBe</th>
<th>Anti HBs</th>
<th>Hep B DNA</th>
<th>Suggested wording of report comment (see footnotes for further information and actions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>14</td>
<td>Reactive</td>
<td>Reactive</td>
<td>Not reactive</td>
<td>Reactive</td>
<td>Reactive</td>
<td>Not reactive or Low Reactive</td>
<td>Detected</td>
<td>Evidence of hepatitis B infection though not of recent onset. The HBe marker pattern is unusual. Please send a repeat sample in 3-6 months to look for changing HBe status. Refer to hepatitis service. Test and vaccinate sexual and household contacts as per guidelines <a href="http://www.dh.gov.uk/greenbook">www.dh.gov.uk/greenbook</a>.</td>
</tr>
</tbody>
</table>

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*Note: DRAFT - THIS DOCUMENT WAS CONSULTED ON BETWEEN 20 AUGUST - 17 SEPTEMBER 2015*
Footnotes relating to the report table for Hepatitis B for immunocompetent individuals

i. HBeAg positive samples are strongly associated with high infectivity unless HBV replication is being suppressed by antiviral therapy.

ii. Anti-HBe positive patients often have low infectivity, but a proportion has precore mutant virus infection with high HBV DNA levels.

iii. HBV DNA PCR is widely available in virology specialist centres and can be used to evaluate the viral load. This has been shown to have prognostic value, independent of HBe status in the evaluation risk of cirrhosis and development of hepatocellular carcinoma in patients with chronic infection. It is also useful to monitor antiviral therapy.

iv. In clinical scenario of recent acute liver failure (fulminant hepatitis) HBsAg may be negative due to the pronounced immune response and rapid viral clearance of HBV; total anti-HBc and anti-HBc IgM may then be the only positive serological markers.

v. Repeat testing for hepatitis B should not be necessary unless the patient becomes immunocompromised.

vi. It is advisable to confirm isolated anti-HBc positive results with a second assay, as isolated anti-HBc sometimes represents false reactivity.

vii. Hepatitis B may reactivate in patients who are immunocompromised.

viii. The detection of HBsAg without evidence of anti-HBc and anti-HBc IgM is associated with early acute infection before antibody production. HBV DNA testing is essential to confirm this. Request repeat sample to confirm identity of patient and to check for confirmation of acute Hepatitis B virus infection by development of other markers, these can take many weeks to evolve and may not be accompanied by symptoms of acute hepatitis.

ix. Please screen and immunise sexual/household contact.

General comments

Acute infectious hepatitis is a notifiable disease. All HBsAg positive patients should be reported promptly: see Notification and Referral section.

The testing algorithm wording of reports assumes this is the first sample received from this patient. Later samples will require modified report comments.

Anti-HBc IgM may be detectable in recent acute hepatitis B or during a flare of viral replication and may be seen in chronic infection with hepatitis B. In determining whether a case is likely to be acute hepatitis B the clinical details as well as any earlier results on record and the level of anti-HBc IgM are useful.

- Acute cases are more likely to have levels over 200 Paul Ehrlich Units/mL.
  Levels between 50 and 200 are probably acute

- Levels below 50 are probably a flare of chronic infection, but may be due to late acute infection

Note: Interpretative comments should be provided on reports: see CPA Standards for the Medical Laboratory (2007) Standard G5.
Patients considered to be at an increased risk of HBV exposure or having chronic liver disease should be tested for anti-HBc when found to be HBsAg negative.

In pregnant patients testing HBsAg positive, additional comments should be added to guide immunisation and follow-up of the baby after birth. See below for further details.

**Hepatitis B in pregnancy**

- The general testing strategies and reporting and notification patterns for hepatitis B infected pregnant women are identical to those for other individuals.
- Additional reporting to specialist midwives or similar healthcare workers responsible for the care of pregnant women and their babies should be in place locally.
- Vertical transmission of hepatitis B to the neonate is a substantial risk and prophylaxis for the neonate should be arranged well before delivery wherever possible. Local arrangements may vary.
- The guidance promulgated by the DH in Chapter 18 of ‘Immunisation against infectious disease’ should be followed taking particular note of online Chapter updates.
- Reference should also be made to DH Guidance ‘Screening for infectious diseases in pregnancy: Standards to support the UK antenatal screening programme’.

All children born to mothers infected with HBV should be followed up to ensure completion of immunisation in accordance with national guidance. Testing for HBsAg at 1 year is currently recommended.
Notification to PHE\textsuperscript{23,24} or equivalent in the devolved administrations\textsuperscript{25-28}

The Health Protection (Notification) regulations 2010 require diagnostic laboratories to notify Public Health England (PHE) when they identify the causative agents that are listed in Schedule 2 of the Regulations. Notifications must be provided in writing, on paper or electronically, within seven days. Urgent cases should be notified orally and as soon as possible, recommended within 24 hours. These should be followed up by written notification within seven days. For the purposes of the Notification Regulations, the recipient of laboratory notifications is the local PHE Health Protection Team. If a case has already been notified by a registered medical practitioner, the diagnostic laboratory is still required to notify the case if they identify any evidence of an infection caused by a notifiable causative agent.

Notification under the Health Protection (Notification) Regulations 2010 does not replace voluntary reporting to PHE. The vast majority of NHS laboratories voluntarily report a wide range of laboratory diagnoses of causative agents to PHE and many PHE Health Protection Teams have agreements with local laboratories for urgent reporting of some infections. This should continue.

Note: The Health Protection Legislation Guidance (2010) includes reporting of Human Immunodeficiency Virus (HIV) & Sexually Transmitted Infections (STIs), Healthcare Associated Infections (HCAIs) and Creutzfeldt–Jakob disease (CJD) under ‘Notification Duties of Registered Medical Practitioners’: it is not noted under ‘Notification Duties of Diagnostic Laboratories’.

https://www.gov.uk/government/organisations/public-health-england/about/our-governance#health-protection-regulations-2010

Other arrangements exist in Scotland\textsuperscript{25,26}, Wales\textsuperscript{27} and Northern Ireland\textsuperscript{28}.
References


