Hepatitis B serology

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This article forms part of our 'Tests and results' series for 2012, which aims to provide information about common tests that general practitioners order regularly. It considers areas such as indications, what to tell the patient, what the test can and cannot tell you, and interpretation of results.

Keywords
hepatitis B; serologic tests

The diagnosis of hepatitis B virus (HBV) infection is established through serological testing. The diagnostic panel for hepatitis B serology – allowing determination of susceptibility, active infection, or immunity through vaccination or past infection – includes testing for:

- hepatitis B surface antigen (HBsAg)
- hepatitis B surface antibody (anti-HBs)
- hepatitis B core antibody (anti-HBc)

(*Table 1*).

What are the indications for testing?

Most people living with chronic hepatitis B (CHB) in Australia were infected at birth or in early childhood, and are from two priority populations: people born overseas in high HBV prevalence areas (especially the Asia Pacific region and sub-Saharan Africa), and Aboriginal and Torres Strait Islander people. One-third of the estimated 170 000 Australians living with CHB[1] remain undiagnosed, facilitating poor outcomes. Primary liver cancer, mostly attributable to chronic viral hepatitis, is one of the fastest increasing causes of cancer death in Australia.[2] Therefore opportunistic testing of all those at risk, particularly from these two priority populations, is essential in preventing these outcomes. Other patients whose HBV status should be determined include:

- pregnant women, due to the need to intervene to prevent vertical transmission
- adults at increased risk of transmission, including sexual and household contacts and family members of people with HBV, men who have sex with men, people who inject drugs, sex workers and haemodialysis patients
- people living with hepatitis C or human immunodeficiency virus (HIV) infection due to increased risk factors, and also the presence of co-infection alters prognosis and treatment
- patients about to commence chemotherapy or immunosuppressive therapy, as HBsAg positive patients may develop a life threatening flare of HBV when undergoing treatment
- people with elevated alanine aminotransferase/asparate aminotransferase (ALT/AST) of unknown aetiology.

When is it not recommended?

There are no contraindications for serologic testing for HBV, although given the potential impact (medical, psychological and social) of the result on individuals and their family/contacts, testing should be conducted within the context of appropriate informed consent.

Where does it fit in a diagnostic approach?

The presence of HBsAg indicates active HBV infection. The reason for requesting all three serological tests – HBsAg, anti-HBs and anti-HBc – in a patient at risk of HBV infection is that systematic interpretation of these results allows categorisation of most patients by their hepatitis B status, be they susceptible, immune through vaccination or resolved natural infection, or chronically infected with HBV. This avoids missed diagnoses, recalling patients or adding tests, and unnecessary vaccination (*Table 1*).

The systematic interpretation of HBV serology results is discussed below.

What should I tell my patient?

Gaining informed consent before testing is essential and needs to be conducted in a culturally appropriate

Table 1. Serological tests that constitute the diagnostic panel for HBV		
HBsAg	Hepatitis B surface antigen	Active infection (acute or chronic)
Anti-HBs	Hepatitis B surface antibody	Immunity (vaccination or infection)
Anti-HBc	Hepatitis B core antibody	Infection (past or current)

and safe manner. Particular considerations should be made with regard to a patient's cultural beliefs and practices, and behaviour and language including assessing the need for an interpreter. The patient needs to be equipped for informed consent by understanding:

- the reason for testing and risk assessment
- confidentiality and privacy issues around testing
- the natural history and transmission of information (including explanation of high prevalence areas and mother-to-child transmission, if appropriate)
- time taken for results to become available and the need to return for results
- implications of a positive and negative result.

Conveying a test result also needs to be conducted in a culturally appropriate and safe manner. Results need to be given promptly and in person where privacy is assured. If the result is positive, the immediate needs of the patient need to be addressed, such as counselling, follow up appointments and referral if needed. It is important to avoid information overload and it is often useful to provide written material (taking language and literacy levels into account) and details of available support services. The importance of ongoing monitoring and the availability of treatment should be made clear, as should the opportunity for testing and vaccination of household contacts and/or family members who may be at risk.

There is no special timing of serologic testing. However, it is important to note that HBsAg (the first marker of HBV infection to become positive following infection) is usually undetectable until an average of 4 weeks after infection. Chronic HBV infection is defined as the presence of HBsAg for more than 6 months.

When required, serological confirmation of immunity following vaccination should be undertaken at least 1 month after vaccination is completed.

What does it involve?

The actual testing is via a blood test, with no special preparation required.

Hepatitis serology tests are eligible for Medicare rebate. However, to be able to order all three diagnostic tests (HBsAg, anti-HBs, and anti-HBc) simultaneously and retain Medicare eligibility, the requesting doctor should write '? chronic hepatitis B', or similar clinical justification for testing on the request slip.

Some doctors are concerned that testing patients from priority populations (such as people born in medium-high prevalence areas such as the Asia Pacific region or sub-Saharan Africa; or Aboriginal and Torres Strait Islander people) falls foul of the 'screening' provisions of the Medicare Benefits Schedule. This is not the case – identifying a person at particular risk of a health condition and then testing for that condition (in this case, CHB in someone from an endemic population) constitutes routine clinical care.

How does the test work?

Serologic testing for HBV infection, like much modern serology, relies on enzyme immunoassay (EIA) techniques for the detection of antigens and antibodies in patient serum. This typically involves incubating patient serum in the presence of reagents within wells coated with antigens or antibodies, which will specifically react with those being tested for.

Modern hepatitis B serology techniques are highly sensitive and specific.

What do the results mean?

Table 2 outlines interpretation of the HBV serology panel. *Table 3* provides an example of test results.

The reporting of thresholds in anti-HBs titre (10–100 and >100 mIU/L) can be confusing. Any immunocompetent patient who has completed a course of vaccination against HBV administered according to an approved schedule is considered immune as long as their anti-HBs titre has ever been measured as being >10 mIU/mL.

What won't the results tell you?

The diagnostic panel for HBV does not itself differentiate between acute and chronic HBV infection – this requires further clinical and laboratory information, including anti-HBc IgM. Discussion with the laboratory or a specialist is advisable if there is uncertainty.

What are the next steps if there is active infection?

If the pattern of HBV serology indicates active infection (HBsAg positive, anti-HBc positive, anti-HBs negative – *Table 2*), a number of steps are required, including:

- conveying the test result and discussing what this means and what happens next with the patient
- notification by the pathology laboratory (and by the treating doctor in many jurisdictions) to the relevant state or territory health department
- testing of household and sexual contacts (and vaccination if they are susceptible – often funded, see below)
- postdiagnosis work-up of patients with CHB.

The approach to further testing of a person diagnosed with HBV includes determination of the

Table 2. Interpretation of HBV serology[3]		
HBsAg Anti-HBc Anti-HBs	Negative Negative Negative	Susceptible (consider vaccination)
HBsAg Anti-HBc Anti-HBs	Negative Positive Positive	Resolved HBV infection
HBsAg Anti-HBc Anti-HBs	Negative Negative Positive	Vaccinated
HBsAg Anti-HBc IgM anti-HBc* (high titre) Anti-HBs	Positive Positive Positive Negative	Acute HBV infection*
HBsAg Anti-HBc IgM anti-HBc* Anti-HBs	Positive Positive Negative Negative	Chronic HBV infection*
HBsAg Anti-HBc Anti-HBs	Negative Positive Negative	Various possibilities (see 'What if the result is inconclusive?')

* Anti-HBc IgM can also be present (usually at a lower titre) in a flare of CHB

phase of infection and therefore the likelihood of progressive disease and need for treatment; the presence of any complicating factors, and degree of liver disease already present. Such testing includes, but is not limited to:

- HBV DNA viral load (Medicare rebatable annually for patients with CHB)
- HBeAg/anti-HBe serology
- liver function tests.

Detailed discussion regarding the approach to a newly diagnosed patient is beyond the scope of this article. A website has been established to assist Australian doctors in this process and is available at www.hepbhelp.org.au.

All patients with CHB require regular monitoring – at least annually – for disease activity, complications and the need for treatment. It is now known that there is no such thing as a 'healthy carrier' – all patients with CHB require active management to detect progressive liver disease and allow intervention to prevent complications including cirrhosis and liver cancer.

What are the next steps if there is no infection?

Negative serology (ie. susceptibility to HBV infection) should prompt vaccination against HBV, particularly those at higher risk of infection, or of severe illness in the context of acute infection. Refer to the Australian Immunisation Handbook website (see *Resources*).

Some patients will be eligible for free vaccine provided by jurisdictions. These can include household or sexual contacts of people living with CHB, people who inject drugs, and people living with HCV or HIV infection. Clinicians can refer to their state or territory health department for eligibility criteria.

What if the result is inconclusive?

One of the more confusing HBV serology results is when the patient is anti-HBs negative and HBsAg negative, but anti-HBc positive, known as 'isolated core antibody positive'. This can have a number of possible interpretations:

- distant resolved HBV infection – the most common interpretation, particularly in people born in HBV endemic areas
- false positive result – more common in people with a low risk of past HBV infection
- resolving acute HBV infection – in the period between HBsAg loss and detectable anti-HBs development
- passive transfer of maternal anti-HBc – in children up to 3 years of age
- occult HBV infection – a rare situation where active HBV infection occurs in the absence of detectable HBV infection. This can be determined by detecting HBV DNA in serum (NB: this test is not Medicare rebatable in the absence of HBsAg). This should be considered if there is clinical or biochemical evidence of active liver disease.

Table 3. An example test result

Your pathology		**Pathology report**
PATIENT:	Mr XX	DOCTOR: Dr XX
ADDRESS:	XXXX	
DOB:	XXXX	
HEPATITIS SEROLOGY (SERUM)		
HepB surface antigen		**: POSITIVE**
HBsAg confirmation test		**: POSITIVE**
HepB surface antibody		**: Negative**
HepB core total antibodies		**: POSITIVE**
HepB core IgM antibodies		**: Negative**
Comment:		
Consistent with chronic hepatitis B infection		
Vaccination of family/contacts advised (funded by state)		
This result has been notified to the Department of Health. NOTIFICATION BY REFERRING DOCTOR also required under state health regulations		
Tests requested	HBsAg anti-HBc anti-HBs	Collected: Reported:
Lab ref:		Dr ref:
	Authorised:	

Resources

- Australasian Society for HIV Medicine – www.ashm.org.au. Includes resources and guidance on the diagnosis of HBV infection and guidelines for the testing and management of HBV infection
- HepBHelp – www.hepbhelp.org.au. Includes guidelines on the initial work-up of a patient newly diagnosed with CHB, a public hepatitis clinic finder and links to further resources
- Gastroenterological Society of Australia – www.gesa.org.au. Includes resources, guidelines and algorithms for the management of HBV infection
- Australian Immunisation Handbook – www.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook–hepatitisb. For comprehensive discussion of Australian hepatitis B vaccination policy, priority groups, vaccination schedules and other related information.

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