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Hepatitis

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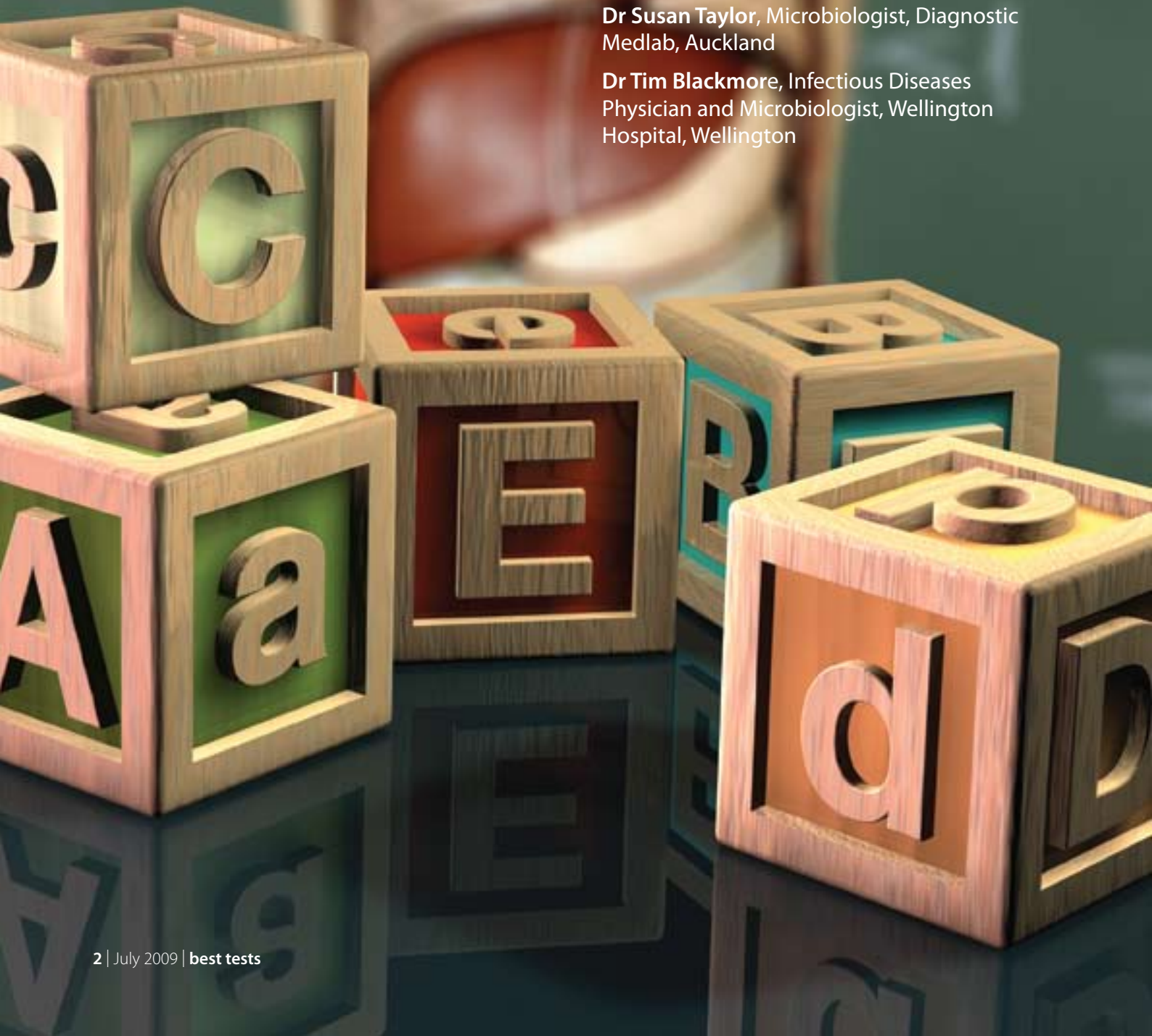


The purpose of this resource is to provide practical guidance for requesting hepatitis tests in common clinical situations.

This guide focuses on some of the situations GPs face in day-to-day practice and provides practical advice for initial testing.

In most situations, when further testing is required, this will be guided by specialist advice and the local laboratory.

Hepatitis is an inflammation of the liver commonly caused by a viral infection. The three main hepatitis viruses are referred to as types A, B, and C. Types D and E occur less commonly.

Symptoms of the different types of hepatitis are similar and can include one or more of the following:

- Fever
- Fatigue
- Nausea/vomiting/diarrhoea
- Abdominal pain
- Clay-coloured bowel motions/dark coloured urine
- Joint pain
- Jaundice

Not all people infected with the hepatitis viruses will display symptoms; children in particular are often asymptomatic.

Viral hepatitis infections

Hepatitis A

The number of cases of hepatitis A has been steadily decreasing since the mid 1990's with 42 cases of hepatitis A notified in 2007.[1] Increases are usually only seen when a small cluster of people are affected by an outbreak. Hepatitis A is a notifiable disease in New Zealand, this is important so that outbreak control measures may be taken, including the protection of contacts by immuno globulin and vaccine.

Hepatitis A is transmitted via ingestion of faecal matter, even in microscopic amounts. Over 50% of people contracting hepatitis A in 2007 had a history of recent overseas travel.

People most at risk for hepatitis A infection are:

- Travellers to regions with intermediate or high rates of hepatitis A
- Sexual contacts of infected people
- Household members or caregivers of infected people, play contacts within day care centres
- Men who have sex with men
- IV drug users

Hepatitis A has an incubation period of approximately 28 days (range: 15–50 days), and is most infectious two weeks before to one week after the onset of clinical illness.[2]

The likelihood of symptomatic infection increases with age. For example jaundice occurs in less than 10% of children under six years, in 40%–50% of children aged 6–14 years and in 70%–80% of people older than 14 years.[2]

Infection with hepatitis A is seldom fatal and does not develop into chronic hepatitis. In pregnancy hepatitis A poses no particular risk to the foetus.

Hepatitis B

In New Zealand hepatitis B is a notifiable disease.[1] Notifications had steadily decreased between 1997 and 2004, but have been increasing since 2004. In 2007 there were 75 cases of acute hepatitis B notified in New Zealand.[1]

It is estimated there are approximately 80 000 people with chronic hepatitis B in New Zealand.[3] There is considerable variation in the rate of chronic hepatitis B virus infection between different ethnic groups with consistently higher rates for Māori, Pacific and Asian peoples than European New Zealanders.[4] Universal infant hepatitis B vaccination introduced in New Zealand in the late 1980s is expected to ultimately have the greatest impact on the control of hepatitis B.

Hepatitis B is transmitted via contact with infected blood, semen, and other body fluids.

Those most at risk for hepatitis B infection are:

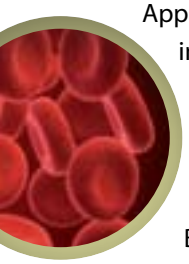
- Infants born to infected mothers
- Sexual contacts of infected people
- People with multiple sex partners
- People with a sexually transmitted infection
- Men who have sex with men
- IV drug users
- Household contacts of infected people
- Healthcare and public safety workers exposed to blood at work
- Haemodialysis patients
- Residents and staff of facilities for developmentally disabled people
- Travellers to regions with intermediate or high rates of hepatitis B (prevalence greater than 2%)
- People who participate in contact sports where there is high risk of bleeding injury

Hepatitis B has an incubation period of 45 to 160 days (average about 120 days).

Many people who contract hepatitis B are asymptomatic. Less than 1% of infants under 1 year develop symptoms, 5%–15% of children aged 1–5 years develop symptoms, while 30%–50% of people older than 5 years develop symptoms.[2]

Most people who develop acute hepatitis B recover with no lasting liver damage and acute illness is rarely fatal.

The risk for chronic infection varies according to the age at infection and is greatest among young children. Approximately 90% of infected infants and 25%–50% of infected children aged 1–5 years will remain chronically infected with hepatitis B. By contrast, approximately 95% of adults recover completely from hepatitis B and do not become chronically infected.[6]



Approximately 15%–25% of people who are chronically infected go on to develop chronic liver disease, including cirrhosis, liver failure, or liver cancer.[7]

Hepatitis C

Between 1998 and 2007, the number of acute hepatitis C notifications has decreased. 32 cases of acute hepatitis C were notified in New Zealand in 2007.[1] Chronic hepatitis C is not notifiable but it is estimated there are approximately 35–40,000 cases in New Zealand.[3]

Hepatitis C is transmitted primarily via contact with infectious blood, and to a lesser extent, via other body fluids.

People most at risk for hepatitis C infection are:

- IV drug users – particularly those who share needles
- Recipients of clotting factor concentrates before 1987
- Recipients of blood transfusions or donated organs before July 1992
- Haemodialysis patients
- HIV-infected people
- Infants born to infected mothers

The most commonly recorded risk factor for hepatitis C in 2007 was intravenous drug use.[1] The role of sexual transmission is controversial. If sexual transmission does occur it is at a very low level. Sexual transmission is likely to be more efficient when there is HIV co-infection and high hepatitis C viral load.

Hepatitis C has an incubation period of 14 to 180 days (average approximately 45 days).

Approximately 70–80% of newly infected people will be asymptomatic, although 75–85% will go on to develop chronic infection.[8]

Subsequently, about 60%–70% of chronically infected people will develop chronic liver disease, 5%–20% will develop cirrhosis over a period of 20–30 years, and approximately 1%–5% will die from cirrhosis or liver cancer.[2]

Hepatitis D

Hepatitis D is also referred to as the delta virus. It is spread through contact with infected blood. This disease is known as a "hitch-hiker" virus as it only occurs in people who are also infected with hepatitis B.[3] Therefore, anyone at risk for hepatitis B is also at risk for hepatitis D. At present it is found mainly in hepatitis B carriers born in certain Pacific Islands (Western Samoa, Nuie and Nauru). It is more common in IV drug users.

Testing would only be indicated following advice from a specialist.

Hepatitis E

Hepatitis E is spread through food or water contaminated by faeces from an infected person. People most likely to be exposed to the hepatitis E virus are those people travelling to countries with endemic infection, e.g. India, Egypt and parts of China. Hepatitis E virus is not commonly transmitted by person-to-person contact although it can be transmitted by blood transfusion.

Animal strains of hepatitis E are common worldwide and there is the potential for zoonotic infection. Locally-acquired hepatitis E has been reported in a number of industrialised countries including New Zealand, UK, US, Europe and Japan. The source and route of transmission of the cases acquired in New Zealand is not yet known.

Detection of hepatitis E is available in New Zealand, but is generally reserved for specialist testing of those with otherwise unexplained hepatitis.

Hepatitis E usually resolves on its own over several weeks to months.[3] Chronic infection does not develop.

Testing for hepatitis

General considerations for ordering laboratory tests

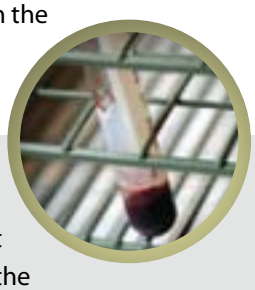
When ordering hepatitis tests, it is important to consider the patient's history, age, risk factors, vaccination status and any previous hepatitis test results.

Diagnostic testing of those with an acute hepatitis may prompt different tests to screening of asymptomatic patients for either infection or evidence of immunity.

Try to be specific when ordering hepatitis tests. Consider the relevant details from the history. For example, has the person:

- Been overseas in the last month – think hepatitis A (incubation period 28 days)
- History of drug use – think hepatitis B and C
- Tattoos and body piercings – think hepatitis B and C
- Contaminated water source – think hepatitis A
- High risk sexual activity – think hepatitis B

Try to avoid writing 'hepatitis serology' on the form. If you are not sure about the most suitable test, it is useful to write relevant clinical details on the laboratory request form, as this can help the laboratory with the most appropriate choice of tests.



Hepatitis serology

Hepatitis serology tests detect either the antigen (virus or part of the virus) or the antibody (the host's immune response).

When an immune response is first initiated, the antibodies are produced as IgM during the initial response, with IgG antibodies being produced later. Differentiation between these antibody classes can provide additional information about the timing of infection.

To remember the "M" and "G" immunoglobulin response, think of the "MG" car. First response is "M" second response is "G".

Immunoglobulin M (IgM) is the major class of antibody secreted first into the bloodstream during a primary immune response however this response is relatively non-specific. Measuring IgM antibodies is of most use in the acute stage of infection, prior to the appearance of IgG. For example, the presence of Hepatitis B core IgM antibody is suggestive of acute infection.

Immunoglobulin G (IgG) IgG antibodies generally appear after IgM, and are therefore a sign of a maturing immune response. They peak with primary infection or vaccination and then may decline over time. An accelerated IgG response is seen if there is immune memory from prior infection or vaccination, and is often the primary means by which protective immunity is generated. IgG antibodies are distributed in extracellular fluid, and is present in milk, and maternal IgG is the only immunoglobulin that normally crosses the placenta. The presence of IgG antibodies generally indicates past or chronic infection or immunity.

What to request – common clinical scenarios

There are a number of situations in which hepatitis tests are frequently considered, this section provides an overview of common clinical scenarios with advice about the initial approach to testing.

Further testing is variable and will depend upon initial results. In many cases the laboratory may provide additional guidance and recommended further testing.

Scenario 1: Acutely unwell patient, suspected hepatitis[10]

Initial tests	
✓	ALT (if not already done)
✓	Hepatitis B surface antigen
✓	Hepatitis B core IgM antibody
Include	
✓	Hepatitis A IgM antibody if symptoms following travel or an outbreak
✓	Hepatitis C antibody if a history of IV drug use
Not usually required:	
✓	Epstein-Barr virus
✓	Cytomegalovirus

Notes:

1. Patients with acute hepatitis of viral etiology, generally have dramatic elevations of ALT (up to 5 or more times the upper limit of normal) therefore patients with normal ALT levels are extremely unlikely to have acute viral hepatitis.
2. Acute hepatitis C illness is usually an asymptomatic or a mild non-specific illness.
3. Epstein-Barr virus and cytomegalovirus generally do not cause hepatitis outside a generalised febrile illness with lymphadenopathy, and they do not cause chronic hepatitis in healthy people.

Scenario 2: Follow up of abnormal ALT/? Chronic hepatitis[6]

Initial tests	
✓	Hepatitis C antibody
✓	Hepatitis B surface antigen

Notes:

1. In chronic viral hepatitis the ALT level may be normal or elevated.
2. Hepatitis A does not causes chronic hepatitis.
3. Less than 5% of adults infected with hepatitis B will go onto develop chronic infection, although approximately 90% of infants and 25–50% of children will go onto to develop chronic infection. Therefore, if an adult who has not had a recent illness with jaundice is found to be Hepatitis B surface antigen positive, they were probably infected as a child.
4. Approximately 80% of people who are infected with hepatitis C will go onto develop chronic infection.

Scenario 3: Blood and body fluid exposures, e.g. Needlestick injuries[12]

From the source person:	
✓	Hepatitis B surface antigen
✓	Hepatitis C antibody
✓	HIV antibody
From the exposed person:	
✓	Hepatitis B surface antigen
✓	Hepatitis B surface antibody
✓	Hepatitis C antibody
✓	HIV antibody (only if the source is HIV positive)

Notes:

1. Blood from the source person should be collected as soon as possible (preferably immediately).
2. Blood from the exposed person should be collected as soon as practicable (within a day or so of the exposure incident).
3. When the source person is known to be positive for hepatitis A, B or C or HIV, immediately consult a specialist to discuss requirement for post-exposure prophylaxis.

Scenario 4: Checking response post Hepatitis B immunisation [11]

Initial test	
Only recommended for babies born to Hepatitis B surface antigen positive mothers and high risk occupational or exposure groups	
Babies born to Hepatitis B surface antigen positive mothers	
✓	Hepatitis B surface antibody
✓	Hepatitis B surface antigen
High risk occupational or exposure groups	
✓	Hepatitis B surface antibody

Notes:

1. Approximately 5–10% of adults do not respond to the primary vaccine course, therefore for high risk occupational or exposure groups it is important to determine immunity after vaccination. Hepatitis B surface antibody levels >10 IU/mL are considered to indicate protection from future Hepatitis B exposure.
2. Babies born to Hepatitis B surface antigen positive mothers should be tested at 5 months of age to ensure that they are protected and have not become infected after delivery. A Hepatitis B surface antibody result >100 IU/mL indicates an adequate response to the primary vaccine course. Whereas results of 10–100 IU/mL may be due to residual Hepatitis B immunoglobulin. In this case, Hepatitis B surface antibody testing should be repeated in one to two months.

Scenario 5: Pre-immunisation screening[11]

Initial tests	
Hepatitis A	
Only if history of possible previous infection	
✓	Hepatitis A IgG antibody
Hepatitis B	
Only in people at high risk of being a carrier for hepatitis B.	
✓	Hepatitis B surface antigen
✓	Hepatitis B surface antibody

Notes:

1. Pre-immunisation screening for hepatitis A antibodies is not routinely recommended but should be considered for those who may have already been infected, including:
   - those who are likely to have been exposed as children (born in a country of high endemicity) or in the course of their employment
   - those with a history of jaundice
   - men who have sex with men
   - IV drug users
   - individuals who have frequently visited areas of high endemicity.
2. **Pre-immunisation screening for hepatitis B not usually indicated. It is encouraged for those at higher risk of being a carrier for Hepatitis B, while those at low risk may be vaccinated without prior screening.**
3. Co-existence of Hepatitis B surface antigen and Hepatitis B surface antibody occurs in a small proportion of patients with chronic Hepatitis B infection. For this reason, testing Hepatitis B surface antibody alone to evaluate "immune status" without measuring Hepatitis B surface antigen is not advised.

Scenario 6: Screening for Hepatitis C infection

✓	Hepatitis C antibody

Notes:

1. Most acute Hepatitis C infections are asymptomatic or result in only mild illness, i.e. many infected patients will not be diagnosed without specific screening.
2. Testing for Hepatitis C is recommended in patients at increased risk for infection, including those who:
   - ever injected drugs
   - received blood, blood products or organs before 1992
   - children born to Hepatitis C infected women (test with either Hepatitis C antibody testing after 12 months of age or Hepatitis C RNA PCR at 4–6 months of age)
   - those with HIV infection
   - those with unexplained abnormal ALT level
3. If hepatitis C is suspected, the appropriate initial test is the Hepatitis C antibody. However, the appearance of Hepatitis C antibody may take many weeks to develop. In acute Hepatitis C infection, Hepatitis C antibody is detected in 50–70% of patients by the time symptoms develop and are usually present in the rest after a further 3–6 weeks.
4. If Hepatitis C antibody testing is positive, Hepatitis C viral testing (Hepatitis C RNA PCR) is required to confirm current infection. Patients positive following Hepatitis C viral testing should be referred to the local hepatitis clinic for assessment and consideration of anti-viral therapy.

References

1. ESR Annual Outbreak Summary 2007, April 2008. Available from: www.surv.esr.cri.nz/PDF_surveillance/AnnualRpt/AnnualOutbreak/2007OutbreakRpt.pdf
2. Centers for Disease Control and Prevention, July 2008. Available from: www.cdc.gov/hepatitis/
3. The Hepatitis Foundation of New Zealand. Available from: www.hepfoundation.org.nz/
4. Robinson T, Bullen C, Humphries W, et al. The New Zealand Hepatitis B Screening Programme: screening coverage and prevalence of chronic hepatitis B infection. NZ Med J 2005;118;1345. Available from: www.nzma.org.nz/journal/118-1211/1345/content.pdf
5. Weilert,F. Practical approach to viral hepatitis in New Zealand. N Z Fam Physician 2003;30(242). Available from: www.rnzcgp.org.nz/assets/teach_prac/NZFP/Oct2003/Weilert_Oct03.pdf
6. bpac^{nz} Liver Function Testing in Primary Care. July 2007. Available from: www.bpac.org.nz.
7. University of Auckland. Immunisation Advisory Centre. Available from: www.immune.org.nz/
8. Chen SL, Morgan TR. The Natural History of Hepatitis C Virus (HCV) Infection. Int J Med Sci 2006; 3(2): 47–52.
9. British Columbia Medical Association. Viral Hepatitis Testing. 2005. Available from: www.bcguidelines.ca/gpac/pdf/vihep.pdf
10. Aotea Pathology Ltd. Viral Hepatitis Testing made easy. 2008. Available from: www.apath.co.nz/BULLETINS/AoteaNews_Sept08.pdf
11. Ministry of Health. 2006. Immunisation Handbook 2006. Wellington: Ministry of Health.Available from: www.moh.govt.nz/moh.nsf/indexmh/immunisation-handbook-2006
12. Morris AJ, Ellis-Pegler RB, Thomas MG. Management of occupational exposure to blood or body fluid. Diagnostic Medlab. 2003. Available from: www.dml.co.nz/downloads/1281_BulletinExposureBloodBodyFluid.pdf