

best tests

JULY 2009

Hepatitis

Therapeutic Drug Monitoring

STI Quiz Feedback



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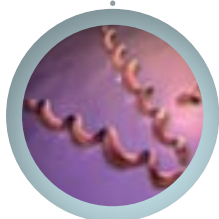
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What test is needed and when?

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 immunoglobulin 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.

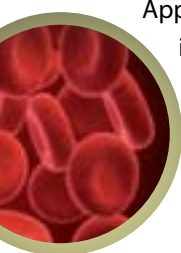
Hepatitis C has an incubation period of 14 to 180 days (average approximately 45 days).

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, Niue 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.

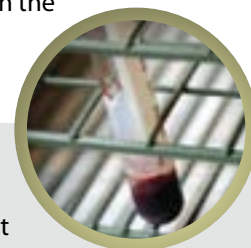
Diagnostic testing of those with an acute hepatitis may prompt different tests to screening of asymptomatic patients for either infection or evidence of immunity.

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 hepatitis¹⁰

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 hepatitis⁶

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 cause chronic hepatitis.

3. Less than 5% of adults infected with hepatitis B will go on to develop chronic infection, although approximately 90% of infants and 25–50% of children will go on 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 on to develop chronic infection.

Scenario 3: Blood and body fluid exposures, e.g. Needlestick injuries¹²

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 screening¹¹

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

Practical considerations for Therapeutic Drug Monitoring

Key reviewer:

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www.bpac.org.nz keyword: tdm

Therapeutic drug monitoring (TDM) is the measurement of the concentration of specific drugs at intervals in order to adjust dosage regimens to achieve a desired clinical effect and avoid toxic effects.

TDM is used where:

1. There is an established relationship between blood drug concentration and therapeutic response and/or toxicity

2. There is a poor relationship between blood drug concentration and drug dosage
3. There are clear clinical indications for the test (such as: no response to treatment; suspected non-compliance; signs of toxicity)
4. The specimen can be provided, appropriately timed and dated, with identifiable patient information
5. Adequate clinical information is supplied to allow the interpretation of results

In order to get meaningful results when undertaking therapeutic drug monitoring, the following needs to occur:

- All dosing and collection time details should be included on the request form (see Table 1)
- Samples should not be collected until drugs have reached steady state (five half lives) (see Table 2)
- Bloods should be collected at the recommended sampling time (see Table 2)

The timing of blood collection is important

Sample once steady state achieved

In most cases blood samples should not be collected until concentrations have reached steady-state. This occurs when the rate of drug administration and drug elimination are equal, for most drugs this is achieved after 4–5 half-lives. If a loading dose has been administered, steady state may be achieved earlier. Drug concentrations may be determined earlier if toxicity is suspected. It is important to wait for steady-state both at initiation and following any dosage change.

Sample at the appropriate time in relation to last dose

When a drug is administered, it goes through the stages of absorption, distribution, metabolism and elimination. Drug concentrations are generally measured in the elimination phase (correlates with trough) as this gives a more predictable and reliable guide to drug dosing.

Different drugs have variable pharmacokinetic characteristics, for instance, digoxin and lithium have extended distribution phases following dosing. This means, that if blood is taken too soon after administration, the level will appear to be elevated.

Details to include on the request form

To accurately interpret results, it is important the request form contains all relevant information. See Table 1.

It can be difficult to make sense of a result unless collection time and previous last dose is known. For example, drug levels that are in the toxic range may have been taken only a few hours post dose, and therefore the drug was still in its distribution phase.

It is important to note how long the person has been on the drug, to ascertain they have achieved steady-state. If there are any known issues with compliance, include on the form.

It is also useful to include on the request form any co-morbidities or other medications, as these may effect the drug pharmacokinetics. For example, steady-state for digoxin is 5–7 days, but may take up to three weeks in a person with renal failure.

Table 1: Information required on request form¹

Time sample collected
Time dose given
Dosage regimen (dose, duration, dosage form)
Patient demographics (age/sex)
Other medications
Other relevant co-morbidities (e.g. renal/liver disease)
Indications for testing (e.g. ? toxicity, non-compliance)

Table 2: Recommended sampling times^{2,3}

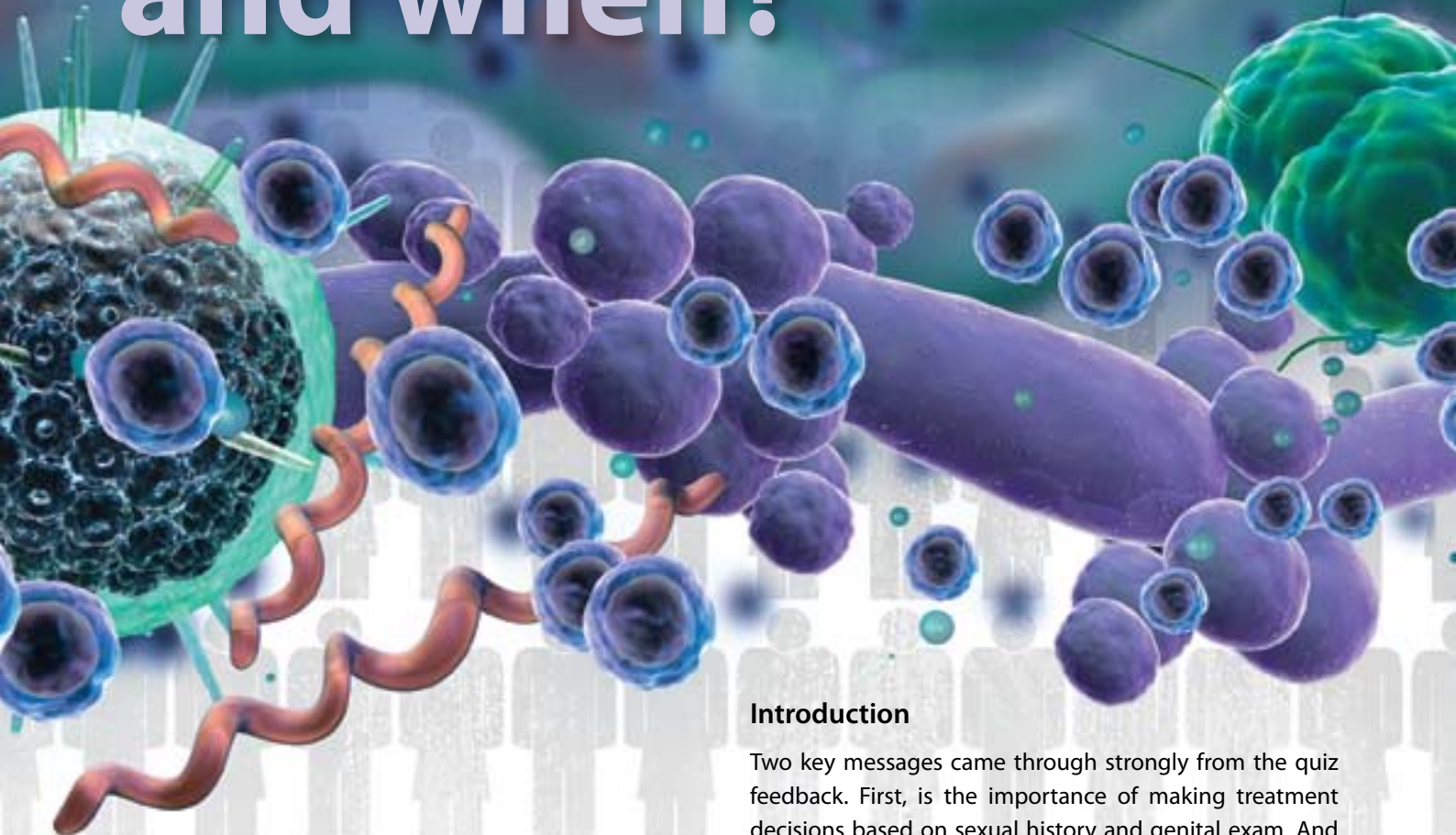
	Time to steady state	Recommended sampling time	Half-life	Note
Carbamazepine	14 days	Immediately pre dose	10–20 hours	Reduced clearance can occur in children, after chronic therapy and with other anti-convulsants.
Digoxin	7 days	6–24 hours post dose	36 hours	In renal failure, may take up to 3 weeks to reach steady state. Routine monitoring not recommended.
Lithium	5 days	12 hours post dose or Immediately pre dose	10–35 hours	Reduced clearance in children. Decreased renal function may lead to increased concentration, especially in the elderly. Drug accumulation is enhanced by dehydration.
Phenytoin	14 days	Immediately pre dose	6–24 hours	Time to steady state may depend on dose. Altered clearance when taken with other anticonvulsants.
Theophylline	2 days	2–4 hours post dose	4–16 hours	Prolonged clearance in neonates, reduced clearance in children. Prolonged clearance in severe illness notably respiratory failure and CHF.
Valproate	3 days	Immediately pre dose	11–17 hours	Reduced clearance when taken with enzyme inducers e.g. phenobarbitone, phenytoin. There is poor correlation between valproate levels and clinical effect. The main reason for measurement is to assess compliance.

References

1. Gross AS. Best practice in therapeutic drug monitoring. *Br J Clin Pharmacol* 1998;46:95-99
2. Medicines information centre, Calderdale Royal Hospital. Available from: http://www.formulary.cht.nhs.uk/Guidelines/Hospital_Based/TDM/TDM.htm
3. Kyle C (Ed), *A Handbook for the Interpretation of Laboratory tests*. 4th Edition, 2008, Diagnostic Medlab.

QUIZ FEEDBACK

Sexually transmitted infections – What test is needed and when?



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Acknowledgement:

bpac^{nz} Ltd would like to thank the GP review panel and Dr Rosemary Ikram for their expertise and guidance on the development of this resource.

Introduction

Two key messages came through strongly from the quiz feedback. First, is the importance of making treatment decisions based on sexual history and genital exam. And second, not to make assumptions about anyone's sexual behaviour – if you are not sure, it is much better to ask the patient.

This quiz feedback includes the aggregated responses from GPs that completed the quiz, comments from the GP review group and specialist commentary from Dr Rosemary Ikram.

All GPs who have responded to this quiz will receive CME credits. This quiz is also available online. There are now over 25 interactive quizzes available at www.bpac.org.nz, all are accredited for CME points.

1. According to the MOH Chlamydia Management Guidelines,¹ what group of patients would benefit most from asymptomatic opportunistic testing for Chlamydia?

	Your peers	GP panel
<input type="checkbox"/> All females, under 25 years old	55%	
<input type="checkbox"/> All women less than 25 years after a recent partner change	78%	•
<input type="checkbox"/> Annually for all people less than 25 years	16%	
<input type="checkbox"/> Every three years for people over 25 years	2%	

GP panel:

This question emphasises the importance of not making assumptions when considering any aspects of sexual health and ensuring all decisions are guided by sexual history. For example, although women under the age of 25 years are most at risk for Chlamydia, it is worth remembering not all women will be sexually active or at increased risk. Therefore, MOH recommends opportunistic testing is targeted at women under the age of 25, who have had two

or more sexual partners in the last 12 months or a recent partner change.

The panel noted 22% of their colleagues indicated they would not do Chlamydia testing following a recent partner change. There was a discussion about the reasons behind this; which may include low perceived risk by either the patient or the GP.

Once a person is found to have a positive result, the panel were aware that contact tracing remains an essential part of Chlamydia management. There are many means of contacting previous sexual partners; this may include phone, email, texting, face-to-face or letter. Patient and provider should come to an agreement of how this is best achieved. Patients can be offered the choice of either patient referral (where the patients notify their sexual contacts) or provider referral (where the health care provider agrees to undertake the task of notifying sexual contacts)

Specialist comment:

As already mentioned partner change is a risk factor regardless of perception. Another high risk group which is not discussed here are those who have been infected previously.

2. What infections are more prevalent in men that have sex with men (MSM) than heterosexuals?

	Your peers	GP panel
<input type="checkbox"/> HPV	23%	
<input type="checkbox"/> Gonorrhoea	82%	•
<input type="checkbox"/> Syphilis	79%	•
<input type="checkbox"/> Gardnerella	4%	
<input type="checkbox"/> Chlamydia	38%	

GP panel:

This generated an interesting discussion with the panel, as they emphasized the importance of taking a thorough sexual history, and not making assumptions about the nature of any relationship.

Generally MSM are at higher risk of STIs, due to different patterns of sexual partnering for MSM than for the heterosexual population. At the NZ Sexual Health Society

conference in 2008, there was a presentation of a study² of the structure of sexual partnering among gay and bisexual men in NZ. The study revealed many MSM have high partner turnover (some very high), partnering histories are complex for the majority of MSM and over half of MSM currently in long-term regular relationships have sex with other men.

Gonorrhoea and Syphilis are considered to be more prevalent in MSM, but the panel also queried if Chlamydia is more prevalent. The panel considered doctors may be more aware of Chlamydia in MSM due to the association with Lymphogranuloma venereum (LGV), even though the overall number of cases identified in New Zealand has been low.

LGV is another presentation of Chlamydia which should be considered in MSMs with symptomatic anorectal disease who are Chlamydia positive but not responding to normal therapy.

Specialist comment:

I am unaware of any New Zealand data relating to the prevalence of *Chlamydia trachomatis* (*C. trachomatis*) in MSM vs MSW (men that have sex with women). Some studies have looked at *C. trachomatis* infection rates in males with urethritis and MSM were not significantly

different to those in MSW. Another study looking at *C. trachomatis* infection in men with gonorrhoea found a significantly higher number of *C. trachomatis* infections in MSW from urethral samples (MSW 31% vs MSM 12%). In the same study 24% men with rectal *Neisseria gonorrhoeae* were found to be also infected with *C. trachomatis*.

3. Which statements are true about STIs in general?		
	Your peers	GP panel
<input type="checkbox"/> All people under 25 years should be routinely checked for STIs	48%	
<input type="checkbox"/> NSU in males is frequently caused by Gonorrhoea	6%	
<input type="checkbox"/> Chlamydia may be the cause of a sterile pyuria	95%	●
<input type="checkbox"/> Prevalence data suggests STIs are generally well controlled in New Zealand	1%	

It is reassuring to note that most GPs are aware that STIs in New Zealand are generally poorly controlled. Chlamydia in particular has been the focus of the recent MOH management guidelines,¹ in an attempt to address this increasing health burden.

Most GPs are aware Chlamydia may be the cause of sterile pyuria, and that Gonorrhoea is generally not implicated in NSU (formerly known as non-gonococcal urethritis).

Specialist comment:

A study performed at Diagnostic Medlab looking for *C. trachomatis* in urines with sterile pyuria from patients in at risk age groups yielded about one third positive. These tests were performed on urines submitted for culture and were not therefore the ideal sample for detection of *C. trachomatis*. In our laboratory we occasionally isolate *N. gonorrhoeae* from such samples, this relies on technical staff inoculating extra media and is not recommended for detection of this organism.

GP panel:

Again this question generated discussion about making assumptions about sexual health. While not all people under 25 should routinely tested for STIs, it would be reasonable to enquire about risk and offer testing.

4. In a patient requesting an STI test, following unprotected intercourse, what is recommended?		
	Your peers	GP panel
<input type="checkbox"/> Self collection is a good option for first line testing	41%	
<input type="checkbox"/> All patients should have genital examination, and swab collection	50%	
<input type="checkbox"/> Laboratory tests should be delayed for about 2 weeks after exposure	83%	●
<input type="checkbox"/> Contact tracing is the responsibility of the patient	8%	

GP panel:

This question provided a good opportunity to reflect on appropriate use of laboratory tests. The incubation periods for different pathogens vary, so incorrect timing of testing may provide misleading results. For example incubation times: Chlamydia is 7–21 days, Gonorrhoea is 2–5 days, Trichomoniasis is 4–28 days. It is useful to remind patients, that while laboratory tests can exclude some organisms, not all sexually transmitted infections can be excluded. In particular screening is not currently recommended for HSV and HPV.

While it is prudent to delay STI testing for approximately 2 weeks, empirical treatment may be commenced. In most cases this would be azithromycin for Chlamydia, although

empirical treatment for other STIs may be indicated in high risk situations.

When a patient requests an STI test a full sexual history and examination is indicated to help determine risk and guide testing. This would typically include a swab (for women) or first void urine (for men) for Chlamydia, collection of a separate swab for gonorrhoea and trichomonas. Serology testing for HIV, hepatitis B and C, and syphilis will be guided by findings from history and examination.

Because a range of tests is indicated for patients requesting an STI check, self testing is generally not a recommended alternative. However the panel were interested to know if a self taken swab or a first void urine (FVU) for gonorrhoea is useful if a swab is refused.

Some of the panel were also familiar with practice in Australia, in which a single swab is used for both Chlamydia and gonorrhoea, and they wondered if this approach could be used in New Zealand.

Specialist comment:

The self collected vaginal swab has been found to be a more sensitive test than FVU for identifying *C. trachomatis* in females. While many of the tests used for detection of *C. trachomatis* also can be used for the detection of *N. gonorrhoeae*, this is not recommended. There are some issues with using a single swab, including poor specificity (false positive), increased cost, and it is also not possible to perform susceptibility testing on these samples.

5. A 25 year old, predominantly heterosexual, man presents for an STI test several days after a sexual encounter with another man. Which of the following is true?

	Your peers	GP panel
<input type="checkbox"/> Immediately test for the conditions associated with MSM eg Gonorrhoea, Syphilis, LGV, and HIV	27%	
<input type="checkbox"/> Sexual history will guide the testing	75%	●
<input type="checkbox"/> Empirical treatment may be indicated	32%	+/-
<input type="checkbox"/> All MSM should also have swabs collected from the rectum and pharynx	48%	

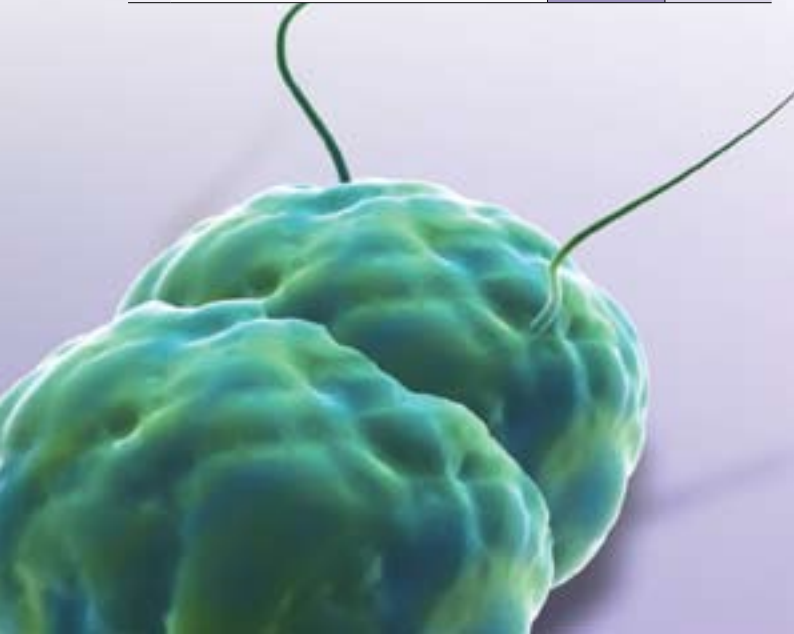
GP panel:

The panel was surprised that about half of their colleagues would think rectum and pharynx swabs are indicated in MSM, especially when “Sexual history will guide the testing” was given as an alternative. This reinforces the importance of not making assumptions about what type of sexual activity has taken place. History taking is of key importance in situations in which you may not be familiar.

In addition, it may be worth considering that a patient presenting in this situation may have associated psychological issues that require further discussion.

Specialist comment

Some guidelines suggest sampling urethral and rectal sites in MSM regardless of history. This relates to a number of common receptive anal sexual practices that do not constitute receptive anal intercourse but have been shown as risk activities for rectal infection.³ However if none of these occurred then urethral alone would suffice.



6. A patient presents with his first clinical episode of genital herpes, what is indicated?		
	Your peers	GP panel
<input type="checkbox"/> Viral swab testing for HSV-1 and HSV-2	82%	●
<input type="checkbox"/> HSV serology	1%	
<input type="checkbox"/> Full STI screening	76%	+/-
<input type="checkbox"/> Contact tracing	27%	

GP panel:

The panel acknowledged the when a patient has their first outbreak of herpes, it requires sensitive management. Many patients are alarmed by the diagnosis of herpes, as there is often a stigma attached to the diagnosis; they may worry about the long term consequences, and may assume it is the result of a partner’s infidelity.

Herpes has both variable incubation and latency periods and most people are asymptomatic carriers, making

it difficult to determine when it was first contracted. Furthermore, although high numbers of sexually active people are sero-positive for herpes, appropriately 80% will be asymptomatic carriers, and be unaware of their carrier status. Contact tracing is therefore not recommended because it is difficult to trace, and there is no recommended treatment of potential contacts.

Further STI testing will be guided by history, and depend on individual patient circumstances.

Specialist comment:

A diagnosis of genital herpes often raises many issues as the panel have discussed. It is important to remember that 20% of infections are asymptomatic 20% have typical symptoms and signs but the vast majority (60%) have atypical recurrent symptoms. Also data relating to serologically discordant couples ie one positive and the other negative show a seroconversion rate of about 10% per year.

7. Which of the following is true about Gonorrhoea?		
	Your peers	GP panel
<input type="checkbox"/> Patients are frequently co-infected with another STI	100%	●
<input type="checkbox"/> People are mostly asymptomatic	5%	
<input type="checkbox"/> Self testing is appropriate	2%	
<input type="checkbox"/> Gonorrhoea is more prevalent in the 35-50 year old age group	6%	

GP panel:

It is clear from these responses, that GPs are aware to consider other STIs in a patient with gonorrhoea.

The panel was interested to know the prevalence of gonorrhoea in the general practice community, and the overall trends in New Zealand. They were aware that current NZ data available from ESR is predominantly from sexual health clinics, and they wanted to know if there are differences between the two.

Also, the panel were aware of the fastidious nature of gonorrhoea, and wondered if delayed transportation of swabs from GP surgeries to the laboratory would affect overall pick up rates of gonorrhoea.

Specialist comment:

The ESR data is the only all New Zealand data I know of. Recently at Medlab South we analysed the data from Nelson Marlborough, which included the community samples and the findings were consistent with the ESR. It was interesting that the majority of cases were diagnosed in GP surgeries.

Delayed transport of samples can lead to a failure to culture *N. gonorrhoeae*. It is therefore not ideal to have samples that will be cultured after more than 24 hours. The sooner the laboratory receives the sample the better. A gram stain of a genital swab is made in the laboratory and this helps confirm the culture result, particularly for males. As previously mentioned, NAAT testing is possible in some laboratories but although sensitivity is good, specificity is a problem as well as lack of susceptibility testing and increased cost.

8. Which of the following statements is true about Chlamydia testing?		
	Your peers	GP panel
<input type="checkbox"/> All people < 25 should be offered self testing	67%	•
<input type="checkbox"/> Collection of a first void urine is suitable for most young people	34%	+/-
<input type="checkbox"/> Testing should be offered in the first trimester of pregnancy	94%	•
<input type="checkbox"/> Most people with Chlamydia will have at least some symptoms	1%	

GP panel:

The panel was surprised that the response rate for offering testing to all under 25 years, was not higher. Again, not all people in this group will be at risk, but at least a discussion around sexual health will need to be done, before this can be determined.

It was interesting to note the high numbers of doctors who agree that Chlamydia testing is indicated in the first trimester of pregnancy. While in the past this was not always considered, it is now recommended by the MOH that women are tested for Chlamydia in the first trimester of pregnancy (and then again in the last trimester for those with ongoing risk factors).

The panel were familiar with the long term consequences for patients following symptomatic PID caused by Chlamydia, but they are interested in the long term consequences of asymptomatic Chlamydia.

Specialist comment:

It is difficult to give a definitive answer regarding the course of PID because the number of cases varies with the population group studied. In one study of 109 women with asymptomatic infection, 16.5% became symptomatic during 2 month follow up while 1.8% developed PID. This number has been found to be much higher if *N. gonorrhoeae* infection is also detected and treatment given for gonorrhoea alone, in this case 30% developed PID.

References

1. Ministry of Health. Chlamydia Management Guidelines, 2008. Available from: [http://www.moh.govt.nz/moh.nsf/pagesmh/8210/\\$File/chlamydia-management-guidelines.pdf](http://www.moh.govt.nz/moh.nsf/pagesmh/8210/$File/chlamydia-management-guidelines.pdf) (accessed April 2009)
2. Saxton P, Hughes A, Dickson N, Sharples, K. Boyfriends, fuckbuddies and casual sex: The structure of sexual partnering among gay and bisexual men in NZ. New Zealand Sexual Health Society Conference, Dunedin, Aug 28-30 2008. Powerpoint presentation available from http://www.nzshs.org/dunedin/peter_saxton_08.pdf (accessed April 2009)
3. Jin F, Prestage GP, Mao L, et al. Incidence and risk factors for urethral and anal gonorrhoea and chlamydia in a cohort of HIV-negative homosexual men: the Health in Men Study. *Sex Transm Infect* 2007;83:113-119.



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