Summer
2007

Clinipath Pathology Newsletter

- C^{14} Urea Breath Testing for *Helicobacter Pylori* in General Practice
- A Guide to Ordering Hepatitis Serology
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CLINIPATH PATHOLOGY

"we take it personally"

From the CEO

Welcome to the summer 2007 edition of our newsletter. In our last newsletter we included a questionnaire regarding your interest in future education topics. We had a fantastic response and your feedback was most appreciated. Your responses have enabled us to plan an educational program which is relevant and meets your needs.

This newsletter includes articles on topics identified by you in the questionnaire as being clinically relevant. Dr Michael Watson has written an article on serological testing for Hepatitis in some of the more common scenarios encountered in routine clinical practice. He has also contributed an article on C^{14} Urea Breath testing and its applications in general practice.

In recent months we have also produced a number of new publications including:

- The new Cervical Smear Guidelines
- Clinipath Pathology Diabetes Registry
- Clinipath Pathology Billing Guidelines
- On-line Computer Solutions

If you would like a copy of any of this information, please contact our marketing department on 9476 5275.

We hope this edition of our newsletter provides you with useful information and we are looking forward to working with you in 2007.

Red cell antibody screen in the context of the Rh (D) antenatal Prophylaxis Program

Current Australian guidelines recommend that all Rh (D) negative women should have red cell antibody screening performed at their initial antenatal visit and at least once between 28 and 36 weeks gestation. In the context of routine antenatal prophylaxis, collection of a blood sample for antibody screening should be undertaken prior to the administration of the 28 week dose of Rh (D) immunoglobulin.

Two recent Australian cases of significant adverse foetal outcomes have highlighted the importance of clinicians ensuring the correct timing and interpretation of red cell antibody screening in the context of the Rh (D) antenatal prophylaxis program.

These two cases have reportedly been attributed to a lack of clarity as to whether the presence of Rh (D) antibodies was due to active alloimmunization or prophylaxis. In both cases the Rh (D) immunoglobulin was given prior to blood sample collection thus further complicating laboratory findings.

Fig. 1 DIAMED SWING used at Clinipath Pathology for automated blood grouping and antibody screening

When antenatal red cell antibody testing is indicated e.g. at 28 weeks gestation, the blood sample should be collected prior to the administration of Rh (D) immunoglobulin. If the Rh (D) immunoglobulin has already been administered, the test should still be performed and the prior administration of Rh (D) immunoglobulin should be highlighted on the laboratory request form.

For further information please contact:

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Bunker Bay winner

Congratulations to the winner of our luxury weekend for two at the Bunker Bay resort. The winner was Dr Jack O'Connor from the Oxford Street Medical Centre. Once again thank you to all who participated in the questionnaire from our last newsletter.

A note from our IT department

The ability to receive patient results by secure electronic download allows practitioners to receive their results efficiently and accurately.

We would like to remind you that the direct download of results can be affected by changes made to the computer system within your practice. If you are intending to make changes to your practice computer software or hardware this could temporarily affect your automatic download of patient results.

Our IT or Marketing departments are available, if necessary, to provide advice on how planned changes within your practice could affect the download of results.

Please feel free to contact them on:

Marketing Department
Mr Clinton Pike
T: (08) 9476 5275

Information Technology
Mr Martin Cullen
T: (08) 9476 5276

C^{14} Urea breath testing for *Helicobacter pylori* in general practice

What is a C^{14} Urea breath test and how does it work?

Helicobacter pylori (the major cause of gastric and duodenal ulcers) is a fastidious bacterium which is known to be a potent producer of the enzyme urease. Urease splits urea to hydrogen and ammonia which raises the pH of the environment surrounding the organism and allows it to survive in the acidic environment of the stomach. The C^{14} Urea breath test works on the principle that a capsule containing radioactive C^{14} labelled urea, when ingested by a fasting patient, will be broken down by the organism (if present). The C^{14} Urea is broken down by the bacteria to $HC^{14}O_3$ which is later transported to and excreted by the lungs as $C^{14}O_2$. This can be readily measured in the laboratory.

What Medications can interfere with the test?

Other organisms may produce the urease enzyme and can give a false positive reading. Usually these other organisms do not survive in the acidic environment of the stomach. Urease producing bacteria do however live in the mouth and so it is important that during the test the capsule be swallowed and not chewed. Prior use of a range of medications (see Table 1) can interfere with the test, either by partially suppressing *H.pylori* growth (rendering the test falsely negative) or by reducing gastric acidity (proton pump inhibitors) which can enhance the growth of other organisms that produce urease (resulting in false positive tests). It is therefore important that patients carefully follow the medication restrictions, outlined in Table 1, before undergoing the test.

Performing C^{14} Urea Breath test

Fig. 1 (left) Patient swallowing capsule

Fig. 2 (below) Patient blowing into foil balloon

continued overleaf

C^{14} Urea breath testing for Helicobacter pylori in general practice continued

What does a positive C^{14} Urea breath test tell you about your patient's symptoms?

It is important to remember that a positive C^{14} Urea breath test simply tells you that the patient is actively infected with *H.pylori*. Clinical interpretation is still very important as not all patients that are actively infected with *H.pylori* will have symptoms that can be attributed to the infection. Gastro-oesophageal reflux is a common example of this, and is usually unrelated to *H.pylori* infection.

How does C^{14} Urea breath test differ from H.pylori serology?

The major difference between *H.pylori* serology and a C^{14} breath test is that a true positive C^{14} Urea breath test tells you that the patient is actively infected with *H.pylori*. *H.pylori* serology cannot reliably distinguish between past or present infection and will also not reliably tell you whether or not you have achieved eradication of the organism. This is because even after successful treatment, serology may remain positive for 6 months or longer. A C^{14} Urea breath test may demonstrate eradication just 4-6 weeks post treatment.

Table 1.

Type	Name			Exclusion period
Antacids	ALU-TAB Algicon Amphojel Andrews Tums Antacid Antassa De Witts Antacid Powder Dexsal Antacid Liquid Dexsal Granules Eno	Gastrogel Gaviscon Gelusil Medefoam 2 Meracote Mucaine 2 in 1 Mucaine Suspension Mylanta Double Strength Mylanta Heartburn Relief	Mylanta Original Rennie Rennie Digestif Salvital Sigma Liquid antacid Simenco Titralac Titralac SIL	Fasting period and during test
Antibiotics**	**Multiactives** Flagyl Flagisyn Helidac Losec HP7 **Amoxycillins** Alphamox Amoxil Amoxoheal Augmentin Bgramin Cilamox	Clamoxyl Clavulin Moxacin **Ampicillin** Alphacin Austrapen Ampicin **Erythromycin** EES E-mycin Eryc Erythrocin	**Tetracycline** Achromycin Helidac **Doxycycline** Doryx Doxsig Doxy Doxylin Doxyheal Vibramycin **Minocycline** Akamin	For 30 days prior to test
Bismuth	De-nol	Helidac		For 30 days prior to test
Cytoprotectives	Carafate	Sucralfate	SCF Ulcyte	For 30 days prior to test
H2 Antagonists	Amfamox (famotidine) Ausran Cimehexal (cimetidine) Cimetidine Cimetax DBL Ranitidine Magicul (cimetidine)	Pepcid (famotidine) Pepcidine (famotidine) Rani 2 Ranihexal Ranitidine Ranoxyl SBPA Cimetidine	SBPA Ranitidine Sigmetadine Sigmetidine Tagamet Tazac (nizatidine) WL-cimetidine Zantac (ranitidine) Zantac Relief	Fasting period and during test
Proton Pump Inhibitors	Acimax Esomeprazole Lansozaprole Losec Tablets Losec Intravenous	Maxor Nexium Omeprazole Pantoprazole Pariet	Rabeprazole Somac Somac Injection Zoton	For 7 days prior to test

*** NB: All antibiotics except Vancomycin and Sulfa drugs (Bactrim etc) be withheld for 4 weeks for maximal accuracy*

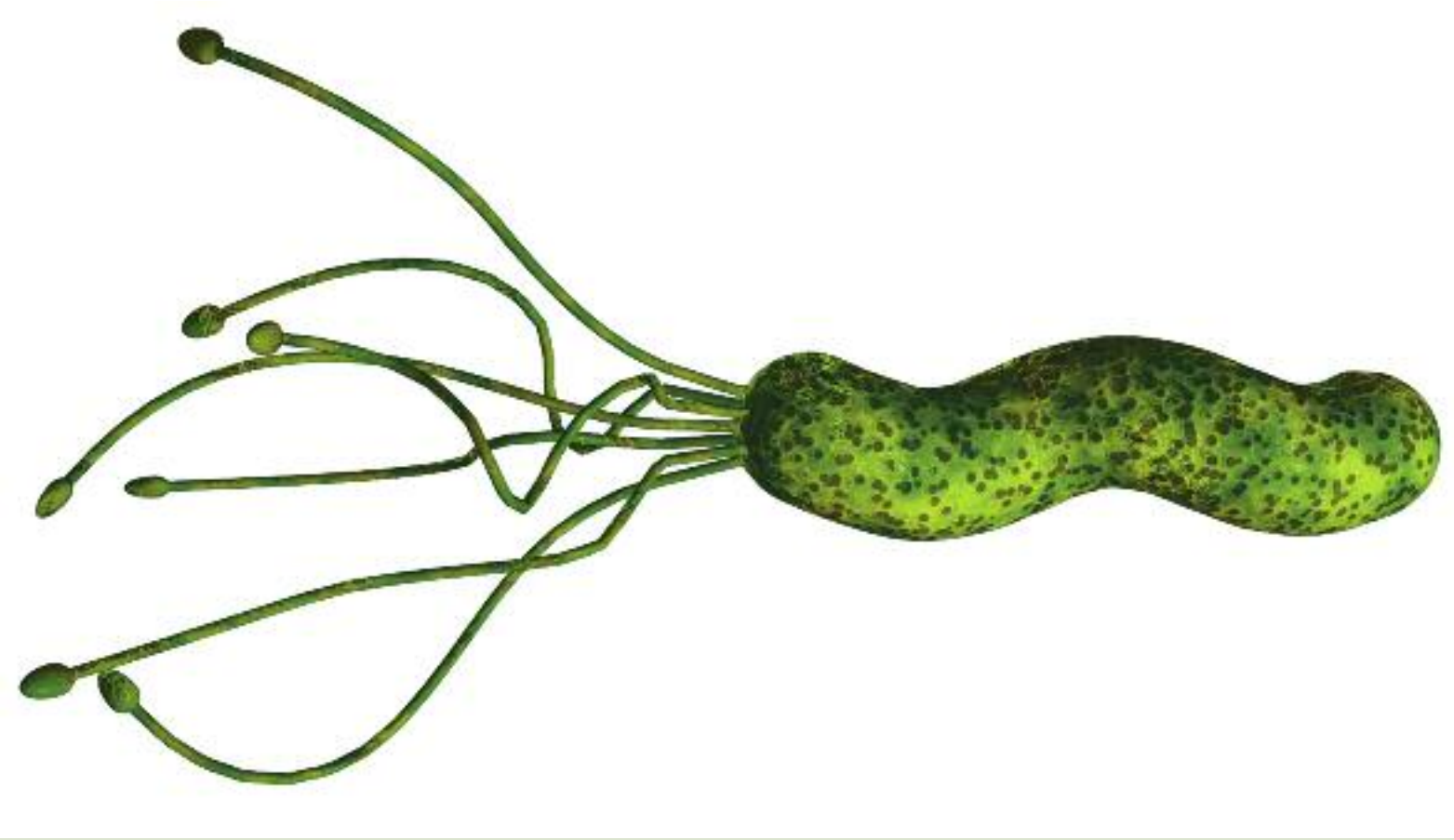

Fig. 1 Helicobacter pylori (H.pylori image courtesy of www.hpylori.com.au)

What are the indications for the C^{14} Urea breath test?

Medicare Australia has recently changed the rules for the C^{14} Urea breath testing rebate. Testing is now at the discretion of the ordering doctor and all requested tests will attract the Medicare rebate.

There is currently no consensus on the role of C^{14} Urea breath testing in general practice in Australia. It is however, generally accepted that it is a valid test for determining if a patient is actively infected with *H.pylori* both pre and post therapy. Some would also argue that it may prevent patients with positive *H.pylori* serology (but no active infection) being unnecessarily treated with broad spectrum antibiotics. It should always be remembered however, that the clinical interpretation of symptoms and signs is paramount in arriving at the correct diagnosis of your patient, and that a positive C^{14} Urea breath test only tells you that the patient is actively infected with *H.pylori*. If there is doubt about the cause of your patient's symptoms, or if symptoms persistent following successful eradication of the organism then referral to a gastroenterologist for further investigation is strongly recommended. This is particularly important in patients over 40 years of age. The C^{14} Urea breath test is generally accepted as the non-invasive test of choice for determining whether or not eradication of *H.pylori* has been achieved.

Are there safety concerns about C^{14} Urea breath testing?

An issue that is frequently raised is the dose of radiation from C^{14} Urea breath testing. Placed in perspective, the dose of radiation received during the test is equivalent to only three microsieverts (this is one tenth the dose of a plain Chest X-ray and equivalent to half the normal daily background exposure to radiation for everyday living).

Where can C^{14} Urea breath testing be performed?

All Clinipath pathology collections centres are able to perform this test. A booking is not essential but patients can contact their nearest collection centre for further information. It is important that your patients are given the appropriate information prior to testing. This includes the medication restrictions outlined previously and the requirement to fast (no food or water) for a minimum of six hours prior to testing.

Where can I receive advice about interpretation of the C^{14} Urea breath test?

Clinipath Pathology microbiologists will be happy to help with interpretation of your patient's test results. In addition, you may wish to discuss clinical interpretation with the gastroenterologist that you regularly refer to, particularly in the setting of atypical clinical presentations that may require expert advice on the differential diagnosis of the clinical symptoms that your patient is experiencing.

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A guide to ordering Hepatitis Serology

Introduction: Hepatitis virus serological testing is carried out in a number of different clinical situations. This article provides a guide to hepatitis serology ordering in some of the more common scenarios seen in everyday clinical practice. A summary table for requesting Hepatitis serology is provided at the end of this article for your convenience; Table 1.

Suspected acute hepatitis

Patients who present with suspected acute hepatitis could be infected with a number of different viruses. The usual hepatitis panel includes Hepatitis A, B and C. It should however be remembered that Epstein Barr Virus (EBV) and Cytomegalovirus (CMV) are also very common causes of inflammation of the liver particularly in children and young adults. For Hepatitis serology it is sufficient to request "Hepatitis A, B and C serology" on the request form provided that in the clinical notes section of the request form that "?hepatitis" or "?abnormal LFTs" is written. Further clinical history (eg overseas travel) is important for the pathologist to ensure that the appropriate testing has been carried out. The Clinipath Pathology testing protocol is to perform Hepatitis A IgM (and if this is detected we will confirm it with a Hepatitis A IgG antibody test), Hepatitis B surface antigen (HBsAg), Hepatitis B core antibody (HBcAb) and a Hepatitis C antibody in this clinical setting. If EBV is clinically suspected, then this should be specifically requested. Writing "EBV serology" is sufficient. A monospot may also be ordered, it is not as sensitive as EBV serology but may give a rapid answer. Hepatitis E virus should be considered in patients who have travelled to developing countries and who have proven hepatitis and are negative for Hepatitis A, B and C. Hepatitis E virus is a particularly severe infection in pregnant women. Hepatitis D virus can only occur in patients who are Hepatitis B surface antigen positive as it requires Hepatitis B virus replication to exist.

Sexually transmitted disease screening

Hepatitis B may be transmitted by sexual contact and serological testing for patients at risk of Hepatitis B through sexual exposure should be considered. In this instance, we are interested in;

a) whether or not the patient has acquired Hepatitis B in the past (it should be noted that screening immediately following sexual exposure will not detect acute infection and follow up serology would be required) and

b) whether or not the patient is immune to Hepatitis B.

We therefore recommend a Hepatitis B surface antigen (HBsAg) test for the former and Hepatitis B surface antibody test (HBsAb) for the latter. If a request is made for "Hepatitis B serology" as part of an STD work up, then we will routinely perform a Hepatitis B surface antigen but will also do a Hepatitis B surface antibody if specifically requested.

Although Hepatitis C is rarely transmitted by sexual contact, testing is indicated if there are risk factors such as a history of injecting drug use or previous tattooing. Follow up serology in 3 months including Hepatitis B surface antigen and Hepatitis C antibody may be considered in order to detect acute infection following exposure. Please note that Hepatitis B surface antigen testing if performed within several weeks of a Hepatitis B immunization may give a false positive result due to the presence of synthetic Hepatitis B surface antigen in the vaccine.

Immunity following immunization or natural infection

Vaccines are now available for Hepatitis A and Hepatitis B and testing for immunity may sometimes be indicated. It is sufficient to write on the request form "Hepatitis A and B serology" and in the clinical notes write "? Immunity to Hepatitis A and B" or "Post Hepatitis A and B vaccination ? immune". In this scenario, the Clinipath Pathology protocol would be to perform a Hepatitis A IgG antibody and a Hepatitis B surface antibody (HBsAb). Alternatively "Hepatitis A IgG antibody" plus "HBsAb" may be specifically written on the request form. These tests can of course also be ordered as individual tests if required.

Antenatal screening

Hepatitis B may be transmitted at delivery and in the post natal period. Hepatitis B screening is routinely recommended during pregnancy and if Hepatitis B carriage is detected, then prophylaxis for the neonate is indicated. The Clinipath Pathology protocol is to perform a Hepatitis B surface antigen (HBsAg) test to screen for Hepatitis B in pregnancy. It is sufficient to request "Hep B serology" provided that in the clinical notes "antenatal screen" is written. Hepatitis C testing is funded by Medicare Australia for screening during pregnancy. Although its value in helping to prevent neonatal infections is currently limited, this may soon change as we better understand the role of Hepatitis C viral load testing. This will help to define the risk of transmission of Hepatitis C during breast feeding and the role of the mode of delivery (eg Caesarian section) plays in prevention of transmission of infection to newborns. Hepatitis C testing is always indicated in patients with risk factors such as injecting drug use or previous tattooing. Requesting "Hepatitis C serology" is sufficient information on the request form. The current prevalence of Hepatitis C seropositivity in our antenatal population is 0.5%.

Blood or body fluid exposure

The recipient (the person that was exposed)

Where a blood or body fluid exposure has occurred, it is of value to determine a patient's baseline status for Hepatitis B and C (and HIV) and to follow the patient up to monitor for acquisition of these viruses. Immediately post exposure, the aim is to establish a baseline for the person's immunity or

Table 1. Summary Table

Clinical situation	Tests requested *	Tests Performed by Clinipath Pathology	Clinical information required on form
Suspected acute hepatitis	**Hepatitis A, B, C serology**	**HepAIgM, HepBsAg, HepBcAb, HepCAb** – Note: suggest adding Hepatitis E serology in overseas traveller and always consider EBV and CMV serology in acute hepatitis in younger patients	? Hepatitis or abnormal LFTs
STD screen or post sexual exposure	**Hepatitis B serology** **Hepatitis C serology**	**Hepatitis B surface Antigen (HepBsAg)** – this will be done routinely in an STD screen. This will need to be followed up to detect acute infection. **Hepatitis B surface Antibody (HepBsAb)** – measures baseline immunity as a guide to immunization. This will be done if specifically requested. **Hepatitis C Antibodies** – indicated in IV Drug users ,tattoos etc	STD screen
Immunity post immunisation	**Hepatitis A serology** **Hepatitis B serology**	**Hepatitis A IgG Antibody** **Hepatitis B surface Antibody (HepBsAb)** – guidelines for re-vaccination are available in the Australian Immunisation Handbook Note: These can be ordered individually	? immunity post Hep A and B vaccination
Antenatal screen	**Hepatitis B serology** **Hepatitis C serology**	**Hepatitis B surface Antigen (HepBsAg).** Follow up serology may be required later in pregnancy if the patient is exposed to Hepatitis B. **Hepatitis C Antibodies** – always indicated in IV Drug users, tattoos etc	Antenatal screen
BLOOD/ BODY FLUID EXPOSURE RECIPIENT (Initial testing)	**Hepatitis B and C serology (and HIV serology)**	**Hepatitis B surface Antibody (HepBsAb)** – this establishes immune status and guides Hep B prophylaxis **Hepatitis C Antibody** – important for OH&S reasons and establishes baseline	RECIPIENT – baseline post blood/body fluid exposure or RECIPIENT – baseline post needle-stick exposure
DONOR (Initial testing)	**Hepatitis B and C serology (and HIV serology)**	**Hepatitis B surface Antigen (HepBsAg)** **Hepatitis C Antibody**	DONOR – baseline post blood/body fluid exposure or DONOR – baseline post needle-stick exposure

** Please note that this table only includes the Hepatitis serology testing required and other serological tests may be indicated in specific clinical situations e.g. HIV serology etc.*

prior exposure to these viruses. We therefore recommend Hepatitis B surface antibody (HBsAb) testing be performed on the person who was exposed. This will help guide the Hepatitis B prophylaxis required for the exposed person. The current edition of the Australian Immunisation Handbook is the best guide to this prophylaxis. Documenting the patient's Hepatitis C antibody status is also important for legal and occupational health and safety reasons. It is sufficient to write on the request form "Hep B and C serology" provided that in the clinical notes you state "RECIPIENT – baseline test post blood exposure" or "RECIPIENT – baseline test post fluid exposure" or "RECIPIENT – baseline testing – needle stick injury". Follow up testing will be determined by the results of initial testing of the recipient and donor.

The "donor" or "source" (the source of the blood or body fluid)

In cases where the source of the blood or body fluid is known, it is of value to determine the person's infective status for Hepatitis B and C (and HIV). We therefore routinely recommend testing for Hepatitis B surface antigen (HBsAg) and Hepatitis C antibodies (and HIV serology). If HBsAg is detected, then further testing such as Hepatitis B e Antigen (HBeAg) may be indicated to better define the risks of transmission to the recipient. We recommend discussing this further testing with the clinical microbiologist. Likewise, if Hepatitis C antibodies are detected, then there may be benefit in some circumstances for testing the donor for Hepatitis C RNA by nucleic acid testing such as PCR.

Summary

Although Hepatitis serological testing is complex, provided the appropriate clinical information is provided to the laboratory, we will be able to ensure the most appropriate testing is performed for your patient.

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New Protein Electrophoresis (QEP) Machine for Biochemistry

Fig. 1 Helena Spife 3000

As of November 2006 as part of our ongoing commitment to quality, Clinipath Pathology has introduced a new Protein Electrophoresis system, the Helena SPIFE, see Fig 1. This replaces our previous capillary electrophoresis system and offers the following advantages:

- More reliable identification and typing of paraproteins occurs, as the SPIFE electrophoresis gel is directly visualized (Fig. 2), whereas capillary electrophoresis relies on an indirect scan.
- Ability to now perform urine protein electrophoresis inhouse. This will improve our turnaround time, as previously this could not be reliably performed on capillary electrophoresis and thus had to be referred.
- Reliable quantitation of IgM paraproteins. Capillary electrophoresis is known to markedly underestimate these para-proteins on occasion.
- The SPIFE is the most widely used method in Australia, thus results are comparable with many other laboratories.
- Improved instrument reliability and thus more reliable turnaround times.

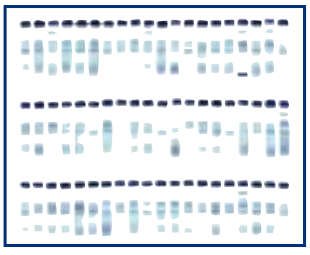

Fig 2 Spife Electophoresis Gel

Dr Sydney Sacks
Chemical Pathologist

A note from our Microbiology department

1. Swab for Microscopy, Culture and Sensitivity (Bacterial)

Collection:
Blue top swab with transport medium. Record the site of collection on swab container and request form.

Storage:
Store specimen at room temperature.

Note: Specimen collected in transport medium (Blue top) cannot be used for PCR.

2. Swab for PCR testing

Collection:
Orange top wire swab (dry) in empty sheath. Record the site of collection on swab container and request form.

Storage:
Store specimen at room temperature.

Common tests requested include:
N.gonorrhoea, Chlamydia, Ureaplasma/Mycoplasma
Herpes I/II, Influenza, Adenovirus, Enterovirus, Bordetella.

Note: Orange top (dry) swabs are unsuitable for microscopy, culture and sensitivity.

To ensure that we can provide you with a fast and accurate service, please clearly indicate on the request form the microbiological tests required.

Collection Centre News

New centres

Perth City
713 Hay Street Mall
Mon-Fri 8.00am-5.00pm
Sat 10.00am-1.00pm
T: (08) 9226 0128

Kelmscott
53 Railway Avenue
Mon-Fri 8.00am-1.00pm, 1.30pm-5.00pm
Sat 8.30am-11.00am
T: (08) 9390 4736

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