

Message from the Director

I would like to welcome readers to the 2003 Spring edition of this newsletter. There are a number of articles that we hope you will find educational. We have also provided information on IPath services together with proposed changes that will lead to improved service delivery.

- **Laboratory Information System (LIS) (Omnilab) Changes**

IPath will be separating the Omnilab LIS and patient data base from South East Health (SEH) and operating independently, commencing the 11th October, 2003 using the same version 9.4.2 of software. Initially this will involve copying of the combined SEH and Illawarra Health (IH) patient database, converting to a new and improved operating system and loading the programs and data base onto servers in IH. On the 6th December the software will be updated to version 9.5.2.

Currently the LIS uses a combined patient database of SEH and IH patients with the management of the LIS network based at SEH. It has now become apparent that the combined data base has the potential for breaches of patient confidentiality. Therefore IPath have decided to separate the patient database and program management from SEH and to manage the program locally within the Illawarra. This will have the benefit of improving the performance of our LIS and will enhance the speed with which problems can be resolved and improvements made. Users will notice several immediate changes to the use of the system as a result of this separation.

- **Improved features of the data base separation**

IPath will now be able to print patient reports, in response to medical officers requirements, at scheduled times throughout the day. This option has not been available to IH previously as report printing has only been available at night due to limitations of the network arrangements with SEH.

IPath will be able to provide both electronically selected fax reports and also encrypted emailed reports to those medical officers requiring this service. This will be available following the upgrade to version 9.5.2 on the

6th December.

An improved results enquiry program will be available known as "Courier", which provides direct access to the data base and up to date laboratory result information to the enquirer. Results can be presented either cumulatively or non-cumulatively. These results can be printed and appear very similar to our routinely printed pathology reports. Dr Anthony Elderfield (02 4222 5406) can be contacted to provide training and instruction on the use of this program if a scheduled training session cannot be attended.

- **Unavailable features with the new data base**

The **Ward Information System (WIS)** will no longer function as the laboratory result enquiries program as this is a SEH program which has been superseded and is to be replaced by the use of the Omnilab program "Courier".

SEH patient results will no longer be accessible on the new patient database.

- **LIS, IT communication or data base problems – HELP REQUIRED**

All help calls between 7:30am to 5:30pm on normal working days are to be logged via IH ISD Help desk (02 42225522 or helpdesk@iahs.nsw.gov.au) or, after hours, to the Central Specimen Reception (CSR) of IPath on 02 4222 5008. These calls will be co-ordinated and triaged to IPath IT Support "IPITS" group. You will be provided with a log number for the call and, where required, this can be used to follow up progress or resolution of any problems.

- **Review of Pathology Services in NSW**

NSW Health is undertaking a review of public pathology services in NSW. This review is aimed at improving the pathology services and detailed terms of reference have been established. Consultants have been contracted to undertake the review and their report, due at the end of October, is to be reviewed by a committee of Department of Health Officers, Area Health Service CEO's, Directors of Finance and Directors of Pathology Services. I will keep you informed as to the recommendations of this review.

Dr Gary Schier

Laboratory Diagnosis of Pertussis

Introduction

Pertussis (whooping cough) is a notifiable respiratory infection caused by the fastidious Gram-negative bacterium, *Bordetella pertussis*. It is highly contagious, spreading by airborne respiratory droplets. Despite a dramatic reduction in the incidence of pertussis and its complications since the introduction of infant vaccination in the 1950s, outbreaks continue to occur every 3-5 years. The last peak in pertussis notifications in NSW occurred in 2000/2001 suggesting that we can expect a rise in the number of cases in the next year or two. Immunity following childhood vaccination wanes after 7-12 years while immunity after natural infection wanes after approximately 15 years. Consequently adolescents and adults are potentially susceptible to pertussis and, in NSW during 2000, the peak incidence occurred in the 10-19 year age group. Such individuals usually have milder disease and are rarely affected by serious complications but can serve as a reservoir of infection for unvaccinated children and infants, the group at highest risk of complications and pertussis-related mortality.

Clinical Features

The clinical course of classical pertussis can be divided into 3 stages:

- 1. Catarrhal or coryzal stage (days 1-7):** a prodromal phase consisting of mainly upper respiratory tract infection symptoms such as a runny nose.
- 2. Paroxysmal stage (weeks 2-4):** characterised by coughing paroxysms with an inspiratory “whoop” and often associated with post-tussive vomiting. Lymphocytosis may be noted on a full blood count and differential during this stage.
- 3. Convalescent stage (weeks 5-12):** a non-productive cough may persist for up to 3 months.

The clinical manifestations of pertussis in adolescents and adults with waning immunity are often less severe and may be atypical. Such individuals generally present with nothing more specific than a prolonged non-productive cough, often associated with post-tussive vomiting. Pertussis needs to be considered in any person with a persistent coughing illness.

Laboratory Tests for Pertussis

Laboratory confirmation of a clinical diagnosis of pertussis is important for public health responses. Laboratory tests are increasingly relied upon to establish a diagnosis of pertussis in cases with atypical clinical manifestations such as a prolonged dry cough, which can be caused by other respiratory pathogens such as *Mycoplasma pneumoniae*, *Chlamydia pneumoniae* or even *Bordetella parapertussis*.

The laboratory tests that can be used to diagnose pertussis are:

1. Pertussis Culture

Culture of *Bordetella pertussis* from nasopharyngeal secretions collected by pernasal swab or via nasopharyngeal aspirate. This method has excellent specificity but low sensitivity, particularly after the first 2 weeks of the illness. Sensitivity is significantly reduced by prior antibiotic therapy and culture is useful only in the catarrhal and early paroxysmal stages of the illness in individuals not already exposed to antibiotic therapy.

For culture of pernasal swabs a fine wire swab is inserted pernasally to collect nasopharyngeal secretions. Best results are obtained by inoculation of selective Pertussis agar plates at the time of specimen collection (i.e. at the bedside) together with the use of specialised charcoal-based transport media.

Bordetella pertussis generally takes at least 3-4 days to grow and cultures are routinely incubated for 7 days before a negative result is issued.

2. Pertussis PCR

Nucleic acid amplification by use of the polymerase chain reaction (PCR) is more sensitive and more rapid than culture for the diagnosis of pertussis in the catarrhal and paroxysmal stages of the illness. This test is less likely than culture to be adversely affected by prior antibiotic therapy. It is unlikely to be useful in the convalescent stage of the illness. Occasional false positive results can occur.

Suitable specimens include dry nasopharyngeal swabs, nasopharyngeal aspirates or even dry throat swabs. Swabs should be fine wire pernasal swabs of the type used for pertussis culture but should be submitted to the laboratory DRY in their original container, not in any type of transport medium.

3. Pertussis Serology

Demonstration of a *Bordetella pertussis* specific antibody response can be used to diagnose pertussis after 2 weeks of

illness and serology is the only valid diagnostic method in the latter stages of the illness.

Pertussis IgG seroconversion or demonstration of a rising pertussis IgG antibody level on paired serum samples collected 10-14 days apart can confirm recent *Bordetella pertussis* infection but can also be seen in response to pertussis vaccination. Likewise pertussis IgM antibodies also rise after pertussis vaccination. Most partially immune individuals with pertussis already have high pertussis IgG antibody levels by the time they present for assessment of their symptoms and it can be difficult to know whether these high IgG levels are due to recent pertussis infection or are a response to prior vaccination or past natural infection. In contrast, pertussis IgA antibodies rise only transiently after *Bordetella pertussis* infection and don't tend to rise after vaccination. Consequently assay for pertussis IgA antibody is the main serological method used in the diagnosis of pertussis. Detection of pertussis IgA antibodies in serum from a patient with a cough of more than 2 weeks duration is considered as presumptive serological evidence for a diagnosis of pertussis.

The specificity of detection of pertussis IgA antibodies is quite high (~98%) but the sensitivity of this test is low (~25%). In addition, the IgA system is not fully developed until adolescence and IgA responses in children may take several weeks to occur. IgA responses in infants less than 2 years old are often poor, limiting the utility of this test in that age group.

Because of these problems with sensitivity, a negative pertussis IgA result does not exclude a diagnosis of pertussis and repeat testing may be required, particularly in children.

There is currently no reliable serological test to demonstrate protective immunity to pertussis.

Pertussis Diagnosis: which test, when?

The choice of diagnostic tests for pertussis depends on the duration of symptoms:

Symptoms < 2 weeks:

- Pertussis Culture and PCR are most useful
- Serological diagnosis not possible but collection of a serum sample is useful as a baseline to demonstrate an antibody rise in a subsequent sample

Symptoms for 2–4 weeks:

- Pertussis PCR and IgA serology are most useful

Symptoms for 5-12 weeks:

- Pertussis IgA serology is the only useful test

Pertussis culture is performed daily on-site at IPath Illawarra Pathology's Wollongong Hospital laboratory. Samples for pertussis PCR and serology are referred to a Sydney teaching hospital reference laboratory where the testing is performed once or twice weekly depending on demand.

Pernasal swabs for pertussis culture and PCR, pertussis selective agar and transport media can be obtained by contacting the IPath Illawarra Pathology Microbiology Department (phone 42225008). The Clinical Microbiologist is available (phone 42225008 or on call via Wollongong Hospital switchboard) for advice and assistance in the collection of pernasal swabs for culture and PCR testing.

Opening of New Shellharbour Laboratory

A new Shellharbour pathology laboratory is due to open mid next year as part of the A&E redevelopment at Shellharbour Hospital. This laboratory will provide routine diagnostic testing for Clinical Chemistry, Haematology and Transfusion with all other testing being done at the Wollongong laboratory. As a prelude to opening the new laboratory IPath have employed outpatient collection staff to provide a much needed service to the residents and medical staff. The collection rooms are located in the existing laboratory area and are staffed from 7:30am to 5:30 pm Monday to Friday and 7:30am to 12:30pm on Saturdays.

Improved Courier Service to the Milton and Shoalhaven Areas

A new twice daily courier service has commenced that will provide courier services between Wollongong Hospital, Shoalhaven Hospital and Milton Ulladulla Hospital. Where urgent work is to be couriered outside of the scheduled times this has also been provided, although this will be at an additional cost. Any feedback on this service or additional services required can be directed to Mr Andriske (02 42225353).

• 24 Hour Service – Shoalhaven Laboratory

The Shoalhaven laboratory is now staffed seven days per week 24 hours per day. Staff are no longer required to be recalled after hours to perform urgent testing. The staffing for the after hours period has been provided mainly to ensure that timely testing of urgent work occurred. This now enables clinicians to undertake appropriate treatment of patients, based upon their pathology results, in a more timely manner.

Both the Wollongong and Shoalhaven laboratories now have pathology staff available on the premises on a 24 hour basis, 7 days a week.

The Numbers Do Add Up Dr Fernando San Gil

Clinical Chemistry Department
IPATH: Illawarra Pathology

The IPATH Clinical Chemistry Department reports over 1 million test results per year. A great deal of effort goes into ensuring the analytical validity of the end-result that appears on a Doctor's report, but there are a host of pre-analytical, analytical and post-analytical variables that can exert an effect. This article briefly outlines the measures taken by the laboratory to minimize analytical influences, and maximize the reliability of test results and ensure the confidence of clinicians.

Choosing the Right Assay Methodology

Choosing the most appropriate assay methodology is first, and possibly the most important step, to achieving analytically valid results. Generally, there are a number of alternative methodologies, and suppliers, of assay reagents for a given analyte. The laboratory chooses the most appropriate assay methodology after assessing a range of different factors, such as: the type of equipment and infrastructure needed, staffing requirements, expected frequency of testing, reputation and reliability of manufacturers and suppliers, assay performance in in-house and independent evaluations, precision, stability of reagents, known interferences, analytical range, robustness, standardization, acceptance in laboratories generally, cost etc. Once an assay methodology is chosen, it is always performed strictly according to manufacturers' instructions.

Internal Quality Control

Whether an assay is run as a batch or continuously throughout the day, the laboratory checks the analytical validity of patient results before their release. For all assays, commercial quality control (QC) fluids are analysed concurrently with patient samples to achieve this step. This process identifies variations in analytical accuracy or precision, within and between runs, that may affect the validity or interpretation of individual and cumulative patient results.

Assaying QC fluids is a powerful tool that allows the laboratory to assess the analytical performance of an assay. First, because the concentration of the analyte in question is known, the laboratory can quantitatively assess the accuracy (or closeness to a predefined target value) and precision (the spread of results away from the target value) of an assay before results are

released. Second, because the analyte in different QC fluids are present at known concentrations, the performance of an assay across a wide analytical range can be determined quantitatively. Third, by collecting analytical data for QC fluids over long periods of time statistical algorithms may be applied to uncover unfavourable trends (Table 1), such as systematic (bias) or random (imprecision) errors, that may affect assays from time-to-time (Table 2). For patient results to be accepted, results for QC fluids must demonstrate both accuracy and precision as determined by the QC rules. This process provides confidence in an assay and allows problems to be resolved quickly, without impacting on patient results. Fourth, properly applied QC rules have predictive value. The "process capability", calculated from the medical allowable limits (see below) and the precision of the methodology used, is a measure of the performance and stability for an assay over time. Fifth, QC fluids are tailored specifically to have the same analyte concentrations and fluid matrix as the patient samples being tested. So, QC fluids with serum, urine or CSF matrices are used as appropriate to mimic any matrix effects of the sample type in an assay.

3. External Proficiency Programs

Commercially available External Proficiency Programs provide the laboratory with another powerful tool to confirm the analytical validity of patient results. The iPATH Clinical Chemistry Department currently participates in 18 national and international external proficiency programs that cover all the analytes tested by the laboratory. Examples of external proficiency programs include the RCPA Australian Quality Assurance Programs and the UK-based International Cyclosporin Proficiency Testing Scheme. Specimens (whose analyte concentrations are known only to the organizers) are sent to the laboratory throughout the year, assayed by the laboratory, and the results sent back to the organizers. Regular reports sent back by the organizers give the laboratory an independent (or external) assessment of the laboratory's performance for the different assays. Reports give the accuracy and precision achieved over time for the different assays, the laboratory's performance compared to other laboratories performing the same assay, and the assay's performance compared to other methodologies, instruments or reagents for the same assay.

4. Defining Clinical Performance Limits

The purpose of the quality process used by the laboratory is to detect errors, arising from both systematic and random variability, that make a patient result invalid. However, there is no doubt that setting the limits for medically acceptable errors is problematic. For example, limits for error detection have no relevance if the inherent imprecision of an assay is so poor it cannot identify genuine, clinically relevant, changes in the concentration of an analyte (false negatives). Likewise, limits have no relevance if they flag changes in the concentration of an analyte that are due to normal biological variation (false positives). Different strategies (Table 3) are

used to define the clinical performance limits for an assay, but no single strategy is universally applicable. For many analytes, a system based on a fraction of normal biological variation provides the most widely accepted solution. Tables documenting the total allowable error are available (e.g. www.westgard.com; RCPA). By incorporating these published allowable limits into the statistical algorithms used by the laboratory rejection limits can be set for an assay.

5. Laboratory Accreditation

Clinicians have an expectation of high quality results, enabling them to make clinical decisions. Testing laboratories have an obligation to ensure that the assays performed meet the end users' expectations. As mentioned above the laboratory monitors its own short and long-term performance with internal quality control and external proficiency programs. But, in addition to these self-evaluation measures, the laboratory undergoes regular assessment of global practices and policies in a process called "laboratory accreditation". In Australia, the National Association of Testing Authorities (NATA) fulfils the task of assessing and accrediting laboratories. Accreditation is a rigorous process that assesses the laboratory's policies and performance against a written and internationally recognized standard, currently ISO17025, and against other peer laboratories. Continued accreditation by NATA is, therefore, confirmation of a laboratory's ongoing high standard of performance.

The different facets of quality used by the laboratory and summarized in this report are designed to ensure the analytical validity of results, but more importantly, to provide confidence in the results within objectively defined tolerance limits.

Rule	Explanation
	One QC value exceeds +/- 2 sd from target mean
1 _{3s}	One QC value exceeds +/- 3 sd from target mean
2 _{2s}	Two consecutive QC values exceed +/- 2 sd from target mean
R _{4s}	The difference between the high and low QC value within a run exceeds 4 sd
10 _x	Ten consecutive QC values fall on one side of the target mean

Systematic Error	Random Error
Method bias	Chemical interference
Instrument bias	Instrument faults
Reagent lot bias	Analytical faults
Calibration bias	Specimen integrity

Fraction of reference range	Based on current rather than appropriate assay performance
Physician surveys	
Consensus values	
State-of-the-art technology/methodology	Determined objectively using external proficiency programs
Biological variation	Imprecision related to normal biological variation. Imprecision is arbitrarily set to some proportion of the biological variation.

Challenges in Cytology workshop

On Saturday the 13th September 17 Cytotechnologists and pathologists from IPATH, Southern.IML and the south Sydney area attended the "Challenges in Cytology Workshop" held on level 8 at Wollongong Hospital. The workshop was a collaboration between IPATH Illawarra Pathology and The NSW Cervical Screening Program.

Facilitated by Dr Stephen Braye from Hunter Hospital, the workshop was designed to highlight the reasons why cytological errors occur & to provide participants an opportunity to view and discuss diagnostically difficult cases.

New Pathology Tests now available ON-Site

Effective from the week commencing 25 August 2003, the assays shown in the table below will be performed routinely by the Clinical Chemistry Department of iPATH: Illawarra Pathology.

These assays were previously referred to laboratories in Sydney.

Analyte	Days Assayed	Specimen type	Reference Interval
Tacrolimus	Tuesday & Thursday	EDTA whole blood	*
Homocysteine	Monday	Serum	<15 umol/L
Beta-2-Microglobulin	Monday	Serum	<3.0 mg/L

* 12 hour trough blood level 20ug/L for first 2 weeks and 15ug/L for next 12 weeks is recommended for renal transplant recipients.

Outpatient Pathology Tests Available Through Illawarra Health Pathology Service

Medical practitioners and other health care workers in the Illawarra and Shoalhaven will be aware of the quality clinical consultative service provided by the specialist pathologists of IPath Illawarra Pathology, the area-wide pathology service of Illawarra Health. You may not be aware that IPath Illawarra Pathology also welcomes referral of patients from private medical practitioners for outpatient pathology tests.

IPath Illawarra Pathology is committed to providing a quality diagnostic and consultative pathology service locally in the Illawarra and Shoalhaven regions. Its quality system is certified to ISO17025 and the service is accredited with the National Association of Testing Authorities and the Royal College of Pathologists of Australasia.

Illawarra Health welcomes and actively encourages referral of patients by local medical practitioners for pathology tests at IPath Illawarra Pathology. Such outpatient test referrals show active support for the local public hospital pathology system so that it can continue to provide the quality clinical advice you know and expect. This support will allow IPath Illawarra Pathology to continue to improve on the provision of a comprehensive 24 hours a day, 7 days a week pathology service for the facilities of Illawarra Health and the communities of the Illawarra and Shoalhaven.

To improve our outpatient service to patients and health care workers of the Illawarra, in the last 6 months IPath Illawarra has extended the outpatient blood collection service at Shellharbour Hospital to include Saturday mornings and has introduced a Community Home Blood Collection Service.

Experienced and dedicated nursing and technical staff now perform blood collections for pathology tests at each of the following IPath Illawarra Pathology outpatient collection facilities:

So, the next time your patients need pathology tests, think about the option of referring them to IPath Illawarra Pathology and support your local public pathology service.

Shellharbour Hospital (located near the Emergency Dept.)

Phone 42952487

Monday to Friday 7.30 am – 5.00 pm

Saturdays 7.30 am – 12.30 pm

Wollongong Hospital (located on level 2, Cancer Care Centre)

Phone 42225472

Monday to Friday 8.00 am – 5.00 pm

Shoalhaven District Memorial Hospital (Nowra)

Phone 44239235

Monday to Friday 9.00 am – 5.00 pm

Generally no prior appointment is necessary but some complex tests may require a pre-arranged appointment. If in doubt please phone one of the outpatient collection facilities on the numbers listed above.

For the convenience of people who find it difficult to attend one of our outpatient collection facilities, IPath Illawarra Pathology, in partnership with Illawarra Community Health, are able to provide a Community Home Blood Collection Service. This allows patients in the Northern Illawarra (from Kiama through to Helensburgh) to have blood collected by skilled and dedicated community nurses in the comfort of their own homes. This service is available Monday to Friday 8.30 am – 4.30 pm and on weekends 8.30 am – 11.30 am. You can refer your patients for **Home Blood Collection** by phoning **1300 792 755**. Pathology request forms should be **faxed to 42285623**. Feedback received so far has indicated that this service has been immensely beneficial to patients of the Northern Illawarra and it is hoped that we can extend the service to include the Shoalhaven region in the not too distant future.

IPath Illawarra Pathology bulk bills and so your patients are not confronted with any out of pocket expenses for specimen collections or tests performed by IPath Illawarra Pathology.

Pads of personalised IPath Illawarra Pathology request forms can be obtained by contacting our Customer Liaison Officer, Mr David Andriske, on 0411446169. David also welcomes any feedback, comments, suggestions or enquiries about our service.

HAEMATOLOGY PATIENT SUPPORT GROUP

IPath's Haematology Department, in consultation with the Leukaemia Foundation, are piloting a new Mentoring Programme in the Illawarra for patients with haematological malignancies (ie leukaemia, lymphoma, myeloma). This involves selected Mentors (patients currently in remission from their own disease) providing emotional support to newly diagnosed patients (or patients receiving active treatment). If you have any patients who may benefit from this type of service please contact Kerrie Jones at IPath on 42534570 who will be more than happy to discuss this service further