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Inside this issue

Gordon Purdie and colleagues recently published a study in the *Journal of Rheumatology* documenting that medical laboratory workers in New Zealand who had worked with solvents had more than double the rate of severe Raynaud's Phenomenon (RP). Eight percent of those who had worked with solvents had severe RP compared with 3% among those who had not worked with solvents. In this issue they comment on their findings as well as linking other solvent exposures to RP and connective tissue diseases. They give advice on minimising solvent exposure, when to seek medical advice, and when to eliminate exposure.

Elly Sekikawa and colleagues compared chromogenic and conventional media in the isolation and identification of urinary tract pathogens. Eighty nine clinically significant organisms were isolated from 239 urine specimens with white cell counts of greater than 50 million/L. Chromogenic media were able to identify 70% of the isolates on Day 1 compared to 12.2% by conventional methods. The replacement of blood agar/MacConkey agar plates and Cystine-Lactose-Electrolyte-Deficient agar plates with the chromogenic BBL CHROMagar Orientation was recommended based on its superior ability to detect mixed cultures, the ability to directly identify common urinary tract pathogens and its higher isolation rate of micro-organisms.

Sandy Leverett conducted a retrospective audit on tumour marker requests at the Hawke's Bay District Health Board Hospital laboratory to determine if the requests had been ordered appropriately according to the Best Practice Advocacy Centre (BPAC) guidelines. With a few exceptions, the hospital based requests were found to be appropriate by the BPAC guidelines. However, about half of the requests from community General Practitioners were inappropriate by the same criteria.

One of the most commonly encountered primary immunodeficiency is common variable immunodeficiency (CVID). Christian Christian presents a case study of CVID and used lymphocyte surface markers and B-cell memory cell studies to confirm the cause in a nine-year old patient.

Earlier this year the NZIMLS conducted a survey among members that aimed to find out how well it, and the services it provides, performs. Rob Siebers and Ross Hewett, on behalf of Council, analysed the results and present them in a special article in this issue. Top services and activities rated by the members were the journal, Council newsletter, CPD programme and the Executive Office; while the web site and promotion of the profession were rated low. Top activities of importance to members were Council governance, web site, CPD programme and QMLT/QSST examinations. Although the response rate was low, results from the survey will be valuable for the NZIMLS Council in improving its services to its members.

In this issue is another journal questionnaire for members to obtain CPD points. As from now, the NZIMLS CPD Co-Ordinator, Jillian Broadbent will take over from the Editor in marking the questionnaires and informing members if they have achieved 5 CPD points. The questions will continue to be set by the Editor and Deputy-Editor from articles in the Journal.

Correction

In the August 2011 issue (volume: 65: page: 68) questions 6 and 7 of the April 2011 journal questionnaire had identical answers. The correct answers for these two questions are:

6. Why is early identification of cefotoxin-resistant organisms necessary.

Early identification is necessary as the appropriate treatment might reduce the spread of the resistant strains, consequently reducing patient mortality in hospitalised patients.

7. Why should a genotypic test be used for detection of AmpC producers.

As a significant number of isolates harbouring the bla AmpC gene could not be detected by the TDET phenotypic method.

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Raynaud's Phenomenon and other serious health risks from laboratory work with solvents

Gordon L Purdie, Dianne J Purdie and Andrew A Harrison

Because Raynaud's Phenomenon (RP) appeared to be common in a cytology department, where it was thought of as a normal part of growing old for women, we suspected something in the work environment or a work practice might be causing RP. RP is associated with many conditions and is normally seen as colour changes in fingers in cold, typically white and blue. When considering conditions associated with RP and possible work-related causes we thought that, if there is a high rate of RP among cytology department workers, it might be caused by solvent exposure. There is evidence that solvent exposure causes scleroderma (1,2), an autoimmune connective tissue disease with RP being a common symptom. The solvent xylene is normally used in cytology and histology. We conducted a postal survey of scientists, technicians and laboratory assistants from cytology, histology and transfusion medicine departments. It was hoped that most of those from transfusion medicine would have not worked with solvents.

Raynaud's Phenomenon and solvents

We found that laboratory workers who had worked with solvents had more than double of the rate of severe RP and have published the survey in the *Journal of Rheumatology* (3). Eight percent of those who had worked with solvents had severe RP compared with 3% among those who had not worked with solvents. After adjusting for age and sex, those who had worked with xylene or toluene and either acetone or chlorinated solvents had an almost nine times greater risk of severe RP. Higher rates of severe RP were associated with longer durations of working with xylene or toluene.

Given the evidence that solvents might cause scleroderma and undifferentiated connective tissue disease (signs, symptoms and laboratory abnormalities that suggest a connective tissue disease, but which do not meet criteria for any specific rheumatic disease) (4,5), these increased rates of severe RP could be early preclinical scleroderma or another connective tissue disease. Other signs of early scleroderma include antibodies and nail-fold capillary abnormalities. RP, with some of these signs, is predictive for scleroderma (6,7). Our findings could be of serious concern since scleroderma and some other connective tissue diseases have high morbidity and mortality.

Other solvent related diseases

As well as this evidence linking solvent exposure to RP and connective tissue diseases and there is also some evidence linking solvent exposure to multiple sclerosis (8). Solvent exposure also causes central neurotoxicity, peripheral neuropathy, acute poisoning and contact dermatitis (9). Solvent exposure has also been linked to renal failure, reproductive disorders, multiple chemical sensitivity, and several cancers, particularly laryngeal, naso-pharyngeal, bladder, leukaemia, non-Hodgkin's lymphoma and multiple myeloma (9).

Minimising solvent exposure

There is no known safe level of solvent exposure. Solvents are absorbed through our lungs and skin. Skin absorption occurs from the air and from direct contact (10). The Department of Labour also produces Workplace Exposure Standards (WES) (11). Its levels are not upper limits of safe exposure. We do not know what vapour levels have been in medical laboratories. However, there

are historical references to high levels in medical laboratories. One study reported xylene concentration in the atmosphere at a hospital laboratory well above the Threshold Limit Value (12). Another found, with no extraction fans operating, a xylene level of 75 ppm, above the WES of 50 ppm, and a formaldehyde level of 13 ppm (the WES has a ceiling of 1 ppm) (13). For xylene the WES does not consider skin contact. It also does not consider interactive effects of simultaneous exposures. Ketones interfere with the metabolism of several solvents (14). Acetone is a ketone that is used in medical laboratories. In rats and mice, blood concentration of xylene was higher with simultaneous acetone exposure and its decline slower than without acetone exposure (15). This was a large effect and suggests the WES should be considerably reduced when both these solvents are used. Xylene is not cleared within 24 hours, hence with daily exposure there will be increasing body levels (16).

In our survey 81% of people working in histology or cytology departments had handled wet slides without gloves. Skin absorption models have been developed (10), showing that when air levels are low skin contact with xylene could be the main exposure source. For example, they suggest that there is similar absorption of xylene from having 100cm² of skin exposed for 10 minutes to inhaling vapour for 8 hours at one fifteenth of the WES.

In 1992 the Department of Labour produced guidelines for the safe use of organic solvents (17). These recommend elimination, if not practicable isolation, and if exposure was unavoidable then minimisation.

Wearing appropriate gloves is a simple way to reduce one source of exposure. At the time of our survey, mid 2006, 49% of people working in histology and cytology had worked with xylene or toluene wet slides without gloves during 2006. The 1992 Department of Labour guidelines recommend the use of viton gloves for xylene and toluene as it provides excellent protection. Nitrile gloves provide fair protection from xylene and toluene and are not recommended. Nitrile is permeable to some organic solvents, including xylene and toluene which come through the gloves after about an hour and half an hour respectively (18). Different solvents require different gloves, for example, viton and nitrile are rated as poor for acetone and butyl excellent.

When to go the doctor

RP is common. Our research has confirmed a prevalence in New Zealand comparable with countries with a similar climate; about 20% of women and 5% of men (19). In most cases it is a relatively benign complaint. Cold hands and colour changes are the most common symptoms, but in some cases pain and numbness can interfere with daily activities. In rare cases it may be severe enough to cause digital ulcers and even gangrene. RP is sometimes associated with chilblains, especially in younger people, causing transient localised red plaques, itch and a burning sensation in the affected areas. People with RP should see their general practitioners if the symptoms are easily provoked, occur in warm temperatures, impinging on function or causing concern or significant discomfort. Investigations may be performed if the history and examination suggest that RP may be a symptom of a more generalised autoimmune condition, particularly in cases of new-onset RP in adults.

Medical advice should be sought in all cases where the onset of symptoms follows exposure to solvents. This is because solvent exposure can, in rare cases, lead to the development of connective tissue diseases, of which RP may be an early manifestation.

When to eliminate exposure

If you are concerned that solvent exposure is giving rise to problems with your health, or may do so in the future, you may wish to eliminate your exposure to solvents. We do not know if solvent exposure only initiates these diseases or whether continued exposure makes them worse. Cancers might be initiated, and neurotoxicities made worse. Magnant et al found some differences in patients with scleroderma between those occupationally toxically exposed and others, suggesting that the exposures influence the severity of scleroderma (20). They hypothesized that toxic agents may amplify the cellular response rather than the humoral response and that people with scleroderma should stop continued exposure. If you have signs or symptoms that could be early CTD a precautionary approach would be to eliminate your solvent exposure.

Author information

Gordon Purdie, BSc, Senior Research Fellow¹
Dianne Purdie (nee Stanley), CT(ASC) CT(IAC)²
Andrew Harrison, MB ChB FRACP PhD, Rheumatologist and Associate Professor³

¹Dean's Department, University of Otago Wellington, New Zealand

²Wellington, New Zealand

³Department of Medicine, University of Otago Wellington, New Zealand

Corresponding author

Gordon Purdie, Department of Public Health, University of Otago Wellington, PO Box 7343, Wellington South, New Zealand. E-mail: Gordon.Purdie@otago.ac.nz

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Comparison of two chromogenic media and conventional media in the primary isolation and identification of urinary tract pathogens

Elly Sekikawa, Miomir B Vidicki and Mary K Bilkey

Abstract

Objective: To evaluate the performance of two chromogenic media, UriSelect 4 (US, Bio-Rad Laboratories) and BBL CHROMagar Orientation (CO, Fort Richard Laboratory Ltd), compared to that of a conventional method, for the primary isolation and identification of urinary tract pathogens.

Methods: A total of 239 urine specimens (with white blood cells >50 million/L) processed in the LabPlus Microbiology Laboratory (Auckland City Hospital) during the period of January-February 2009 were tested. Each specimen was routinely processed using a conventional method which utilises a split Blood agar/MacConkey agar plate (BA/MC, Fort Richard Laboratory Ltd) and Cystine-Lactose-Electrolyte-Deficient agar plate (CLED, Fort Richard Laboratory Ltd). Specimens were also inoculated onto US and CO. The resulting cultures were enumerated and isolates identified when defined criteria were met. The results were compared and any discrepancies investigated.

Results: A total of 89 clinically significant organisms were isolated. The number of organisms which were isolated and identified correctly by US, CO and BA/MC was 87 (97.7%), 88 (98.9%) and 84 (94.4%) respectively. The chromogenic media were able to identify 70% of the isolates on Day 1 compared to 12.2% by conventional methods.

Conclusion: The replacement of BA/MC and CLED with CO was recommended and implemented at LabPlus based on its superior ability to detect mixed cultures, the ability to directly identify common urinary tract pathogens and its higher isolation rate of micro-organisms.

Key words: culture media, chromogenic substrates, microbiological technics, urinary tract infection, laboratory diagnosis

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Introduction

Urinary tract infections (UTIs) are prevalent worldwide and are considered to be the most common type of bacterial infection in humans. In the community, the majority of UTIs are uncomplicated but are often recurrent. The incidence of these infections is high, with an estimated 80-90% of women experiencing at least one episode during their lifetime (1). Its importance in the hospital setting is also profound, where they are responsible for 40-60% of all nosocomial infections (2). The aetiology of nosocomial UTIs are often more diverse than uncomplicated community-acquired infections and can be frequently polymicrobial (3).

The role of the microbiology laboratory in the diagnosis and monitoring of UTIs is extensive and comprises a significant part of the daily workload. At LabPlus, the microbiology department receives approximately 40,000-50,000 urine specimens a year. The laboratory protocol for processing these specimens includes urine dipstick chemistry, microscopy and the utilisation of CLED agar for a colony count (4). The decision to culture the urine is then based upon microscopy results, primarily the presence of bacteria and number of white blood cells (>10 million/L). BA/MC is used as the primary plate for recovery of urinary pathogens. In addition to the split plate, a Colistin-Nalidixic acid-Agar plate (CNA, Fort Richard Laboratory Ltd) is also inoculated if the patient is pregnant

or is catheterised to better visualise Gram positive organisms. Identification of bacteria recovered from these media is then based upon colonial characteristics and the results of biochemical tests.

Since 1990, chromogenic culture media have been commercially available as an alternative way to detect bacterial pathogens (5). Such media contain specific enzyme substrates which when utilised release coloured dyes resulting in pathogens forming coloured colonies.

Currently, there is a range of chromogenic media that is available commercially for the isolation and identification of urinary tract pathogens. This study focuses on two of these media – US and CO. Both media incorporate chromogenic enzyme substrates which allow for the detection of bacterial enzymes -glucosidase (-GLU), -galactosidase (-GAL) and tryptophan deaminase (TDA) (6,7). Utilisation of these substrates results in the development of unique coloured colonies. In addition, both media also have the ability to prevent swarming of *Proteus* spp.

The aim of this study was to evaluate the performance of two chromogenic media, CO and US, compared to the conventional method for the isolation, enumeration and identification of urinary tract pathogens. This study also aimed to investigate incubation time flexibility of chromogenic media. Finally, the possibility of replacement of conventional media with one of the chromogenic media was explored.

Materials and methods

Specimens

Urine specimens sent to LabPlus Microbiology for microscopy, culture and sensitivities (MCS) were used. A total of 239 samples were included – 174 midstream urine specimens, 29 catheter urine specimens, 35 casual urine specimens and 1 bag urine specimen. The samples were collected during the months of January and February 2009. A criteria of white blood cells >50 million/L or the presence of bacteria seen in microscopy was utilised in order to increase the chance of isolating clinically significant cultures for the study.

Chromogenic media

Quality control of the media was performed for each new batch to check for correct colour development for a range of organisms. Half of a plate was used per sample. Both chromogenic media require 18-24 hours of incubation.

Day 0

Urine specimens meeting the criteria for the study were inoculated onto both US and CO using a 0.001mL disposable plastic loop to achieve isolated colonies. The laboratory number of each specimen was noted to allow access to information on the paperless Delphic Micro system (e.g., microscopy results, specimen type). The media were placed in a box (to protect the chromogenic substrates in the media) and incubated initially for 18 hours at 35 ± 2°C in ambient air.

Day 1

To test the flexibility of the incubation time, both media were read at 18 hours, 24 hours and prolonged incubation (40 hours).

Identification procedures were performed at 18 hours unless the culture looked in need of longer incubation. Each plate was enumerated and a code given (0 = A0, 10^7 = A1, 10^7-10^8 = A2, >10^8 = A3; organisms/L). A0 and A1 cultures were not identified (insignificant). A2 and A3 cultures were identified if there was a pure growth of an organism, or, if a mixed sample had <math><10</math> million epithelial cells per litre on microscopy in which case the predominant or up to two organisms were identified. If an A2 or A3 sample had >10 million epithelial cells per litre on microscopy and three or more organisms upon culture, no organisms were identified (likely contamination). Any amount of *Streptococcus agalactiae* (Group B streptococci, GBS) was reported for specimens of colony was recorded for both media.

from pregnant patients.

Presumptive identification of the organisms by colour was made according to the manufacturers' instructions (both media had the same colour reactions). Confirmatory tests for *Escherichia coli*, *Enterococcus* spp. and *Proteus mirabilis* were performed as suggested by the manufacturers, allowing their identification on Day 1. The presumptive identification of the other organisms was confirmed by conventional methods used in LabPlus. Table 1 shows the identification chart used in this study. At both 18 and 24 hours incubation, a detailed description of the appearance of each type

Table 1. Identification chart based on chromogenic colour production (references 6 &7).

Colour of colony	Presumptive identification	Confirmatory tests
Pink (β-GAL +)	<i>Escherichia coli</i>	Spot indole – positive*
Blue-green small (β-GLU +)	<i>Enterococcus</i> spp.	Gram stain – gram positive cocci*
Beige with brown halo (TDA +)	<i>Proteus mirabilis</i>	Spot indole – negative*
Large blue/purple (β-GLU +)	<i>Klebsiella</i> , <i>Enterobacter</i> , <i>Serratia</i> , <i>Citrobacter</i> spp. (KESC group)	Remel RapID ONE identification kit
Beige with brown halo (TDA +)	<i>Proteus</i> , <i>Morganella</i> , <i>Providencia</i> spp. (PMP group)	Spot indole – positive Remel RapID ONE identification kit
Diffuse sheeny pale orange often with greenish pigment	<i>Pseudomonas aeruginosa</i>	Oxidase – positive Cetrimide plate - pigment
Small white dry	Yeast (<i>Candida</i> spp.)	Wet film – budding yeast CHROMagar™ Candida
Small cream/yellow	<i>Staphylococcus aureus</i>	Catalase – positive
Small pale pink	<i>Staphylococcus saprophyticus</i>	5% Salt Agar, DNA agar and Trehalose Mannitol Phosphatase Agar (TMPA)
Small white (catalase positive)	<i>Staphylococcus</i> spp.	
Small translucent pale blue	<i>Streptococcus agalactiae</i> (GBS)	Streptococcal Grouping Latex kit – Group B
Very fine blue	<i>Lactobacillus</i> spp.	Gram stain – Gram Positive bacilli typical lactobacilli
Other	Unknown	Investigation required

*recommended by manufacturer and allows confirmation of identification on Day 1

Day 2

Cultures were examined for the final time at 40 hours incubation and any differences in appearance were noted. Any confirmatory tests put up the previous day were examined and results recorded.

Day 3

The results from conventional routine cultures of each specimen in the study were obtained from the Delphic Micro system and recorded. Any discrepancies between the results obtained by the conventional method and the chromogenic study were investigated.

Results

Culture results

Of the 239 samples cultured, 155 (65%) were not identified, 76 (32%) were followed up and identified and 8 (3%) were isolated and identified by some but not all three media (i.e., discrepancies). Out of the 76 specimens which met the criteria for identification, 62 grew single organisms and 6 grew two clinically significant organisms. The remaining 8 specimens revealed GBS from urine specimens of pregnant patients.

Table 2 summarises the 74 isolates identified in the study (excluding GBS recovered from pregnant patients). *E. coli* was the primary isolate in the study (55.4%), followed by the KESC group (9.5%) and *Enterococcus* spp. (9.5%).

Table 2. A summary of the 74 isolates identified in the study (excluding GBS from pregnant patients).

Organism	Exact match			Same ID but difference in purity	Total number of isolates
	Pure	Mixed predominantly	Two isolates	Pure or mixed predominantly	
<i>E. coli</i>	24	6	2	9	41 (55.4%)
KESC group					7 (9.5%)
<i>E. cloacae</i>	3				
<i>K. pneumoniae</i>	2		2		
<i>Enterococcus</i> spp.	3	1	3		7 (9.5%)
<i>P. aeruginosa</i>	2		2	1	5 (6.8%)
<i>C. albicans</i>	2	1		1	4 (5.4%)
<i>S. aureus</i>	1	1		1	3 (4.1%)
CNS*	1		1		2 (2.7%)
Other <i>Candida</i> spp.	1		1		2 (2.7%)
GBS				1	1 (1.4%)
<i>P. mirabilis</i>	1				1 (1.4%)
<i>Lactobacillus</i> spp.				1	1 (1.4%)
All species	40 (54.1%)	8 (10.8%)	12 (16.2%)	14 (18.9%)	74

*CNS, coagulase negative staphylococci

Fourteen of the cultures obtained the same final identification by all three media, but media differed greatly in their ability to demonstrate mixed growth (i.e., detection of a pure growth compared to detection of a mixed growth with a predominant isolate). Mixed growth was seen in 11 (78.6%), 6 (42.9%) and 5 (35.7%) cases in US, CO and BA/MC respectively.

During the study a total of 45 urine specimens from pregnant patients were cultured. Eleven out of 45 (24.4%) were found to

harbour GBS. Eight cases were recovered from all three media, the remaining 3 cases showed discrepancies in isolation of this organism.

Table 3 summarises the discrepancies found in the study. Of the eight discrepancies, seven should have resulted in identification. Of the eight discrepancies, CO was correct in six of the cases, US in five and BA/MC in two.

Table 3. Summary of discrepancies

Organism(s)	Medium with correct interpretation	Description of inconsistency
GBS (in pregnant female)	US and CO	Both US and CO recovered A2 growth with a mixture of organisms which included GBS. BA/MC recovered A1 growth with no GBS
GBS (in pregnant female)	US and CO	
GBS (in pregnant female)	BA/MC	Both US and CO grew a mixture of organisms but not GBS. However, GBS was recovered on BA/MC
<i>C. albicans</i>	US and CO	Both US and CO recovered A2/A3 growth whereas the conventional method recovered A1 growth resulting in no identification
<i>P. aeruginosa</i>	US and CO	
<i>Lactobacillus</i> spp.	US and CO	
GBS, <i>Enterococcus</i> spp. and <i>Staphylococcus</i> spp.	CO (≥3 organisms carried out) ID not	CO grew an equal mixture of 3 organisms and thus were not identified. US grew an equal mixture of GBS and <i>Enterococcus</i> spp. which were identified. BA/MC grew an equal mixture of GBS and <i>Staphylococcus</i> spp. which were identified
<i>Streptococcus bovis</i>	BA/MC	Colonies on US and CO were identified as <i>Enterococcus</i> spp. based on colour formation and Gram stain. The identification of <i>S. bovis</i> was made by conventional method on Day 5 using Crystal GP (BBL)

A total of 89 clinically significant organisms were isolated in the study (74 non-GBS organisms + eight GBS organisms + seven organisms which should have been identified from the discrepancies). The number of organisms which were isolated and identified correctly by US, CO and BA/MC was 87/89 (97.7%), 88/89 (98.9%) and 84/89 (94.4%) respectively.

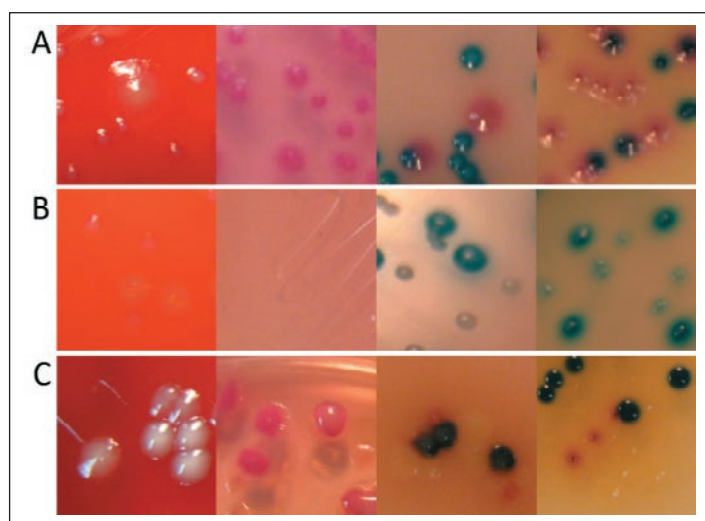
Isolates were identified faster by chromogenic media compared to conventional methods. 69.5% of all significant isolates were identified on Day 1 on both chromogenic media compared to 12.2% using conventional methods.

Incubation times and colour production by chromogenic media

24 hours of incubation was the most reliable period for observing cultures. The major concern at 18 hours of incubation was in regards to some of the Gram positive organisms. There were a few cases in which white non-distinct colonies (mostly *Staphylococcus* spp.) at 18 hours looked pure but on review at 24 hours colour development of some of these colonies had occurred (e.g., light pink or light yellow). Prolonged incubation (~40 hours) yielded bigger colonies and sometimes irregular looking colonies, however, the colour of the colonies did not change.

Colour production by the majority of organisms was accurate and corresponded well with the manufacturers' descriptions. However, presumptive identification of *S. aureus* based only on colour production was not reliable. The US reading chart showed *S. aureus* as yellow colonies, while CO described the colonies as opaque cream. During the study, white, cream and yellow colonies of *S. aureus* were encountered.

Figure 1. Colonial appearance on BA, MC agar, US and CO (from left to right). A. *E. coli* and *Enterococcus* spp.; B. *Enterococcus* spp. and GBS; C. *E. coli*, *K. pneumoniae* and *P. mirabilis*.



Discussion

The gold standard for the diagnosis of UTIs is the quantitative culture of urine samples on solid media. Traditional media include CLED agar, BA and MC agar. Presumptive identification of urinary pathogens and detection of mixed cultures on such media can be difficult, time consuming and requires experience. The development of media which utilise various chromogenic substrates has made the process of interpreting urine cultures easier and faster. Previous researchers have demonstrated the equal or superior performance of various chromogenic media compared to conventional media for the isolation and identification of urinary tract pathogens (8-18). The results from this study were in agreement with prior findings.

In this study, isolation and identification of isolates was found to be best on CO (98.9%), followed closely by US (97.7%) and least favorable by the conventional method (94.4%). Chromogenic

media carry many advantages which can be seen at every point of the culture reading and identification process. The initial visual screening of a chromogenic plate compared to BA/MC is easier, faster and more reliable (Figure 1). Coloured colonies also allow for more accurate detection of mixed cultures which help to identify contaminated specimens, leading to reduced workload and unnecessary work up of clinically insignificant organisms (8,10). With regards to quantification, chromogenic media allow for a more accurate count since very small colonies are easier to see and stand out from the media compared to CLED agar. Importantly, enumeration and identification can be performed on the same plate unlike the conventional method (CLED for enumeration, BA/MC for identification).

Most organisms isolated in the study were correctly presumptively identified based on colour production as described by the manufacturers. However, colonies of *S. aureus* exhibited a range of colours. This observation was consistent with the findings of Scarparo et al. (17). It is recommended, therefore, that colonial colour should not be used for the presumptive identification of *S. aureus* due to its unreliability.

Definitive identification of *E. coli*, *P. mirabilis* and *Enterococcus* spp. is possible on Day 1 with the use of chromogenic media and a rapid test allowing for earlier antibiotic therapy initiation. Spot indole (for confirmation of *E. coli* and *P. mirabilis*) was used without difficulty and the colouration of the colonies did not interfere with the positive reaction. The confirmatory test for enterococci is a Gram stain. This step may be unnecessary as the colonial morphology was very distinctive and there was no confusion with other blue colony producing organisms (GBS, lactobacilli, KESC). Many studies did not perform any type of confirmatory test for enterococci (8-11,13,14,16).

Although there were no issues in this study regarding the identification of these three organisms, other studies have discussed some problems which should be considered. These include the ability of some *Enterobacter* spp. and *Citrobacter* spp. to produce pink colonies (emphasising the importance of a spot indole test) (10-12,17); the ability of *E. coli* to produce cream-coloured colonies (although rarely) (17); and false positive spot indole test for *P. mirabilis* when isolated with indole positive strains of *E. coli* or *K. oxytoca* (17).

Organisms from the KESC group were recovered well and easily distinguished from other Gram negative bacilli. This study showed that a RapID ONE could be inoculated straight from the chromogenic plate to give an identification on Day 1 and was performed on 5 out of the 7 isolates of KESC organisms with no errors. The chromogenic media's ability to detect mixtures was utilised to ensure that a pure growth was present before the test was put up.

Vaginal colonisation with GBS in pregnant patients can lead to neonatal infections thus identification of these organisms in urine specimens is crucial (19). GBS grew on both US and CO as translucent, light blue colonies. However, the colour chart provided by US showed colonies that were translucent and white/grey. This colour discrepancy again raises the issue of the validity of the colour chart and suggests that a more reliable chart should be produced.

There were only 8 discrepancies identified (Table 3) i.e. no correlation between the three methods with regards to isolation and identification of urinary tract pathogens. Three of the cases were due to differing colony counts in which *C. albicans*, *P. aeruginosa* and *Lactobacillus* spp. grew as A2/A3 on chromogenic media but A1 on CLED agar. This observation may be explained by the introduction of technical error in the inoculation and reading of the CLED plate (which uses a calibrated filter strip), or, the chromogenic media's ability to grow and visualise these organisms better. The latter explanation could also account for 2 of the 3 discrepancies regarding GBS in which both chromogenic media

detected GBS not seen on either BA/MC or CNA plates. However, this is contrary to an observation made by Aspevall et al. (11) who found that chromogenic media did not consistently support the growth of Gram positive and fungal urinary tract pathogens. Further investigation of this matter is recommended. The third discrepancy regarding GBS was in favour of the conventional method. This could be explained by the greater inoculum size (0.01mL on CNA compared to 0.001mL on US and CO) which would increase the chance of growing GBS if a patient had a low level of colonisation. Another discrepancy involved the identification of *S. bovis*, an organism that is rarely isolated in urine as a cause of UTI. However, isolation of this organism is significant as faecal carriage is associated with carcinoma of the colon (4,20). An incorrect identification of enterococci was made on the chromogenic media based on the Gram stain reaction and colony colour. It is important when questionable colony colours and morphology are seen that the colony is investigated fully by conventional identification methods.

A limitation of the study was the moderate number of urine samples tested. This was due to the limited time of specimen collection. Only samples received in January and February 2009 were included in the study. In addition, a predefined criteria for specimen inclusion was put in place to increase the probability of processing only positive samples. This further reduced the number of analysed specimens.

Cost is an important issue if a laboratory is considering introducing a new method. Although chromogenic media are more expensive, there may be cost savings due to easier recognition of significant isolates during culture reading and faster, more accurate detection of mixed cultures. A reduction in error may be seen in tests as picking an isolated colony from the plate is easier and more accurate when the colonies are coloured. This in turn will reduce workload by avoiding unnecessary repetition of tests. With time, these savings may be significant and will also result in faster reporting of isolates. Previous researchers have shown that the use of chromogenic media can be less expensive than conventional methods (8,13,17,18). Their conclusions however were based on cheaper chromogenic media (price varies depending on country) (17), unnecessarily excessive methodology (18) and unrealistic labour times (8). The conclusion made by Retelj and Harlander (13) seems to be the most reasonable. They stated that the use of chromogenic media for urinary tract pathogens is cheaper than conventional methods only when there is a high proportion of bacteriuria positive samples and a high isolation rate of *E. coli* and *P. mirabilis*.

A cost analysis was performed on the isolation, enumeration and identification of these two organisms to check the validity of the statement made by Retelj and Harlander. The cost for *E. coli* using conventional methods was \$0.97. This included BA/MC, ¼ CLED agar, spot indole test, ¼ MacConkey agar, ¼ Citrate agar and associated labour costs. The cost for *P. mirabilis* using conventional methods was \$2.20. This included BA/MC, ¼ CLED agar, spot indole test, ornithine test and associated labour costs. Isolation, enumeration and identification of either *E. coli* or *P. mirabilis* using chromogenic media cost \$1.01 and \$0.88 by US and CO respectively. This included ½ chromogenic agar, spot indole test and associated labour costs. Therefore, in the context outlined by Retelj and Harlander it is very likely that the use of chromogenic agar would result in cost savings, especially with the less expensive CO.

The application of chromogenic media for routine use would require some changes. Notably, the incubation time must be strictly controlled as sufficient time is required for the bacteria to convert the chromogenic substrates into colour. Eighteen hours of incubation is minimal while 24 hours is optimal and the most reliable. To ensure this, a rearrangement of the schedule for reading cultures would need to be made. Twenty four hours of incubation was necessary for the complete colour development of staphylococci. This was observed when a pure looking culture at 18 hours revealed mixed growth when re-read at 24 hours. This

phenomenon was not mentioned in the available literature and should be considered. The use of CLED for enumeration and the selective inoculation of BA/MC and CNA plates for identification could be removed and replaced with inoculation of half a plate of chromogenic media for all urine specimens. This would streamline urine processing and will reduce the frequency of technical errors. In addition, if culture is performed on all urine specimens, results from a urine dipstick are unnecessary and could also be eliminated especially as studies have shown that urine dipstick results have low specificity and variable sensitivity (21,22).

The use of chromogenic media will not affect antibiotic susceptibility testing as demonstrated by other researchers (8,9,17,18). The number of mixed susceptibilities that must be repeated on isolated colonies will likely be reduced with the regular use of chromogenic media (8). Antibiotic susceptibilities were not performed in this study and could be investigated to validate this point.

Following the study, BA/MC, CLED and CNA plates were replaced with CO as part of a planned process review of urine processing and culture. Implementation of CO to the routine process at LabPlus required additional training of staff in the use of chromogenic agar. However, once staff were confident in differentiating colonies by colour the time to read plates was consequently reduced.

In conclusion, in this study both chromogenic media were superior to the conventional method and offered additional advantages in the detection and identification of urinary tract pathogens. These chromogenic media can: a) prevent the swarming of *Proteus* spp. and spreading of mucoid *E. coli* and *K. pneumoniae*; b) enable accurate enumeration of isolates; c) enable direct identification of common urinary tract pathogens by colony colour and a rapid test; d) enable faster and more accurate detection of mixed cultures resulting in increased detection rates of contaminated samples; and e) allow susceptibility testing to be performed directly from the plate.

The most common isolate responsible for UTI (*E. coli*) can be identified a day earlier than by conventional methods, allowing the clinician to commence an initial course of antibiotics based on the organism's most common susceptibility pattern. This is important especially in the setting of a nosocomial UTI when patients are often immunocompromised (23). In the laboratory, the use of chromogenic media will significantly reduce the daily workload and will result in cost-savings with time due to improved efficiency.

Conclusions

Due to the slightly better isolation and identification rate of isolates CO was superior to US. The substitution of BA/MC with CO for the primary isolation of urinary tract pathogens was recommended and implemented successfully at LabPlus. Furthermore, the elimination of the CLED agar count and CNA plate from the routine processing of urine samples was possible with the use of CO and helped to improve the overall culturing process.

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Author information

Elly Sekikawa, BMLS, Medical Laboratory Scientist^{1,2,3}
Miomir B Vidicki, MD, Specialist Clinical Microbiologist and Senior Lecturer¹
Mary K Bilkey, BSc PGDip, Section Leader Microbiology²

¹ Auckland University of Technology, Auckland

² Department of Microbiology, LabPlus, Auckland City Hospital, Auckland

³ Currently Medical Student, University of Auckland

Author contributions

Elly Sekikawa carried out the project and was the primary author. Miomir Vidicki and Mary Bilkey conceived and supervised the project and contributed to the writing of the article. The authors have no conflicts of interest to declare.

Author for correspondence

Elly Sekikawa, P O Box 2738, Auckland 1140.
E-mail: elly.sekikawa@gmail.com

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Are tumour markers requested appropriately: a one-month audit of tumour marker requests at Hawke's Bay District Health Board laboratory

Sandy Leverett

Abstract

The objective of this paper was to complete a retrospective audit on tumour marker requests at the Hawke's Bay District Health Board Hospital Laboratory to determine if the requests had been ordered appropriately according to the guidelines issued by the Best Practice Advocacy Centre (BPACnz). A sample period of one month of tumour marker requests from 16.5.11 to 15.6.11 for AFP, β -hCG, CA 125, CA 15-3, CA 19-9 and CEA were viewed to identify whether the clinical information conformed to BPAC guidelines. Where no clinical details were provided, cumulative history was viewed to establish, if possible, the reason for the test request.

Requests were divided between the community General Practitioners and those that were hospital based as either in or out-patients. With a few exceptions, the hospital based requests were found to be appropriate by the BPAC guidelines. However, there were a large number of requests from the community General Practitioners (49% overall) that were inappropriate by the same criteria.

Key words

Tumour markers, BPAC, guidelines, appropriate requests.

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Introduction

Best Practice Advocacy Centre (BPACnz) is an independent New Zealand organization that examines evidence based information, cost effectiveness and New Zealand specific needs to make recommendations to primary health care professionals in New Zealand (1).

Tumour markers are a valuable addition to the test panel used for monitoring disease progression. However, their limitations must be kept in mind in order to ensure they are appropriately requested. Generally there is poor sensitivity and specificity for tumour markers. Values may not rise early enough, they may not rise in all occasions or they may rise due to other factors such as other concurrent disease, transient response to treatment or artefactual results due to testing limitations such as haemolysis, sample quality or delayed testing. This is undesirable, not only as a waste of resources, but also because it can be misleading giving false reassurances or false concern.

Methods

As a response to the BPAC publication entitled 'Appropriate Use of Tumour Markers' (BPAC, July 2010) it was decided to complete a retrospective audit on tumour marker requests at the Hawke's Bay District Health Board Hospital laboratory. Requests were reviewed over a one month period from 16.5.11 to 15.6.11 for AFP, β -hCG, CA 125, CA 15-3, CA 19-9 and CEA to determine whether the clinical information provided with the request corresponded to the BPAC guidelines of appropriate use. Where no clinical details were provided, cumulative history was viewed to establish, if possible, the reason for the test request.

Results and Discussion

Alpha fetoprotein

Alpha fetoprotein (AFP) is a glycoprotein produced initially in the embryonic yolk sac and then later in the foetal liver thus foetal blood concentrations are relatively high (2 – 4 g/L). After birth AFP decreases to reach adult levels of 0-6 μ g/L by about 10 months of age (2).

Analysis of AFP, outside of prenatal screening, takes place because it is raised in various cancers such as liver, germ cell testicular, bowel, stomach, lung, breast and lymphomas. It can also be raised in other situations such as chronic hepatitis or cirrhosis. As a tumour marker, AFP is most often used for testicular cancer or hepatocellular carcinoma (HCC).

With regards to testicular cancer, BPAC states that diagnosis should be made on "clinical signs and symptoms [and] investigations including ultrasound and CT scans" (3). AFP should be analysed for non-seminomatous tumours following diagnosis but before treatment with the rate of marker decline reflecting the response to treatment. BPAC guidelines indicate AFP measurements are not useful for seminomas (3).

The American Association for Clinical Chemistry produces the National Academy of Clinical Biochemistry (NACB) Laboratory Medicine Practice Guidelines. Their current guidelines on tumour markers indicate there is no place for screening for testicular cancers using AFP and that diagnosis is usually confirmed by ultrasonography. AFP, β HCG and LD are "mandatory" before treatment and that AFP is important in evaluating the response to treatment and in early recognition of relapse (4).

The International Germ Cell Cancer Collaborative Group use AFP along with β HCG and LD in a scheme to classify metastatic germ cell tumours and selection of treatment is based on tumour type and prognostic group (4).

In preparation of the NACB guidelines other group studies were evaluated, including those of the European Group on Tumour Markers (EGTM), the European Association of Urologists (EAU), the European Society of Medical Oncology (ESMO) and the National Comprehensive Cancer Network (NCCN), and all groups concur that AFP is important for staging/prognosis, detecting recurrence and monitoring treatment but not for screening (4).

The use of AFP is, however, recommended by NACB to screen for HCC, in conjunction with liver ultrasound, in high risk but asymptomatic groups in order to give "early identification of tumours while they are still potentially curable" (5). Examples of high risk patients are those with cirrhosis, chronic viral hepatitis, haemochromatosis. NACB state an AFP result greater than 20 μ g/L and increasing should prompt further investigation.

Diagnosis of HCC should be through imaging, with AFP levels used as "an adjunct in diagnosis". The European Association for the Study of the Liver (EASL), the British Society of Gastroenterology and the EGTM also all recommend this (5).

In this audit there were 77 requests for AFP over the month concerned. Of these, 28 came from the community GPs, 27 from hospital in-patients and out-patient clinics, and 22 from the Hepatitis Foundation. Of the 28 GP requests, 18 were hepatitis patients being serially monitored, two others were cirrhosis monitoring and seven were inappropriate requests from primary carers by BPAC recommendations. The inappropriate requests had no cumulative results or past history to indicate a valid reason for testing and had the following clinical details:

- abnormal liver function tests, weight loss
- ? testicular mass
- testicular lump
- ovarian cysts
- seminoma review*
- two samples with no clinical details

*BPAC guidelines state AFP is not useful for seminomas; β -hCG and LD should be used instead, but is useful for non-seminomatous tumours (3).

Of the 27 hospital AFP requests, six were for HCC monitoring in hepatitis patients, 18 were appropriate requests for suitable oncology reviews or high risk patient HCC screening. The three inappropriate hospital requests were for seminoma reviews.

β -human chorionic gonadotropin (β -hCG)

β -hCG is a glycoprotein synthesized mainly in the placenta hence its use as a pregnancy marker. However, it is also produced in small amounts in the pituitary with normal ranges of 0-5 IU/L. The alpha subunit is common to FSH, LH, TSH and hCG but the beta unit is unique to hCG which is why it is used to analyse hCG concentrations (2).

β -hCG is raised in trophoblastic tumours, testicular tumours, melanoma, breast cancer, GI, lung and ovarian cancer. It can also be raised in cirrhosis, duodenal ulcers, inflammatory bowel disease, menopausal women and pregnancy. β -hCG's main use as a tumour marker is for testicular cancer. Recommendations are for its use alongside AFP however it can also be useful for seminomatous tumours where AFP is not (3).

There were 16 β -hCG tumour marker requests during the audited period, three from GPs and 13 hospital based. One of the GP requests was appropriate by BPAC standards as it was a seminoma review. However, the other two GP requests were inappropriate in that they were querying testicular masses and had no cumulative review history or clinical history to indicate a diagnosed cancer. The 13 hospital requests were all considered appropriate, being tumour and seminoma reviews.

Cancer Antigen 125 (CA 125)

CA 125 is raised in ovarian cancer as well as other situations such as during menstruation, pregnancy, benign ovarian cysts and endometriosis. The reference range is 0-35 kIU/L, however, values do decline with menopause and aging (2).

BPAC guidelines recommend that CA 125's main role is in the management of ovarian cancer and that it should not be used for screening or diagnostic purposes as it has poor sensitivity for early stage disease (6). It can be used to monitor serous type ovarian cancers and levels following chemotherapy are a strong indicator of disease outcome. It can also be used to detect recurrent disease.

NACB guidelines agree with BPAC that CA 125 is unsuitable for screening. However, they indicate that it can be used with transvaginal ultrasound in the detection of hereditary ovarian cancer in asymptomatic individuals. The NACB also supports the use of CA 125 in differential diagnosis in post-menopausal women with pelvic masses and in correlating sample concentrations with tumour burden and stage, with declining concentrations showing a response to treatment and rises predicting a relapse (4).

The audit identified 47 requests for CA 125, 13 from GPs and 34 hospital based. Of the GP samples only two were appropriate

by BPAC standards having been requested for ovarian cancer monitoring. The other 11 GP requests were considered inappropriate as they had the following clinical details with no result or clinical history found to support the case for testing:

- RA
- 2 x ovarian cysts
- weight loss, immune suppressed
- pelvic scan
- adenexal mass, ?ovarian
- 5 x no clinical details provided

All hospital CA 125 requests were appropriate by BPAC guidelines as they were for monitoring diagnosed patients.

Cancer Antigen 15-3

CA 15-3 is a MUC1 protein antigen that is elevated in breast cancer and also in cases of cirrhosis and benign diseases of the ovaries and breast (4). Because CA 15-3 testing lacks sensitivity in early disease BPAC consider it to have no role in screening or diagnosis of breast cancer, but that its use should be limited to monitoring for recurrence or treatment effectiveness (3).

NACB guidelines also state "current blood-based biomarkers are of no value in early detection of breast cancer" and even that the clinical benefit of CA 15-3 following primary surveillance is unclear (4). This thinking is echoed by the American Society of Clinical Oncology (ASCO), ESMO and NCCN. These groups also concur that CA 15-3 can be useful in palliative care to help decide if a particular type of therapy should be continued (4).

There were 20 CA 15-3 requests during the period of this audit and all of them were hospital based. Only one of these was considered inappropriate by BPAC standards as it had clinical details indicating colon cancer. However, a further look showed this was probably an error on the request form as the clinical history showed a diagnosis of breast cancer.

Carcinoembryonic antigen (CEA)

CEA is a family of glycoproteins. Production starts during foetal development but is found in low levels (0-3ug/L) in healthy adults (2). One of the first tumour markers to be used, levels are raised in colon cancer but also in lung, breast, liver, pancreas, thyroid, stomach and ovarian cancers as well as in ulcerative colitis, cirrhosis and smoking (3). The most common use of CEA results is in the management of colorectal cancer (CRC) patients. BPAC recommendations are that CEA results not be used for screening or diagnosis due to its poor sensitivity and specificity and the low prevalence of CRC in non-symptomatic individuals. It may provide some prognostic information but should only be requested in management of patients with established malignancy (6).

NACB also recommends that CEA not be used as a screening test. They indicate that a preoperative CEA concentration may be used, with other factors, to plan surgical treatment but not to select a patient for adjuvant chemotherapy (4). CEA is widely used in surveillance of CRC but there is no agreement between groups as to the magnitude of change that would be clinically significant.

During the period of this audit there were 109 CEA requests, 30 from GPs and 79 hospital-based. Of the 30 GP requests, 13 were appropriate by BPAC standards (monitoring of diagnosed CRC patients) and 17 were inappropriate, i.e. clinical information given did not meet BPAC criteria and there was no clinical or result history to indicate otherwise. The clinical details give were:

- adenexal mass, ?ovarian
- alternating D&V, ?diverticulitis or cancer
- 2 x change of bowel habit, tenesmus
- iron deficient anaemia
- weight loss, change of bowel habit
- ?colon cancer
- ovarian cysts
- 8 x no clinical details provided

It is worth noting that two of the requests caveated the CEA request with "yes I know, not for primary screening" yet that is just what they appeared to be.

Of the 79 hospital requests, 78 were appropriate by BPAC guidelines but one was a request from the emergency department with clinical details of constipation and abdominal pain with no indicative result or clinical history.

Cancer Antigen 19-9 (CA 19-9)

CA 19-9 is a glycolipid synthesized by normal pancreatic, biliary duct, gastric, colon, endometrial and salivary epithelial cells. The normal reference range is 0-37 kIU/L but this can be raised in cancer of the stomach, bowel and particularly pancreas (2). BPAC recommends that it is not used for screening but only for monitoring known malignancies. It is recognized that use of CA 19-9 has been proposed to differentiate between benign and malignant situations but this has not yet been established with evidence based studies (3). The NACB guidelines state routine measurement of CA 19-9 is not recommended as it is less sensitive for CRC than CEA (4).

During the audit period there were 38 requests for Ca 19-9. One of these was from a GP and the rest were hospital based. All requests were appropriate as per BPAC guidelines being monitoring of diagnosed CRC patients.

In summary, aside from using AFP for hepatocellular carcinoma in high risk patients, tumour markers should not be used as screening tests for malignancies as the lack of sensitivity and specificity is too great. However, the individual markers do all have a role in the management of the already diagnosed patient when used

appropriately. During the course of the audited period there were 42 inappropriate (as per BPAC guidelines) tumour marker requests, which resulted in a cost of over \$800 for the one month audited.

Author information

Sandy Leverett, BA(Adv) HNC, Medical Laboratory Scientist

Laboratory, Hawke's Bay District Health Board, Hastings

E-mail: sandra.leverett@hawkesbaydhb.govt.nz

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Common variable immunodeficiency (CVID); a case study

Christian Christian

Abstract

Immunoglobulins recognize the antigens and initiate mechanism that destroys them. There are five groups of immunoglobulins in the serum which are IgG, IgA, IgM, IgD, and IgE. Immunodeficiency can be classified to primary or inherited and secondary. One of the most frequently encountered primary immunodeficiency is the autosomal dominant common variable immunodeficiency (CVID), which is characterized by hypogammaglobulinaemia and recurring infections with associated lymphocyte abnormalities. A nine year old Caucasian female presented with chronic cough, lethargy, anorexia, and weight loss. Initial laboratory investigation showed a low IgA concentrations with a normal IgG concentrations due to Intragam infusion given in the previous month. Further testing such as lymphocyte surface markers and B-cell memory cell studies indicate a low number of LGL/NK cells and a B-cell maturation defect suggestive of CVID. A month later, the same patient presented with three days history of becoming unwell following her most recent Intragam therapy. In addition to the blood count results (a low haemoglobin level and an elevated reticulocytes count), an elevated total bilirubin, a very low haptoglobin level and a positive direct antiglobulin test (Coombs test) indicated autoimmune haemolytic anaemia (AIHA). Together with antibiotics therapy, immunoglobulin therapy has greatly improved the prognosis of patients with CVID. This case demonstrates the importance of early diagnosis of CVID and treatment to ensure better prognosis.

Key words: immunoglobulin, immunodeficiency, hypogammaglobulinaemia, Intragam.

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Introduction

Immunoglobulins or humoral antibodies are a group of structurally related proteins that recognize the antigens and initiate mechanism that destroys them. The basic immunoglobulin (Ig) molecule is made up of four polypeptide chains consisting of a pair of heavy (H) chains (M_r 50-75 kDa each) and a pair of light (L) chains (M_r 22 kDa each) (1). There are five types of H chain (γ , α , μ , δ , and ϵ) and two types of L chain (κ and λ). The amino acid sequences of the variable regions at the N-terminal ends of the four chains determine the antigenic specificity of the particular antibody molecules (2). Immunoglobulins are synthesized by plasma cells, the progeny of B-stem cells in bone marrow. More mature B-cells which are found mainly in blood and lymph nodes develop receptor immunoglobulins on their surface membranes (2). In the presence of an antigen, plasma cells are proliferated and developed from these B-cells and then secrete specific antibodies capable of binding additional antigen.

There are three major groups of immunoglobulins in the serum which are IgM, IgG (four subclasses), and IgA (two subclasses) and two minor groups which are IgD and IgE. IgM is the most primitive and least specialized immunoglobulin with a pentameric structure. It is the first antibody that appears in response to antigenic stimulation. IgG is the major immunoglobulin produced by plasma cells, making up 70-75% of the total immunoglobulins, which is produced in response to most bacterial and viral infections (2). IgG is the only immunoglobulin that can cross the placental barrier providing passive immune protection for the fetus and newborn. IgA is a monomer and the idiopathic immunoglobulin present in

the respiratory and gastrointestinal mucosa. It can exist in a dimeric form called secretory IgA due to additional secretory peptide called "J piece" (3). This form can be found in tears, sweat, saliva, milk, colostrum, and bronchial and gastrointestinal secretions. While IgE is known as the idiopathic immunoglobulin associated with allergic and anaphylactic reactions, IgD is the only group of immunoglobulins with unknown function.

Immunodeficiency can be classified to primary or inherited causes (rare) and secondary causes (common). There are more than 200 clinical phenotypes of primary immunodeficiency (PID) identified and about 100 of them now have well-defined molecular genetic basis. One of the most frequently encountered PID is common variable immunodeficiency (CVID) or acquired hypogammaglobulinaemia. Kalha and Sellin, however, argue that CVID is the second most common PID, second to selective IgA deficiency (4). Nevertheless, CVID is the most clinically significant form of PID. The clinical course and the degree or type of serum immunoglobulins deficiency varies from patient to patient, hence, the word "variable".

Case presentation

A nine year old Caucasian female presented to the Paediatric Assessment Unit (PAU) at Southland Hospital in Invercargill with chronic cough, lethargy, anorexia, and weight loss. She had been discharged from Christchurch Hospital recently with related conditions.

Immunoglobulins (IgG, IgA, and IgM) were measured on a Roche Cobas 6000 (C501 unit) using an immunoturbidimetric assay according to manufactures' methods. The immunoglobulins concentrations (Table 1) showed a low IgA concentration but a normal IgG concentration which is an atypical finding for CVID. A normal IgG concentrations in this case however, can be explained by the immunoglobulin replacement (Intragam) therapy given while she was treated in Christchurch Hospital in the previous month. Presumably, early CVID diagnosis had been made by the immunologists team at Christchurch Hospital. Unfortunately, the immunoglobulins concentrations result prior to Intragam infusion were not available. A blood specimen was taken for lymphocyte surface markers studies. The results (Table 2) showed normal amounts of CD4 and CD8. However, a low number of LGL/NK cells were identified in the blood, which indicates that the ability of immune system to recognize virus infected cells and certain tumor cells may have been compromised.

A blood specimen was also sent to LabPlus Auckland for B-cell memory cell studies. The results in Table 3 shows reduced switched memory B-cell, consistent with a B-cell maturation defect. A confirmation of CVID diagnosis was therefore made due to lack of LGL/NK cells and a B-cell maturation defect. The patient was sent to Starship Hospital, Auckland for further assessment due to her chest involvement with cryptogenic organizing pneumonia after no growth was found in the blood cultures. She was later discharged from Starship Hospital with three weekly Intragam infusion of 12 gram (maintenance dose) and 50 mg of Prednisone.

Table 1. Immunoglobulins concentrations.

Immunoglobulins	Result	Reference range
IgG (g/L)	9.2	6.1-15.7
IgA (g/L)	0.2↓	0.3-2.4
IgM (g/L)	1.0	0.5-2.4

Table 2. Lymphocyte surface markers.

T Cells	Result	Reference range
CD3 (x10 ⁹ /L)	1.02	0.60-2.60
CD4 (CD3+) (x10 ⁹ /L)	0.56	0.40-1.70
CD8 (CD3+) (x10 ⁹ /L)	0.46	0.20-1.10
LGL/NK Cells		
CD56 (CD3-) (x10 ⁹ /L)	< 0.02 ↓	0.07-0.70
B Cells		
CD19 (x10 ⁹ /L)	0.51	0.07-0.60
Total lymphocytes (x10 ⁹ /L)	1.6	1.5-5.7

Table 3. B-cell memory cell studies.

Memory naive B-cell	Result	Reference range
CD19	32.2%	
CD20	32.3%	
Naive B-cells	88.5%	57.7-79.7%
Naive B-cell phenotype: CD27-IgD+		
Memory B-cells	6.7% ↓	8.7-18.7%
Memory B-cell phenotype: CD27-IgD+		
Switched B-cells	1.2% ↓	5.0-21.0%
Switched B-cell phenotype: CD27-IgD+		
Immunologist comment: Reduced switched memory B-cells. Consistent with a B-cell maturation defect.		

A month later, the same patient again presented to the PAU at Southland Hospital, Invercargill with three days history of becoming increasingly unwell following her most recent Intragam infusion. She had symptoms of worsening lethargy, anorexia, nausea, and low grade fever. She also appeared pale and jaundiced. Upon examination, she had a mild splenomegaly and a palpable lymph node in her right neck.

The blood count results (Table 4) indicate autoimmune haemolytic anaemia (AIHA) due to a very low haemoglobin level and an elevated reticulocytes count. This finding is supported by an elevated total bilirubin (Table 5), a very low haptoglobin level (<0.05 g/L; reference range 0.30-2.70 g/L) and a positive antiglobulin test (Coombs test). It is not possible however, to decide whether AIHA was due to CVID complication, Intragam infusion, or underlying infection. She was admitted to the Children Ward at Southland Hospital the same day. Blood transfusion was delayed due to the presence of an autoantibody in her serum. A blood specimen was sent to New Zealand Blood Service in Auckland for crossmatch before she was transfused with three units of red blood cells over the subsequent two days. Blood cultures were taken peripherally and via PICC line but no growth reported. Initially, Gentamicin and Vancomycin were given intravenously to treat possible infective cause for AIHA. Later, Vancomycin was replaced by Teicoplanin. After commencing intravenous (IV) antibiotics and transfusion, her clinical condition improved. She was discharged three days later with complete five days IV antibiotics, suspended Intragam infusion, 10 mg daily Prednisone, 20 mg daily Omeprazole, and 5 mg daily Folic Acid.

Table 4. Blood count

	Result	Reference range
Haemoglobin (g/L)	49↓	115-150
PCV	0.15↓	0.33-0.42
MCV (fL)	78	75-92
MCH (pg)	25.3↓	26.0-32.0
Platelets (x10 ⁹ /L)	272	150-430
WBC (x10 ⁹ /L)	9.7	4.0-12.0
Neutrophils (x10 ⁹ /L)	6.7	1.80-7.50
Lymphocytes (x10 ⁹ /L)	2.2	1.40-5.00
Monocytes (x10 ⁹ /L)	0.7	0.20-1.00
Eosinophils (x10 ⁹ /L)	0.0	< 1.0
Basophils (x10 ⁹ /L)	0.1	< 0.3
Retic. Count (x10 ⁹ /L)	160↑	20-90

Table 5. Liver function tests

	Result	Reference range
Total bilirubin (μmol/L)	37↑	2-21
Alk. Phosphatase (U/L)	161	90-420
GGT (U/L)	32	< 51
ALT (U/L)	116↑	8-31
AST (U/L)	106↑	< 40
Total Protein (g/L)	68	60-80
Albumin (g/L)	39	35-50
Globulin (g/L)	29	23-34

Discussion

CVID is a disorder characterized by a low level of serum immunoglobulins and an increased susceptibility to infections. In most patients, there is a decrease level in both IgG and IgA. However, it has been found in some patients that all three major types of immunoglobulins (IgG, IgA, and IgM) are decreased (5). Past studies on the cells of the immune system in patients with CVID have shown a degree of lymphocyte abnormalities. Only less than 1% of patients with CVID have a low number of B-cells with the majority patients are found to have a normal number of B-cells, but they fail to undergo normal maturation which is shown by reduced switched memory B-cells in the B-cell memory cell studies (6). Consequently, they lack the mechanism of plasma cell differentiation. Some patients, however, lack enough function from helper T-cells necessary for a normal antibody response which is shown by a low CD4 count or reversed CD4/CD8 ratio (7).

The lymphocyte surface markers studies of the patient in this case study showed a low number of LGL/NK cells. Beside helper T-cells abnormality, a low number of LGL/NK cells may provide alternative explanation for a finding by Kalha and Sellin that some CVID patients have a lack of proliferative responses to T-cell receptor stimulation and decreased expression IL-2, IL-4, IL-5, and interferon (IFN)-γ (4). LGL/NK cells account for up to 15% of blood lymphocytes and express neither T-cell nor B-cell antigen receptor. They release IFN-γ and other cytokines such as IL-2 when activated, therefore they are essential in the regulation of haemopoiesis and immune response (8). The finding of gene defects in CVID has been difficult because of its heterogeneity. However, it has been proposed to be an autosomal dominant condition, affecting both males and females equally (9). Family studies have suggested that CVID gene defects are found in chromosome 2, 11, 16, 17 and 22. The following table shows the different types of CVID according to its gene defect found in Online Mendelian Inheritance in Man (10).

Table 6. Types of CVID according to its gene defect (Adapted from reference 10).

Type	Gene/locus MIM number	Chromosome	Gene/locus
CVID1	607594	2q33	ICOS
CVID2	240500	17p11.2	TNFRSF13B
CVID3	613943	16p11.2	CD19
CVID4	613494	22q13.1-q13.31	TNFRSF13C
CVID5	613495	11q12	MS4A1
CVID6	613496	11p15.5	CD81

The prevalence of CVID is found to be higher in northern European descent with an estimated incidence of between 1:50,000 and 1:200,000. CVID can develop at any age but in general, it has a bimodal age of onset which peaks between ages 1-5 and 18-25 (11). The mortality rate from CVID remains high despite therapy due to delayed diagnosis and by the fact that the immune defects involve the humoral and cell-mediated system (4).

The signs and symptoms of CVID include hypogammaglobulinaemia (IgG, IgA, and/or IgM), poor titre response to vaccination with polysaccharide and protein antigens (e.g. tetanus and diphtheria), and recurring infections (due to pneumococcus, hemophilus and mycoplasma) which cause bronchitis, pneumonia, sinusitis, conjunctivitis, and otitis (11,12). These infections normally respond well to antibiotics but recur upon the discontinuation of medication. Additional symptoms such as viral infection, enlarged spleen or lymph nodes, fatigue, gastrointestinal problems (often due to *Giardia lamblia*), and polyarthritis/joint pain may also present (4,5,11). Even though antibody responses are depressed, patients with CVID may develop autoimmune diseases (5). These antibodies commonly attack either red cells (autoimmune haemolytic anaemia (AIHA)), white cells, or platelets. CVID may also cause additional complications such as chronic lung disease, liver disease, gastrointestinal disease, lymphoma, and granulomatous infiltration.

Generally, the diagnosis of CVID can be made by demonstrating hypogammaglobulinaemia together with poor or absent response to immunization and characteristic clinical manifestation. This is, however, a diagnosis of exclusion. The signs and symptoms of CVID can be confused with X-linked hypogammaglobulinaemia. A more specific diagnosis of CVID can also be made by performing lymphocyte surface markers and B-cell memory cell studies. Patient with CVID may show a low number of CD4 (therefore reversed CD4/CD8 ratio) and/or a low number of LGL/NK cells in the lymphocyte surface markers studies. On the other hand, the B-cell memory studies may show reduced switched memory B-cells.

The main treatment of CVID is immunoglobulin replacement therapy. It can be given intravenously (IVIG), intramuscularly (IMIG), and subcutaneously (SCIG). The goal of the therapy is to maintain serum IgG above 5 g/L at all time. IVIG Intragam is the most common immunoglobulin replacement therapy in New Zealand. It is a sterile, preservative free solution containing 6 g of human protein and 10 g of maltose in each 100 mL. At least 90% of the protein is IgG monomer and dimer. For CVID patients, the dose of Intragam is individualized in the range of 0.2 to 0.6 g per kg body weight per month (13). It can be given as a single dose or as two equal doses at fortnightly intervals. It can also be given undiluted or diluted with up to 2 parts of 0.9% saline or 5% glucose. Intragam contains trace amount of IgA (< 0.025 mg/mL) which may provoke anaphylaxis in patient with IgA antibodies, such as those with IgA deficiency. Intragam can be given to patients with a complete IgA deficiency if the IgA is completely removed (4). Intragam therapy may induce side effects, such as headache, anaemia, nausea, vertigo, neutropenia, thrombocytopenia, and fatigue (13). Together with antibiotics therapy, immunoglobulin therapy has greatly improved the prognosis of patients with CVID. Steroids may also be given to reduce the inflammatory response. However, the prognosis of

CVID also depends how much damage has been occurred to the organs due to autoimmune diseases, infections, and malignancies (5). While SCIG is relatively new treatment, it is widely believed that IMIG is painful and less effective. Intravenous IL-2 replacement has also been considered since the discovery of IL-2 deficiency in CVID (4).

In conclusion, common variable immunodeficiency is a primary immunodeficiency characterized by hypogammaglobulinaemia and increased susceptibility to infections. This autosomal dominant disorder is mainly caused by lymphocyte abnormalities. Besides measuring immunoglobulins concentrations, further testing such as lymphocyte surface markers and B-cell memory cell studies are necessary for correct diagnosis. It is not possible to heal CVID, but it can be controlled by immunoglobulin therapy replacement.

Author information

Christian Christian, BMLSc MNZIMLS, Medical Laboratory Scientist

Automation Department, Southern Community Laboratories, Southland Hospital, Invercargill

Author contributions

CC conceived and researched the study and substantively drafted the article. The author declares no conflicts of interest.

Author for correspondence

Christian Christian, Automation Department, Southern Community Laboratories, Southland Hospital, PO Box 828, Invercargill. Email: christian.christian@southerndhb.govt.nz

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The New Zealand Institute of Medical Laboratory Science and the services it provides. How well does it perform?

Rob Siebers and Ross Hewett; on behalf of the NZIMLS Council

Abstract

The New Zealand Institute of Medical Laboratory Science (NZIMLS) is the organisation that represents those engaged in the profession of Medical Laboratory Science in New Zealand. Its role is to promote professional excellence through communication, education and a code of ethics to achieve the best laboratory service for the benefit of the patient. As such it provides a variety of services for its members. In 2006 a members survey was conducted to determine how well the NZIMLS, and services it provided, performed. Results from that survey identified various areas of concern. Five years on the survey was repeated. A web-based questionnaire was filled in by 379 members, a response rate of 19.7% of the total membership (n=2,013). Top services and activities rated by the members were the journal, Council newsletter, CPD programme and the Executive Office; while the web site and promotion of the profession were rated low. Top activities of importance to members were Council governance, web site, CPD programme and QMLT/QSST examinations. Results from the survey will be valuable to the NZIMLS Council in improving its services to its members.

Key words: survey, NZIMLS, services, communication, education

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Introduction

The New Zealand Institute of Medical Laboratory Science (NZIMLS) represents scientists and technicians engaged in the profession of medical laboratory science in New Zealand. The NZIMLS provides a number of services for its members including a continuing professional development programme (CPD), medical laboratory technician and Fellowship examinations, an annual scientific meeting and discipline specific seminars, a regular newsletter, and a peer-reviewed scientific journal. It also provides various awards for members, has professional representation on Board of Studies Committees of the three New Zealand universities providing an undergraduate medical laboratory science degree, and promotes the profession. Professional affairs are handled by an elected Council while the day-to-day running of the NZIMLS is handled by the Executive Office. The NZIMLS also employs a CPD co-ordinator and website manager and appoints an Editor for its journal (1).

In 2006 a questionnaire was distributed to members whom were asked to rate the performance of the NZIMLS and the services it provides. Results from that survey identified various areas of concern and was helpful for the NZIMLS Council in focussing on how to improve its services for the NZIMLS membership (2). Five years on it was decided to repeat the survey to gauge how well the NZIMLS was performing in its provision of services to members, to identify areas of concern, and where improvement is needed.

Methods

Early 2011 the same questionnaire as used in the 2005 survey was posted on-line on the NZIMLS web site (www.nzimls.org.nz). An e-mail message was sent to all financial members of the NZIMLS explaining the survey. At the time of the survey there were 2,013 financial members consisting of 1,613 Members, 451 Associate Members and 39 Fellows and/or Life Members. In order to improve the response rate, members were offered 2 CPD points

for completion of the survey on-line.

In section one of the questionnaire members were asked to rate, on a Likert scale of 0 (poor) to 10 (excellent), the various services the NZIMLS provides. These were:

- Journal
- Newsletter
- Special Interest Groups
- Annual Scientific Meeting
- Organisational structure
- Sponsorship
- Promotion of the profession
- Website
- CPD programme
- Executive Office services
- Technician examinations (QMLT/QSST)
- NZIMLS Fellowship

If members did not have an opinion about any question they were asked to leave that question unanswered.

In section two, members were asked to rate on the same Likert scale on the above NZIMLS services/activities that were of importance to themselves. Included in this section was NZIMLS representation on the undergraduate medical laboratory science degree programme Board of Studies.

In section three members were asked how long they had been a NZIMLS member, why they joined the NZIMLS, what their current membership category was and what additional benefits they thought the NZIMLS could offer its members. An additional yes/no question was added on whether the NZIMLS should provide CPD records to employers.

Results are presented as mean scores with 95% confidence interval (95% CI).

Results

Out of a membership of 2,013, 397 returned the questionnaire giving a response rate of 19.7%. Of these 94.1% were members and 5.1% were associate members. About half had been a member of the NZIMLS for more than 10 years (52.3%), 19.4% between 6-10 years, 23.5% between 1-5 years and 4.8% less than 1 year. The majority of respondents joined the NZIMLS for professional responsibility (46.2%), 33.9% as part of joining the CPD programme, 11.0% because of interest in the profession and 8.9% for other unspecified reasons.

No comparisons between members and associate members were done due to the low response rates of the latter group. Tables 1 and 2 show the mean scores (with 95% CI) of the NZIMLS services ratings and the services of importance to members together with the results from the 2006 survey for comparison.

Table 1. NZIMLS services and activities ratings. 2011 compared to 2006.

NZIMLS services	2011 mean score (95% CI)	2006 mean score (95% CI)
Journal	7.6 (6.2-8.9)	7.0 (6.7-7.3)
Newsletter	7.6 (6.9-8.3)	6.8 (6.5-7.1)
SIG seminars	6.8 (5.4-8.2)	8.5 (8.2-8.8)
ASM	7.6 (6.0-9.0)	7.7 (7.4-8.0)
Organisational structure	7.0 (5.4-8.6)	7.1 (6.8-7.4)
Sponsorship	7.1 (5.7-8.5)	6.3 (5.9-6.7)
Promotion of profession	6.6 (5.1-8.1)	5.9 (5.5-6.3)
Website	6.1 (4.3-7.9)	7.6 (7.3-7.9)
CPD programme	7.6 (6.2-9.0)	7.1 (6.8-7.4)
Executive Office services	7.5 (6.0-9.0)	7.3 (7.0-7.6)
QMLT/QSST examinations	7.0 (5.4-8.6)	7.5 (7.1-7.9)
NZIMLS Fellowship	6.9 (5.4-8.4)	6.1 (5.6-6.6)

Table 2. NZIMLS activities of importance to members. 2011 compared to 2006.

NZIMLS activities of importance to members	2011 mean score (95% CI)	2006 mean score (95% CI)
Journal publication	6.5 (5.0-8.0)	7.5 (7.1-7.9)
Continuing education	7.0 (5.2-8.8)	8.5 (8.2-8.8)
Council governance	8.6 (8.1-9.1)	6.9 (6.5-7.3)
ASM	6.8 (5.1-8.5)	7.8 (7.4-8.2)
Special Interest Groups	7.2 (5.4-9.0)	8.8 (8.5-9.1)
Promotion of profession	7.3 (5.5-9.1)	8.7 (8.4-9.0)
Website	8.5 (8.0-9.0)	8.3 (8.0-8.6)
CPD programme	7.7 (6.3-9.1)	8.5 (8.2-8.8)
QMLT/QSST examinations	7.7 (6.1-9.3)	7.7 (7.2-8.2)
NZIMLS Fellowship	6.8 (5.0-8.4)	6.1 (5.5-6.7)
BMLSc representation	5.8 (3.9-7.6)	8.4 (8.1-8.7)

About two-third of respondents (61.4%) agreed that the NZIMLS should provide practitioner CPD records to employers. Members were asked an additional three questions and a summary of their responses follows.

What do you expect from your regional representatives?

The overriding response to this question was to actively communicate between the members and Council in matters of local, regional and national importance within medical laboratory science. This was mainly to represent the views of the members and region to Council and to feedback to the members items of professional and national interest from Council meetings.

A strong theme was to visit all the laboratories within the regional representative's region on an annual basis and to keep membership informed of events. Some members were confused as to what NZIMLS council members did or who they were, whereas others felt communication with their respective council members were excellent.

Another theme was active promotion of the profession by Council members to students and the public with some wanting more political activity by Council members and the NZIMLS.

Are there any areas in which you think the NZIMLS could improve?

There was a significant mixture of responses to this question, with a number of re-occurring themes linked to some extent to the previous question, such as communication. Promotion of the profession to the public, politicians and in healthcare generally was continued, with another area being that the NZIMLS become involved in negotiations of the terms and conditions of employment.

More CPD point's opportunities, like regional meetings and SIG meetings, advanced educational opportunities, scholarships, and online learning were other significant themes along with shopping, software, healthcare insurance and holiday discounts being offered to members.

There was in many responses, support of the NZIMLS and Council and the current activities with an understanding of the time restraints and workload of the current councillors and executive.

A portal on the NZIMLS website for direct feedback and or comments to Council was one suggestion as was an interactive online forum.

Do you have any further comments to make about the NZIMLS?

This by far elicited the most comments, some hugely varied to those above and others very much the same. Promotion of the profession at government and public level was a re-occurring theme once again. Management of Council meetings and Council in general were also commented on including less frequent meetings, "road show" type Council meetings in the regions, less corporate governance, but also significant endorsement and support of the current NZIMLS activities and the work of the NZIMLS and Council.

The role of the annual scientific meeting evoked quite diverse comments ranging from the meeting being too long, need more overseas speakers, the scientific program is not diverse enough or does not cater for all levels, should only be in the major centres, more use of video conferencing, more local meetings, and not annually.

The role of technicians in the profession was extensively commented on with regard to lack of registration of those working in specimen services, how there should be more cross-credits of their qualification for the BMLSc degrees, and questions in the survey specifically for technicians.

The respective roles of the Medical Laboratory Science Board (now Medical Sciences Council) and the NZIMLS was commented on and some members would like the NZIMLS to take over some of the activities of the Medical Sciences Council such as issuing APC's and the registration process for overseas graduates.

Underlining concern for the future of the profession was a constant theme in many of the responses and much of this linked to more active promotion of the profession to government, educational institutes and health agencies. The recognition of the importance of medical laboratory science was also linked to these comments.

Discussion

The mean ratings of the services and activities that the NZIMLS provides ranged from 6.1 to 7.6. However, there was a wide spread of ratings within each category. Top ratings (> mean score of 7.5) were for the journal, newsletter, Annual Scientific Meetings, CPD programme and the Executive Office services. Bottom two ratings were for the web site and promotion of the profession. Comparatively, in 2006 SIG seminars, Annual Scientific Meetings, the web site and technician examinations achieved the top ratings while promotion of the profession and Fellowship were ranked at the bottom then.

Top activities of importance to members in 2011 were Council governance, web site, CPD programme and QMLT/QSST examinations while NZIMLS representation on BMLSc degree committees and journal publication ranked bottom. Comparatively, in 2006 continuing education, journal publication, Annual Scientific Meetings, Special Interest Groups, promotion of the profession, web site, CPD programme, NZIMLS representation on BMLSc degree committees and QMLT/QSST examinations all ranked high as important activities by members. However, these comparisons need to be treated cautiously given the low and different response rates of the 2006 and 2011 surveys.

Although the response rate to the 2011 survey was significantly higher than the 2006 survey, 19.7% vs 7.7%, the results of this 2011 survey and comparison with the 2006 survey should be treated with caution as there could be a significant non-response bias. Also, questions can elicit biased answers. An additional limitation was that some questions were not of relevance to some members and in hindsight "don't know" or "not applicable" categories should have been included in the questionnaire.

A copy of all the comments has been distributed to all Council members and NZIMLS employees. Many of the comments are quite specific and within the context of the overriding themes stated above, will be discussed in more detail at Council meetings and feed-back provided to NZIMLS members.

There will be some actions that can be immediately implemented, such as greater engagement at government level and greater communication about activities already in place, but not necessarily communicated to the membership as well as they could be.

The survey was designed to gather an understanding of the needs of the NZIMLS members and to track how well Council is doing in fulfilling those needs.

References

1. Beechey K, Hewett R. The role of the NZIMLS Council. "What we do" and "What can you do for us". *N Z J Med Lab Sci* 2011; 65: 2-3.
2. Siebers R, Buchanan A, Hewett R. Performance of the NZIMLS and the services it provides. Results from a questionnaire. *N Z J Med Lab Sci* 2006; 60: 102-105.

Author information

Rob Siebers, FNZIC FNZIMLS FSB, Associate Professor¹ and Editor²
Ross Hewett, MNZIMLS, Laboratory Manager³ and Treasurer/
Secretary of the NZIMLS²

¹School of Medicine and Health Sciences, University of Otago, Wellington. E-mail: rob.siebers@otago.ac.nz

²New Zealand Institute of Medical Laboratory Science, Rangiora

³LabPlus, Auckland

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Book Reviews

Mosby's Diagnostic and Laboratory Test Reference - 10th Edition by Kathleen D. Pagana and Timothy J. Pagana. Elsevier Australia. ISBN: 978-0-323-07405-6. AU\$53.99.

This manual of diagnostic and pathology tests is a handy small format guide for health providers responsible for ordering the tests. Tests are arranged alphabetically and each test includes the sections: name of test, type of test, test explanation and related physiology, normal findings, interfering factors, procedure and patient care, abnormal findings, and where relevant, contraindications and possible critical values.

For a student or practitioner of medical laboratory science, the guide is probably too general to be of great educational value. However, the section "test explanation and related physiology" will be useful for medical laboratory scientists (both students and practitioners) who wish to quickly revise their theory, and update themselves on the newer assays in our rapidly evolving field.

Inclusion of electrodiagnostic tests such as Holter monitoring, sleep studies and fetal nonstress test are outside the scope of practice for medical laboratory scientists. Conversely, omissions of some laboratory tests, for example transfusion reaction investigations, may frustrate the medical laboratory scientist student. Therefore the book is more suitable for primary health providers than allied health professionals.

Some examples of confusing information are evident. For example, there is a listing for "Coombs test, indirect (blood antibody screening, indirect antiglobulin test [IAT]". A transfusion scientist would be more comfortable if this entry was "blood antibody screening", as the entry pertains to this application of the IAT (a tool used for several applications). Concepts between the antibody screen and the compatibility test become mixed, and a reassurance is given, that if the test is negative, "transfusion should then proceed safely and without any transfusion reaction". Whilst it is true that haemolytic transfusion reaction is unlikely in the case of a negative antibody screen, causes of non haemolytic transfusion reaction have not been screened for in this test.

The section "contraindications" struck the reviewer as useful for health providers ordering tests, however, this entry was not evident against many of the tests. The "interfering factors" section for each entry is very useful, a feature that could be used by both health providers ordering the test and medical laboratory scientists. However, there is no discussion of uncertainty of measurement. Similarly there are no indications of expected turnaround times for tests. Of course this will vary between pathology providers, but it is useful for clinicians to know if a test takes more than 24 hours (as may be the case in prenatal genetic testing for example)

The book is very accessible with language which is not overly technical or jargonised. The cover is waterproof and easy to wipe down; an advantage in a laboratory or hospital setting. Inside the front and back covers is a list of abbreviations for many laboratory tests. This is a nice feature, but the list is not totally comprehensive and could be expanded. Spelling and reference ranges are from USA and not always the same as those we use in New Zealand.

In summary, this reference book may provide a useful addition to other more detailed texts in a pathology library.

Holly Perry, MSc
Senior Lecturer, School of Applied Sciences, Faculty of Health and Environmental Sciences, AUT, Auckland

Manual of Surgical Pathology – 3rd Edition by Susan C. Lester. Elsevier Australia. ISBN: 978-0-323-06516-0. AU\$174.60.

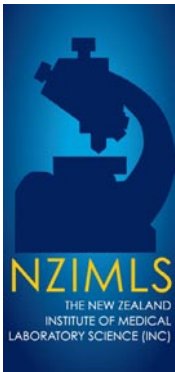
Having reviewed this book in detail we would recommend it to anyone embarking in the direction of dissection in Surgical Pathology. Although it may be more suited to a Pathology Registrar it would be of great benefit to a Medical Laboratory Scientist with a passion for dissection.

The introduction covers basic standard operating procedures such as information that must accompany the specimen such as identification, previous history and current treatment. The author also describes the general principles relating to gross descriptions of specimens. Technical information such as the make up of various Histology fixatives is also included. The pathway through the Histology lab from tissue cassettes to the stained section and final diagnosis is described. The chapter on immunohistochemistry is well set out and easy to understand.

Part two of the book provides a huge amount of detailed information on the dissection of the various tissues that come into the Histology Lab.

In summary this book would be of huge value to anyone who is considering a post graduate course in Histology dissection.

Joe G McDermott, PhD CSci MNZIMLS and Natasha Caldwell, MSc LabPlus, Auckland



Minutes of the 67th Annual General Meeting held at the Labplus, Auckland City Hospital on Friday 5 August 2011 at 4.00pm

PRESENT:

The President presided over approximately 38 members.

APOLOGIES:

Motion:

Moved R Allen, seconded R Siebers

That apologies be accepted from Holly Perry, John Elliot, t Phil Wakem, Christine Story, Rob McKenzie, Tony Mace, Faith Taylor and Kirsten Kelly

Carried

PROXIES

Motion:

Moved W Wilson, B Heaton seconded

That the list of 7 proxies be received.

Carried

MINUTES OF THE PREVIOUS ANNUAL GENERAL MEETING

Motion:

Moved R Hewett, seconded R Siebers

That the minutes of the 66th Annual General Meeting held on 26 August 2010 be taken as read.

Carried

Motion:

Moved C Pickett, seconded R Allen

That the minutes of the 66th Annual General Meeting be accepted as a true and correct record

Carried

BUSINESS ARISING FROM THE MINUTES

Nil

REMITTS AS CIRCULATED

Motion:

Moved R Hewett, seconded W Wilson

That the following Remits be accepted.

1. "THAT Policy Decision Number 3 be reaffirmed

Policy Decision No 3 (1972): Council will make and administer awards to members of the Institute, the details of each award will be recorded and may be amended from time to time by resolution of Council. The summary of these details shall be published annually in the Journal.

2. "THAT Policy Decision Number 5 be reaffirmed."

Policy Decision No 5 (1978): That medical supply companies should not be approached to aid in the finance of Branch or Special Interest Group meetings; companies may be invited to Regional Seminars and although donations may be accepted money is not to be solicited.

Carried

PRESIDENT'S REPORT

Motion:

Moved K Beechey, seconded R Allen

That the President's Report be received. The President acknowledged the work and support that K Taylor had given during his time on Council.

Carried

ANNUAL REPORT

Motion:

Moved R Hewett, seconded J Bird

That the Annual Report be received.

Carried

FINANCIAL REPORT

Motion:

Moved R Hewett, seconded R Siebers

That the Financial Report be received.

Carried

ELECTION OF OFFICERS

The following members of Council were elected unopposed:

President:	K Beechey
Vice President:	C Pickett
Secretary/Treasurer:	R Hewett
Region 2 Representative:	J Bird
Region 3 Representative:	K Allan
Region 4 Representative:	T Barnett
Region 5 Representative:	T Taylor

The results of the elections for:

Region 1 Representative:	L MacDonald	62
	M Matson	110
	S Singh	14

Motion:

Moved R Hewett, seconded T Barnett

That the election of M Matson to the position of Region 1 Representative be accepted.

Carried

Motion:

Moved R Hewett, seconded T Barnett

That the election of officers be approved.

Carried

PRESENTATION OF AWARDS

The award winners were announced and the following awards were presented by the Chairman:

Qualified Medical Laboratory Technician Awards

Donor Services - Elenita Bambol, New Zealand Blood Service
Haematology – Eleanor Claire Hooper, Southern Community Laboratories
Mortuary Hygiene & Technique - Maari Gray, Wellington Hospital
Phlebotomy - Cynthia Robertson, Medlab Hawkes Bay

Honorary Membership

Maurice Sheppard

Life Membership

Robin Allen

HONORARIA

Motion:
Moved R Siebers, seconded W Wilson
That no honoraria be paid.
Carried

AUDITOR

Motion:
Moved R Hewett, seconded W Wilson
That Hilson, Fagerlund Keyse be appointed as the NZIMLS auditors for the 2011/2012 financial year.
Carried

GENERAL BUSINESS

Marilyn Eales acknowledged on behalf of the PPTC, the financial support from the NZIMLS and interest from members.

VENUE FOR THE 2012 CONFERENCE

Science of the Century, Wellington Convention Centre, Wellington, 27-31 August 2012.

VENUE FOR THE 2013 CONFERENCE

Hamilton

Meeting closed 4.45pm

South Pacific Congress Report

What an honour being the first recipient of the Barrie Edwards and Rod Kennedy Scholarship. Barrie was a dear friend and colleague of mine and it was especially poignant for me to honour his memory in this way.

I chose to attend the combined NZIMLS/AIMS South Pacific Congress. This meeting was held on the Gold Coast, Australia on the 8-12 August 2011. The combined meeting offers presenters a platform which is not intimidating, with an audience of peers.

The meeting was opened on Monday by Penelope Wensley, the Governor of Queensland. AIMS and NZIMLS awards were also presented at this time. My scholarship certificate was formally presented to me during the opening ceremony. I think I was more nervous about this moment than my presentation later in the week!

A full and varied program of plenary and concurrent proffered papers followed Tuesday through Friday. Probably the worst part was having to wait until Thursday afternoon to take centre stage myself.

My presentation was entitled Cystic Fibrosis in Adulthood, An Evolving Spectrum Disorder. I described a period of 15 years of sweat testing at Canterbury Health Laboratories, showing the increase in adult sweat test requests, compared sweat chloride

results and CF mutational analysis results and described some atypical findings. The talk went well, apart from a major power point glitch, on my last slide. Apparently I recovered from this very well, though it was a completely different perspective from my side of the lectern, believe me.

For me, the conference was very enjoyable and educational. The congress theme "Lights, Camera, Action" was cleverly incorporated throughout the week's events. The opening cocktail function had movie look-a-likes mingling amongst the delegates. The congress dinner and dance was of a very high standard and most enjoyable.

The meeting came to a fitting close on Friday with the inaugural Bloodisloe Cup. The debate comprised a three person panel from Australia and NZ delegates, thrashing out the topic that there will be no need for pathology laboratories from 2035. Needless to say...we won!

I would like to thank the NZIMLS for making this scholarship possible. I am grateful for the opportunity and the support given to me throughout my journey to presenting at an international conference. I would encourage anyone who might be considering applying for this scholarship to do so- it really is a wonderful opportunity.

Sandy Woods
Canterbury Health Laboratories, Christchurch

President's Report 2011

There was one change to the Council membership this year with Kevin Taylor from Canterbury Health Laboratories standing down as President. The Institute would like to take this opportunity to acknowledge the sterling work and valuable contribution Kevin has made serving the profession over the past seven years on Council. We also appreciate his willingness to continue his involvement in convening scientific meetings. Following this change, Chris Pickett from Medlab Hamilton has been elected Vice President and Council welcomed Jan Bird from Pathlab Waikato as the newly elected region two representative.

Last year's NZIMLS ASM was held in Paihia and despite some prior misgivings concerning the remoteness of the venue proved to be a highly successful event. Sandy Woods from Canterbury Health Laboratories was announced as the inaugural winner of the Rod Kennedy/Barrie Edwards scholarship and more recently Bernard Chambers from Middlemore Hospital was awarded the second scholarship. Our congratulations to both on their achievements and Council looks forward to more applications for these prestigious awards. John Elliott was presented with Life Membership of the NZIMLS for his services to the profession at the ASM and spoke of his work with the Pacific Paramedical Training Centre (PPTC). The PPTC celebrated its 30th Anniversary in 2010; we congratulate them on this milestone and trust they will continue their valued work in providing education and training to staff throughout the Pacific Region for many years to come. This year we join our Australian colleagues for the combined AIMS NZIMLS South Pacific Congress on the Gold Coast. The popular location and expected scientific programme should make this an exciting meeting to attend and we look forward to a good representation from our membership at this congress.

Following the threat of closure of the Medical Laboratory Science courses at Massey University, Council made a submission voicing our concerns on the proposal. Although over recent years problems relating to a shortfall in the workforce have been highlighted, the current provision of the BMLSc and GradDipSci courses throughout NZ have maintained sufficient new graduates to fill the vacancies in our workforce. The full impact of the proposed Massey closure on this situation is unknown and most likely will have significant ramifications for the training of future medical laboratory scientists in NZ. The NZIMLS is keen to enter discussions with the universities and professional bodies to develop a strategic plan that would ensure the future needs of the profession are met, meanwhile the profession continues to monitor the situation and awaits the final outcome.

Further progress has been made this year on the role of clinical scientists within the profession with the RCPA having set up a faculty of science and electing a council to prioritise the career structure and future role of clinical scientists within medical laboratories. This pathway could offer new opportunities in the future for those medical laboratory scientists who wish to undertake additional study and further develop their career.

The first year of the standardized format for the QMLT/QSST examinations passed the initial test with mainly positive feedback on the new style. The moderators and examiners course held in June proved successful in communicating these changes and our thanks go to all the examiners, moderators and Council coordinators whose untiring work has contributed to the continuing success of the QMLT examination programme.

Council recognises the important role of specimen services technicians within medical laboratories and in conjunction with the standardised QSST qualification believe that this route should be an acceptable pathway to registration with the Medical Laboratory

Science Board. With this in mind, Council has reviewed and resubmitted to the MLSB our proposal to include specimen services technicians within the definition of the profession of medical laboratory science with subsequent registration of technicians in this area.

Sound financial governance over recent years has seen the NZIMLS maintain its strong financial position which has allowed Council to continue with its promotional and educational initiatives such as funding the production of the 4th edition of the Standardised Reporting of Blood Film Morphology 2010 booklet. The executive office team also made significant advances in the office protocols and documentation last year and Council decided to commission an external audit of the office against the internationally recognised Quality Management Systems standard. The audit report was very pleasing with only a small number of recommendations made and Council intends to apply for full accreditation against AS/NZS ISO 9001:2008 in the next year. The NZIMLS logo and branding was refreshed this year with positive feedback from the membership on the new look website and membership packs in particular. Council acknowledges the good work by Fran and her team at the office on these fine achievements.

This past year will forever be remembered in our history for the double national tragedies that were the Pike River Mine disaster and the Christchurch earthquakes. Our hearts and thoughts are still with those who were directly affected by these events. The messages and support from the membership was gratefully received and certainly made a difference to those concerned. The reports of the dedication to duty and commitment during and post earthquake are remarkable and serve as a testimony to the fortitude of our profession. I am proud of the way our members have responded in this time of need. It is this spirit and professionalism that gives me the confidence that we will meet the many challenges that face us in the coming year ahead.

Finally I would like to thank my fellow Council members for their support and continued efforts working for our membership and profession over the past year. Also it is appropriate to take this opportunity to thank all the members who have given to the profession during their own time in so many ways, it has been greatly appreciated.

Ken Beechey
President NZIMLS



New Zealand Institute of Medical Laboratory Science

The Barrie Edwards & Rod Kennedy Scholarships



The Barrie Edwards & Rod Kennedy scholarships are some of the most significant awards offered by the NZIMLS. The two scholarships provide winners with support to attend an international or national scientific meeting up to a maximum value of \$7,500 for each.

Applications for these prestigious scholarships are invited from Fellows, Members and Associate Members of the NZIMLS. Applicants must be a current financial member of the NZIMLS and have been a financial member for at least two concurrent years prior to application. To be eligible applicants must make an oral presentation or present a poster as 1st author at their nominated scientific meeting.

All applications will be considered by a panel consisting of the President and Vice-President of the NZIMLS and the Editor of the New Zealand Journal of Medical Laboratory Science (who are ineligible to apply for the scholarships). The applications will be judged on your professional and academic abilities together with your participation in the profession. The panel's decision is final and no correspondence will be entered into.

Application is by letter. Please address all correspondence to:

NZIMLS Executive Officer
PO Box 505
Rangiora 7440

There may be two scholarships awarded in each calendar year. Closing dates are - June 30th and December 20th in any given year.

In your application letter please provide the following details:

- Full name, position, work address, email address and contact phone number
- The length of time you have been a financial member of the NZIMLS
- The conference you wish to attend - please provide dates

- A budget comprising airfares, conference registration and accommodation costs
- The abstract of your intended oral or poster presentation and whether it has been accepted for presentation (proof required)
- Your intentions to publish your results
- State briefly your history of participation in the profession over the last 5 years
- State the reasons why you wish to attend your nominated scientific meeting

Successful applicants will be required to provide a full written report on return which will be published in the Journal. If not intended to publish elsewhere, successful applicants will be required to submit their study results for consideration by the New Zealand Journal of Medical Laboratory Science.

Global Science Journal Award

Global Science & Technology Ltd. offers an award for the best article published during the calendar year in the *New Zealand Journal of Medical Laboratory Science* worth \$300. All financial members of the NZIMLS are eligible. The article can be an Original, Review or Technical Article. Excluded are Editorials, Reports, Fellowship Treatises or Case Studies (Case Studies are judged under the NZIMLS Journal Prize)

No formal application is necessary but you must be a financial member of the NZIMLS to be eligible. The Editor and Deputy Editor will decide in December which article is deemed worthy of the award. Their decision will be final and no correspondence will be entered into.

Fellowship of the New Zealand Institute of Medical Laboratory Science

The NZIMLS encourages members to consider Fellowship as an option for advancing their knowledge and career prospects. Fellowship provides an attractive option to academic postgraduate degrees at a fraction of the cost.



Fellowship of the NZIMLS may be gained by examination, by thesis or by peer-reviewed publications.

Examination

Consists of two parts:

- Part 1: Two written papers each of three hours duration
- Part 2: Upon successful completion of Part 1 a dissertation of 3000 - 5000 words

The dissertation may take the form of a review, development of a hypothesis or any other presentation that meets with the approval of the Fellowship Committee.

Thesis

The thesis must be based on the style of Master of Science by Thesis requirements of New Zealand Universities and not exceed 20,000 words.

Publications

A minimum of seven peer-reviewed publications, of which the candidate must be first author of at least four, may be submitted for consideration. These need to have been published in international or discipline acknowledged scientific journals. A review of the submitted articles of 3000 – 5000 words must also be submitted. The candidate must state the contributions he or she made to the publications.

Exemption

Candidates who are holders of postgraduate or professional qualifications in Medical Laboratory Science may be exempt from the Part 1 examinations but are still required to submit a dissertation for Fellowship.

Qualifications recognised by the NZIMLS for the purpose of exemption to sit the Part 1 examinations are:

- Fellowship of the Australian Institute of Medical Scientists (FAIMS), the Institute of Biomedical Science (FIBMS) and the Australasian Association of Clinical Biochemists (FAACB)
- An academic postgraduate qualification, normally at least a postgraduate diploma, in medical laboratory science or closely related subject. The course of study must meet the minimum requirement of one year's full-time study

For full Fellowship regulations and application process visit the NZIMLS web site: www.nzimls.org.nz or contact the Fellowship Committee Chair: Assoc Prof Rob Siebers at rob.siebers@otago.ac.nz



Dr M Shahid has been awarded Fellowship of the NZIMLS following submission of peer-reviewed publications and successful examination of his treatise "β-lactams vs. β-lactamases – recent evolution of concurrent occurrence of multiple *bla* genes including *bla*_{CTX-M} and *bla*_{ampC}: an Indian scenario" which is published in this issue of the Journal.

Dr. M. Shahid, MBBS, MD, PhD., FZIMLS is currently working as Associate Professor in the Department of Microbiology of the J.N. Medical College & Hospital, Aligarh Muslim University, India. His field of interest and research is confined to the mechanism and resistance to beta-lactam antibiotics, with special interest in CTX-M and AmpC β-lactamases. He also has a research experience on human fungal pathogens such as *Aspergillus* and *Candida* species. His work on Aspergillosis in patients suffering from bronchogenic carcinoma has received high acclaim and recognition in the international scientific community. Moreover, his group is working in the field of histamine-research and produced some pioneer researches related to H1–H4 receptors and their agonists/antagonists. Dr. Shahid has published more than 75 research papers in reputed journals and has five books and more than 25 book chapters to his credit. He is presently the member of many scientific bodies, both international and national. He has also been the member of the reviewer panel and editorial board of various international journals/publication houses, including Lancet and Lancet Infectious Diseases; and also those of Bentham Science Publications, USA, and Global Science Books, UK. He has also worked as an Associate Professor in the College of Medicine, King Faisal University, Al-Hassa, Kingdom of Saudi Arabia; Section of Immunity & Infection, The Medical School, University of Birmingham; and NHS Heartlands Hospital, Birmingham, United Kingdom.

New products and services

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Whether you need a refrigerated or non-refrigerated centrifuge for low, medium or highthroughput clinical applications, the Eppendorf 5702 family of centrifuges is the answer.

With three exceptional and economical models to choose from, the compact Eppendorf 5702 centrifuge models can be used in a range of settings, from specimen collection areas through to clinical laboratories. It holds a remarkable amount of tubes for its size, and it quickly spins a variety of popular cell culture and blood tubes in a choice of rotors.

Accommodating either fixed-angle or swing-bucket rotors, its versatility addresses your exact needs. With state-of-the-art features at an economical price, this centrifuge is sure to please you as well as your budget. A significant advantage is that all rotors within the 5702 line are designed to be interchangeable.

The 5702 centrifuges have a number of clever and well-designed features which make it even more desirable. These include:

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- Digital display for maximum reproducibility
- SOFT brake function for slow acceleration and braking. Optimized for cell separation by gradient centrifugation
- "At set RPM" function starts time counting when selected speed is reached for reproducible centrifugation runs
- Parameter lock prevents accidental changes
- Stainless steel rotor chamber is rust-proof and easy to clean
- Electronic imbalance detection for maximum safety
And with temperature control versions:
- Two programming keys to store routine procedures
- Separate Fast Temp function
- Automatic ECO-shut off mode reduces energy consumption

The 5702 Centrifuges, with its space-saving footprint and innovative design, can accommodate a remarkable 30 x 15 ml round-bottom tubes or 20 x 15 ml conical tubes. Your choice of fixed-angle or swing-bucket rotors provides flexibility for low-speed centrifugation of sensitive cells and blood. The A-4-38 Swing-bucket Rotor can spin up to four 85 ml tubes in aerosol-tight buckets at rcf up to 3,000 x g. A variety of adapters accepts all common standard, conical and blood collection tubes. For applications requiring higher tube capacity, rectangular buckets for up to 24 x 15 ml glass tubes can be used. Two versions of the F-35-30-17 Fixed-angle Rotor are available for a capacity of up to 30 x 15 ml. A simple, eight-place swing-bucket rotor is also available for 15 ml conical tubes.

WHY WAIT!!! There is no better time than now to replace, upgrade and/or simply purchase a brand new Eppendorf 5702 centrifuge for your laboratory. For pricing, specifications and demonstration please contact your qualified professional sales team at Medica Limited on freephone: 0800 106 100 or email: sales@medica.co.nz

Biochemistry Special Interest Group 2011

One could be forgiven for thinking that every second year there is some drama around the organizing of the BSIG seminar. 2009 saw a fire, meaning a last minute venue change. 2011: the morning of February 22, I was in the throes (no pun intended) of putting together the advertisement for this year's seminar for the Journal. Only hours later my world was literally turned end for end. A very big thank you to Ross Hewett from LabPLUS who pretty much took over the running of this year's seminar from that moment on. But despite these biennial, behind the scenes organizer's nightmares, the seminars on the day, have always been perfect. This year the BSIG seminar was held at the Waipuna Motor Lodge, Auckland on 18 June. We had 120 delegates attend.

The scientific program was full and varied, with 13 speakers. The keynote speaker was Professor Geoffrey Kellerman from the AACB who gave the Roman Lecture in the 50th Jubilee Year, entitled *AACB, Past, Present and Future*.

Associate Prof Chris Florkowski, Chemical Pathologist, Canterbury Health Laboratories gave us a very thought provoking presentation about the Canterbury Earthquake and the lessons learned from this event.

The Biorad Best First Time Presenter prize was awarded to Matthew Slater from LabTests, Auckland with a presentation entitled *Falsely Elevated Serum TSH Levels Due To Macro-TSH; Identification, Elimination and Pitfalls*.

The Abbott Best Overall Presentation award went to Max Reed from Aotea Pathology, Wellington for her presentation entitled *Now You See It, Now You Don't*. The judges for the awards at the BSIG have a difficult task as the proffered presentations are always of a very high standard.

Thank you to all the presenters, sponsors, delegates and Mother Nature for putting aftershocks and ash cloud on hold for a few days so we could attend and enjoy the seminar.

Sandy Woods
BSIG Convenor

NZIMLS Journal Prize



Council of the NZIMLS has approved an annual Journal prize (\$300) for the best case study published in the Journal during the calendar year.

Case studies bring together laboratory results with the patient's medical condition and are very educational. Many such studies are presented at the Annual Scientific Meeting, SIG meetings, and the North and South Island Seminars, yet are rarely submitted to the Journal for wider dissemination to the profession. Consider submitting your case study presentation to the Journal. If accepted, you are in consideration for the NZIMLS Journal Prize and will also earn

you CPD points. Please contact the Editor or any Editorial Board Member for advice and help. Contact details are on the NZIMLS web site (www.nzimls.org.nz) as are instructions to authors. Refer to the article "How to write a laboratory-based case study for the journal" published in the April 2010 issue of the journal, pages 22-23, for guidance.

No formal application is necessary but you must be a financial member of the NZIMLS during the calendar year to be eligible. All case studies accepted and published during the calendar year (April, August and November issues) will be considered. The Editor, Deputy Editor and the President of the NZIMLS will judge all eligible articles in December each calendar year. Their decision will be final and no correspondence will be entered into.

Winner of the NZIMLS Journal prize for 2010 was Vichiet Khieng for his case study "Vitamin D toxicity? A case study". *N Z J Med Lab Sci* 2010; 64: 44-50.

The Olympus Journal Imaging Competition



OLYMPUS®

The NZIMLS Journal invites applications for the annual Olympus photo competition giving NZIMLS members the chance to win an Olympus digital camera and have their photo published in the journal.

The general theme is "Medical Laboratory Science", so whether it is related to haematology / histology, laboratory personnel, instruments, humour, or other, there's plenty of scope for

keen photographers to showcase their talents.

Olympus, a leading manufacturer of professional opto-digital products, has generously donated a digital camera as the prize for the best photo.

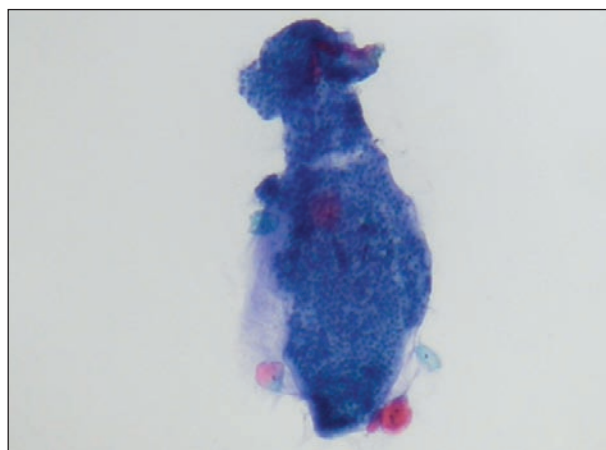
Entries should be submitted as an email attachment to Rob Siebers, Editor of the NZIMLS Journal, at rob.siebers@otago.ac.nz. A title for the photo, together with the entrant's name, place of work and email address, should accompany the attachment. Submissions can be in colour or black and white.

Entries close on **5pm on Friday 14th September 2012**, with the winning photo appearing in the November 2012 issue of the Journal. Previously submitted entries will not be considered.

Judging will be carried out by the Editor, the Deputy-Editor and an Olympus representative. Their decision will be final and no correspondence will be entered into. Entrants must be current financial members of the NZIMLS to be eligible.

The winner of the 2011 Olympus journal imaging competition is Krish Pillay from Diagnostic MedLab, Auckland. His winning entry is shown below.

A group of mucus secreting endocervical cells presenting as a little puppy dog tired of just eating the squamous cells around him all the time, so he begs for some mucus. " *Please sir, can I have more mucus...tired of the same squamous cell diet.*"



Journal questionnaire

Below are 10 questions based on articles in the November 2011 Journal issue. Read the articles fully and carefully, most questions require more than one answer.

Answers are to be submitted through the NZIMLS web site. Make sure you supply your correct email address and membership number. It is recommended that you write your answers in a word document and then cut and paste your answers on the web site.

The site has been developed for use with Microsoft's Internet Explorer web browser. If you are having problems submitting your questionnaire and you are using the Firefox web browser, try resubmitting from a computer or system using Microsoft's Internet Explorer.

You are reminded that to claim valid CPD points for successfully completing the Journal questionnaire you must submit an individual entry. It must not be part of a consultative or group process. In addition, members who have successfully completed the Journal questionnaire can only claim 5 CPD points. You can not then claim additional CPD points for reading the articles from which the questions were derived.

The site will remain open until Friday 24th February 2012. You must get a minimum of 8 questions right to obtain 5 CPD points.

November 2011 journal questions

1. As well as linking solvent exposure to Raynaud's Phenomenon and connective tissue disease, what else can solvent exposure cause.
2. Chromogenic media allow for the detection of which bacterial enzymes.
3. Which microorganism was the primary isolate in the urinary tract pathogen study and which two were the next prevalent isolates.
4. What is the gold standard for the diagnosis of urinary tract infections.
5. Name the types of cancer in which blood alpha fetoprotein levels are raised.
6. Cancer Antigen 19-9 is synthesized by which cells.
7. What determines the antigenic specificity of the particular antibody molecules.
8. Which is the only immunoglobulin that can cross the placental barrier and because of this, what does it provide.
9. What does a low number of LGL/NK cells in blood indicate.
10. What were the top services and activities of the NZIMLS as rated by the members and which were rated low.

Questions and answers for the August 2011 journal questionnaire

1. Which antibiotics are ESBLs able to hydrolyse and which antibiotics are they not able to hydrolyse.

ESBLs are able to hydrolyse oxyimino-cephalosporins (eg. cefotaxime, ceftazidime and aztreonam), but not cephamycins or carbapenems.

2. What is used as a marker of ESBL production and why.
Ceftazidime resistance is used as a marker of ESBL production, as it is hydrolysed by both TEM and SHV type beta-lactamases.

3. What is involved in the mechanism of formation of ring chromosomes.

The loss of varying extents of the telomeric ends of the p and q arms, followed by annealing of the "sticky" ends in order to prevent further loss of genetic material

4. Name the two rings into which ring chromosomes are divided.

Those in which one normal chromosomal homologue is replaced by a ring equivalent, and those in which the ring chromosome is additional to the two normal copies of that chromosome

5. Dynamic mosaicism occurs as a consequence of what and what does it result in.

As a consequence of sister chromatid exchange (SCE) of the ring chromosome during replication, resulting in several unbalanced chromosome outcomes.

6. What should be should be one of the initial tests carried out for referrals of ambiguous genitalia and why.

Routine cytogenetic analysis as an underlying cytogenetic abnormality may be the cause.

7. Name the clinical symptoms associated with *C. difficile* infection.

Mild to severe diarrhoea and more seriously, pseudomembranous colitis, toxic megacolon, bowel perforation, sepsis and death.

8. What laboratory tests are available for the diagnosis of *C. difficile* infection.

Cell cytotoxicity neutralisation assay (CCNA), culture, enzyme immunoassays (EIAs) and PCR.

9. Incorrect laboratory results for *C. difficile* infection diagnosis due to either lack of sensitivity or specificity can lead to what.

Inappropriate patient care with an increased possibility of cross-infections, subsequently increasing the financial burden on the health care system.

10. What was a possible limitation of the *C. difficile* study.

Low sample size and low prevalence of toxigenic *C. difficile*.

Greetings from the PPTC

This year has continued to be very busy for the PPTC especially with country visits, POLHN distance learning and courses held at the Centre. Here are some of the highlights up to the present for 2011.

Courses held at the Centre

A Biochemistry Update course was provided once again this year and as always proved most successful for the eight students who participated. The course was of a three week duration and included the following topics: organisation of phlebotomy collection and laboratory reception; blood collection sets and vacutainer tubes and needle systems; IATA Regulations and packaging techniques for biological substances; basic equipment including pipettes, pH meters, waterbaths, centrifuges, balances etc; an overview of blood gas and other biochemistry analysers; an overview of diabetes in terms of pathology, diagnosis, laboratory management and point of care testing; renal function and renal dialysis; an overview of cardiac enzymes in health and disease focusing on myocardial infarction, diagnosis and laboratory management; advances in protein analysis and specialist biochemical analysis; an overview of thyroid function and associated abnormalities; a molecular approach to biochemical pathology; organisation and effective management of the biochemistry laboratory; quality control, QLab, and external quality. Assessment in the biochemistry laboratory; the use of spreadsheets; and word processing in the biochemistry laboratory. Discussion of quality systems, standard operating procedures, stock control and its management, result processing, audit trails, reducing error and process improvement; an overview of laboratory information systems.

Students attending the course were: Daisy Donna Phal, Yap, Federated States of Micronesia; Peggy Ittu, Kosrae, Federated States of Micronesia; Ischael Ken, Majuro, Marshall Islands; Patricia Miraneta Vaiaso, Samoa; Tiaon Tonganibeia, Kiribati; and George Junior Pakoa, Timothy Phatu and Crystal Tarinavanua all from Vanuatu.

The PPTC would like to thank Dr Michael Crooke, Wellington Hospital Chemical Pathologist, for lecturing the students and presenting the students with their certificates at the final graduation. We would also like to thank the senior medical laboratory scientists from



PPTC staff, students and lecturers. BIOCHEMISTRY 2011

the Division of Biochemistry, Wellington Hospital and those from Aotea Pathology who gave their time freely to provide lectures over the duration of the course. Without their contribution, the provision of such courses by the PPTC could never be possible.

Distance learning programme

Diploma in Medical Laboratory Technology

The Laboratory Technology module introduced in April of this year has been a great success with a total of 26 participants graduating with certificates of completion. Haematology was launched in August of this year and there are currently 21 participants involved in this module.

Laboratory diagnosis of STIs

The teaching of this course commenced in August with over 70 students registered. This is the largest class we have had for any of our on-line courses.

Country visits

Haematology training in Tonga

Phil Wakem returned to Tonga for a week in mid-June of this year as a follow-up to his initial two week teaching and training visit in May. Both visits focused on haematology in terms of its diagnostic processes and associated quality issues. EQA, quality assurance, documentation and blood film examination were just some of the areas covered.

Solomon Islands and Vanuatu

John Elliot visited the Solomon Islands in July and Vanuatu in September. The purpose of these visits was to meet with senior laboratory staff and appropriate Ministry of Health and WHO officials to discuss their draft National Laboratory Policy and plans and determine the role that the PPTC may be able to play in the implementation in both countries. This project is based on the WHO Strategy for Strengthening Health Laboratories and also the Regional Standards which have been published recently by WHO WPRO and in which the PPTC played an important role in developing. John returns to the Solomon's in October to facilitate a workshop on finalising the National Policy and also to commence the training of laboratory staff in Laboratory Quality Management processes. In addition, while in Vanuatu, he had the opportunity to meet with students undertaking our distance learning diploma programme and obtain feed-back on it from them. The photos below are of two of the students.



Amos Temalang, Luganville, Vanuatu ; Noella Tasavi, Port Vila, Vanuatu

Samoa

Phil visited the National Health Laboratory in Apia, Samoa in September to carry out a baseline assessment of the Quality Management System and as time permitted, teach blood film examination; this was most successful. When visiting a laboratory it is always rewarding to see former PPTC students putting into practice their learning and improving their skills in their home laboratory and this was certainly seen in Samoa.

Fiji

From Samoa, Phil travelled to Fiji to visit both hospital and private laboratories throughout the Fiji Islands, firstly visiting Lautoka Hospital, then flying across to Labasa Hospital and finally onto Suva. The main purpose of this visit was to assess external quality assessment in each of the laboratories and to provide teaching and training on site as time permitted. Christine Story, our EQA Co-ordinator, met Phil in Suva towards the end of the week as they were both scheduled to attend the Fiji Institute of Medical Laboratory Science conference. During this conference Phil presented a paper entitled "Quality issues relating to haematology EQA" The whole conference was a great success and the organisers are to be congratulated.

leading to the Diploma in Medical Laboratory Technology [PPTC] commencing with laboratory technology, followed by haematology and biochemistry in 2012 and microbiology and transfusion medicine in 2013. In addition other courses (STI and laboratory management) will also be offered through the POLHN website. Check with your POLHN Country Co-ordinator or the POLHN website and also the PPTC website to keep up to date with these courses.



Attendees at the Fiji Conference 2011

Academic calendar for the remainder of 2011

Blood transfusion course 2011

This course runs from 31st October to 25th November and again this year staff from the Wellington Blood Service will be training the students. The four week lecture series covers routine blood grouping, blood group antigens, crossmatch techniques, antibody detection, transfusion reactions, and haemolytic disease of the newborn, blood donor selection, organisation of a blood bank and the appropriate use of blood components in transfusion medicine. Practical sessions are also provided, focusing on correct technique and fundamental basic procedure. One week of the course is set aside for an overview of current techniques in the detection of transfusion transmissible infections including, HIV, Syphilis, Hepatitis B and C.

Distance learning

The biochemistry module (the 3rd module of the Diploma) will be offered in November of this year followed by microbiology and transfusion science in 2012. This will then complete the first cycle and those who have completed and passed the five modules will be awarded the PPTC Diploma of Medical Laboratory Technology.

It is anticipated that we will offer a second cycle (ie) 5 modules

NICE Weekend

NICE Weekend was held again this year in Taupo at Bayview Wairakei 20th – 22nd May. The venue continues to be a popular one with lots of opportunity for delegates to network between and after sessions over the weekend. The Weekend was attended by 62 delegates (including 1 participating TMS and 4 Australians), 17 Trades representatives and one sponsored student. I think the sponsored student (Jacob Farmer) was a particular highlight in his Bam Bam costume. He seemed to have a lot of followers! Queenie was most upset that she could not run faster!

Overall delegates were exposed to more than just Jacob, with a total of 13 posters and 50 presentations covering, as always, a very wide range of Transfusion topics. The organizing committee would like to thank the following sponsors for their contribution to prizes and other areas of our weekend.

Medtel NZ Ltd, Abbott Diagnostic Division, Murray Craft (for his IT input!), Bio-Rad Laboratories Pty Ltd, Pharmaco (NZ) Ltd, CSL Bioplasma, Lateral Grifols, Ortho-Clinical Diagnostics, Life Pharmacy Rotorua, NZ Blood Service, Abacus – ALS

ABSTRACTS FOR PRIZE WINNERS

Earthquakes and After-effects

(BEST POSTER)

By Julia van Essen

On February 22nd a 6.3 magnitude earthquake struck the Canterbury region. The earthquake caused widespread damage and multiple fatalities in Christchurch City. The purpose of this poster is to describe the impact of the earthquake on the New Zealand Blood Service in Canterbury and to examine the response of NZBS to the disaster. It deals with the events on the day and also in the days of recovery which followed, with the emphasis being on the Donor Centre in Riccarton road. It also looks at the knock on effects for other NZBS centres around the country, which had to take on extra work while the Donor Centre was closed. The disaster has also highlighted the need for laboratory emergency protocol to be updated and the need to have ongoing training and drills for staff. New emergency plans are in draft and work on these is ongoing. New Zealand is a very seismically active country, and earthquakes can strike any time and in any place. All NZBS centres in New Zealand should, therefore, be up to date with the latest emergency plans. Hopefully, Christchurch's experiences can be used as a model for future disaster management planning.



Fiona from Pharmaco presents Julia with her certificate.

Test Tube Babies or a CAT

(BEST VIRGIN – First time attendee)

Melanie Adriaansen (North Shore)

Can column agglutination technology be used in place of the "gold standard" for titration in the antenatal setting and be proved to provide reproducible results? Does literature contradict this or just history?



Steve from Bio-Rad presents Melanie with her certificate.

Factor V111 Inhibitor – Use of Novoseven (rV11a)

(BEST PRESENTATION)

Helen Bardsley (Austin Health Melbourne Australia.)

At a peripheral hospital, a 23yo had a significant post partum haemorrhage. She was G1P1 and had a history of psoriasis. The patient was an 'OVERSEAS' visitor.

Routine FBE and coagulation tests were performed.

Results : Hb 87 g/l INR 1.2 aPTT 56 secs

Group and screen : A RhD Positive Ab screen Negative, 4 units of blood were x-matched.

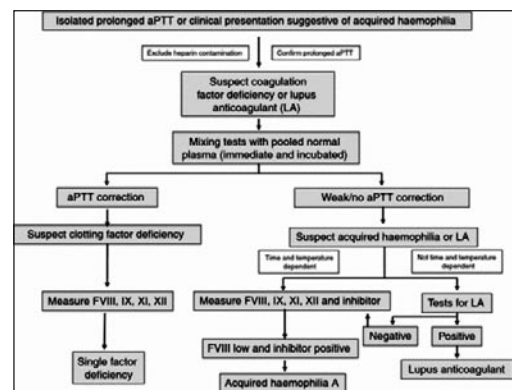
She experienced ongoing bleeding and was transferred to Austin Health.

A further 6 units of blood was x-matched and transfused.

INVESTIGATIVE results: Hb 79 g/l, aPTT 80 secs (see table below)

Factor VIII clotting 3 % (N: 50 – 200)

Factor VIII inhibitor 32 Bethesda Units / ml



Management of patients with a factor VIII inhibitor requires prompt diagnosis. Treatment should be individualised with reference to available recommendations .

The Austin Haematology unit was consulted on the management of this patient. The principles of management are the use of bypassing agents to manage acute bleeding in conjunction with immunosuppression, with the aim of complete inhibitor eradication.

She was commenced on Prednisolone 1mg/kg/d. There was discussion about the use of Novoseven rVIIa for this patient .

Two days later she started to haemorrhage++++ , 9 units of red cells were x-matched, 4 x FFP and 9 vials of Prothrombinex were transfused .

Novoseven rVIIa was given to control the bleeding.

Patient ongoing management: rVIIa 10 days,
Prednisolone 1mg/kg/d
Day 7 Cyclophosphamide commenced
Day 45 Prednisolone weaned
Day 45 Complete inhibitor eradication

Indications for use of Novoseven (rV11a)

Novoseven was developed to treat bleeding symptoms in people with hereditary haemophilia who had acquired high titre inhibitors and were unable to be managed with conventional factor replacement. In pharmacological doses it indirectly results in a thrombin burst, bypassing the inhibitor and resulting in the formation of a stable fibrin clot at the site of platelet activation / bleeding.

However in recent years it has been documented that this agent has a role in the management of non-haemophilia patients with life threatening bleeding post trauma / surgery / delivery , that cannot be controlled by conventional surgical or medical means.

Indications for its use in this context are:

- Life threatening bleeding
- Massive Transfusion requirements, greater than one blood volume in 24 hours.
- Inability to control bleeding by surgical or medical means



Murray from Abbott presents Helen with her award for Best Presentation.

Tony Morgan from Hastings proved to be one of the most intelligent Scientists at the weekend. He correctly answered the most questions in a transfusion spot quiz, earning himself a sponsored trip to NICE Australia, courtesy of Cheng from CSL Bioplasma.



All in all this was another successful Special Interest group weekend. Thanks to all those in the background who helped out (and the judges who had a very tough role!)and also to those who attended. It isn't as NICE without you.

NICE for 2012 is at the same venue, Baywater Wairakei Resort, and 4-6 May 2012.

NICE Co-convenors Raewyn Cameron and Diane Whitehead.

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