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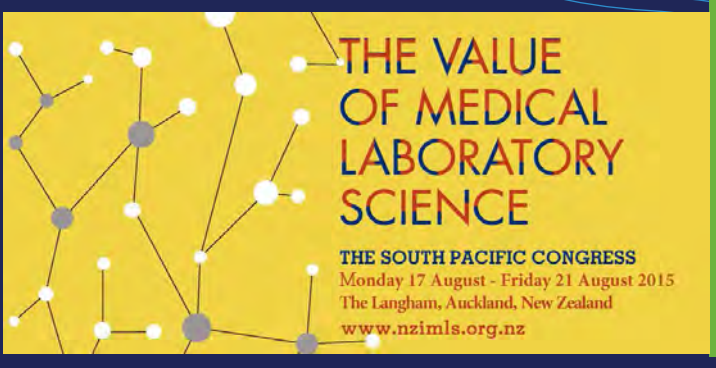

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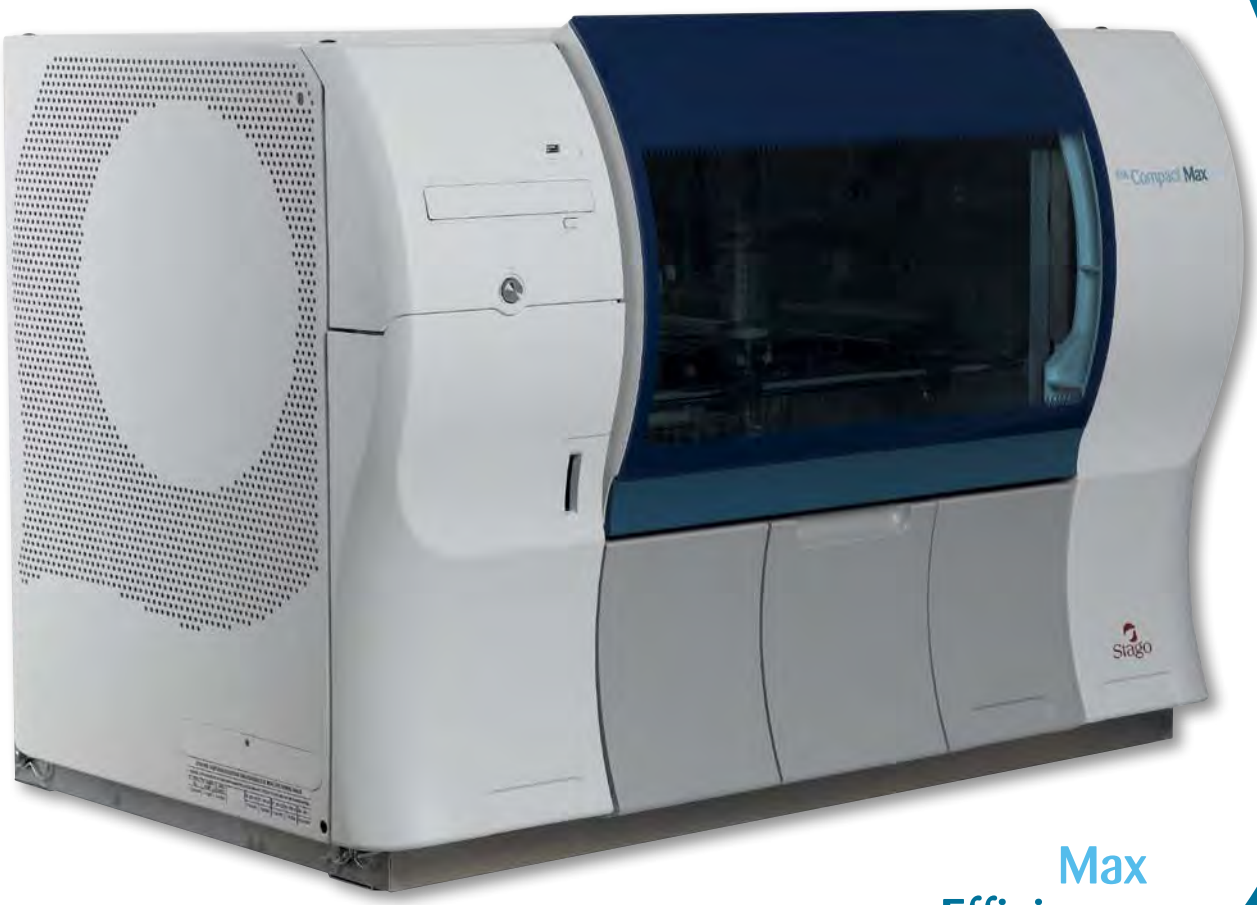

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In this issue

Rob Siebers, Editor

Mackenzie Nicol *et al.* from Aotea Pathology, Wellington characterised four *Neisseria gonorrhoeae* culture collection strains available from ESR, Porirua by three molecular assays designed to predict resistance or reduced susceptibility to penicillin, ciprofloxacin and ceftriaxone. The three molecular assays used produced valid results against each of the strains examined thus making them suitable for use as controls in any new molecular assays being set up by diagnostic laboratories in response to the need for data on resistance to antimicrobial agents in the absence of cultured isolates.

Linda Appleyard from Middlemore Hospital, Auckland reviewed the literature regarding the effect of breastfeeding on reducing pain in infants undergoing heelstick or venepuncture. Published studies have shown that breastfeeding provides significant analgesia for infants undergoing this painful procedure. Maternal holding may also offer some pain relief.

Sharda Lallu *et al.* from Wellington Hospital report the spurious finding of house dust mites in urine samples from two patients. These were initially mistaken for pubic lice. House dust mites are ubiquitous in the indoor environment and have the potential to contaminate urine specimens. In an accompanying Editorial, Rob Siebers from Wellington discusses the potential sources of contamination.

Dr. Alex Dempster from Southern Community Laboratories, Dunedin delivered the TH Pullar Memorial Address at this year's Annual Scientific Meeting of the Institute. In his address he explores the role of the modern laboratory, present issues and our role as laboratory professionals in improving patient care and management. He points out that now that we have academic posts in laboratory technology in health science faculties, the opportunity exists for laboratory scientists to have increasing involvement in the scientific assessment of technological and biomedical developments, the application of which will play very significant roles in future patient diagnosis and management.

You will notice the new look of articles published in the Journal. We hope that it is easier on the eye, more attractive, and welcome your views or suggestions for further improvements as Letters to the Editor.

Rob Siebers, FNZIMLS FSB, Editor

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EDITORIAL

Dust mites in urine

Rob Siebers

School of Medicine and Health Sciences, University of Otago, Wellington

In this issue Lallu et al. report the spurious findings of dust mites in urine samples from two patients (1). They were originally mistaken for pubis lice, but upon referral to a parasitology laboratory were identified as dust mites. As only one specimen was found in both urine samples, and a further urine sample from one patient did not reveal dust mites, the authors conclude that the presence of these dust mites were most likely contaminants from the environment.

Dust mites were first reported in urine samples in the literature in 1953 (2). Infrequent reports of their presence in urine followed (3-7). The first comprehensive survey of dust mites in urine came from China where 3.46% of urine samples from 1,994 subjects were found to contain up to 17 different species of dust mites (8). This incidence of urinary acariasis was positively linked to individuals working in environmental occupations with high densities of dust mites, such as rice storehouses and mills.

The presence of a single or few dust mites in urine is most likely an artifact due to contamination of the specimen. Dust mites are ubiquitous in the environment. The presence of house dust mites in New Zealand were first reported in this journal by Brian Cornere who studied 22 dust samples from homes in Auckland (9). All dust specimens revealed the presence of the house dust mite, *Dermatophagoides pteronyssinus* along with a number of other dust mite species. He extended his study to other centers and confirmed *D. pteronyssinus* as the dominant house dust mite species in New Zealand (10). New Zealand has a very large density of house dust mites in the indoor environment as evidenced by some of the highest levels of Der p 1 in the world (11). Der p 1 is the major group one allergen from *D. pteronyssinus* and induces an IgE response in susceptible individuals contributing to the prevalence and severity of asthma in New Zealand (12).

Not only are house dust mites found in homes, but are also present on clothing (13) and thus have the potential to contaminate urine specimen containers if strict hygiene conditions are not adhered to when collecting the sample. House dust mite allergen has even been detected on human skin and in hair (14,15) suggesting that these sites may also be a potential source of house dust mite contamination of urine samples. A further source of dust mite presence in urine could come from ingestion of mite-infested flour products (16).

It is surprising that more reports on the presence of dust mites in urine are lacking given their high presence in the New Zealand environment. I am aware of only one other (unreported) finding of dust mites in urine in New Zealand. The reason might be their misidentification as lice, or that they resemble food contaminants. Also, in unstained preparations dust mites are transparent and thus may be overlooked. Species identification requires specific expertise of which only a few specialists in New Zealand have this experience. An excellent pictorial guide to dust mite identification has been published and may serve as a resource (17).

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N Z J Med Lab Sci 2014; 68: 83.

ORIGINAL ARTICLE

Detection of molecular markers associated with resistance (PPNG, gyrA, mosaic penA) in Neisseria gonorrhoeae isolates from the New Zealand culture collection

Mackenzie Nicol[1], Mary Nulsen[2] and Collette Bromhead[1]

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ABSTRACT

Objectives: To share information and genetic characterization of the New Zealand culture collection *Neisseria gonorrhoeae* isolates. This information makes the isolates suitable as quality control material for diagnostic laboratories considering setting up molecular assays to predict susceptibility profiles of clinical *N. gonorrhoeae* where a culture isolate is not available.

Methods: DNA was extracted from cultured isolates on the Cobas 4800 CT/NG platform. Taqman PCR assays with specific primers and probes were used to detect a sequence in penicillinase producing *Neisseria gonorrhoeae* (PPNG) or associated with reduced susceptibility to the cephalosporins (mosaic *penA)* and run on the LightCycler 480. The *gyrA* assay utilised a melt curve analysis to detect the Ser91→Phe mutation which occurs in ciprofloxacin resistant *N. gonorrhoeae*.

Results: The three molecular assays used to predict resistance (or reduced susceptibility) produced valid results against each of the ESR culture collection strains examined, namely the WHO-K calibrator strain, the PPNG positive isolates (222, 3330 and 4543), the *gyrA* Ser→Phe positive isolates (4033 and 4543) and the mosaic *penA* positive isolate (4543).

Conclusions: The *N. gonorrhoeae* isolates held by the New Zealand culture collection have been validated and characterised as positive or negative for three molecular markers associated with resistance to penicillin (PPNG), ciprofloxacin (*gyrA)* and ceftriaxone (mosaic *penA*). This goes some way to resolving the ever present issue of a lack of suitable control material when diagnostic laboratories are setting up bespoke and new molecular assays.

Key words: *Neisseria gonorrhoeae*, antimicrobial susceptibility, genotyping, PCR, quality control.

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INTRODUCTION

In the age of molecular diagnostics an ongoing challenge for any laboratory setting up new molecular testing is the availability of suitable quality control material (1–3). This study characterises the *Neisseria gonorrhoeae* culture collection strains available from Institute of Environmental Science and Research (ESR) in Kenepuru, New Zealand by three molecular assays designed to predict resistance or reduced susceptibility.

New Zealand sexual health treatment guidelines state that empiric treatment in New Zealand should be with 500 mg IM ceftriaxone plus 1 g azithromycin. The guidelines also state that ciprofloxacin is an alternative treatment option if the *N. gonorrhoeae* has tested as susceptible. (http://www.nzshs.org/guidelines/Gonorrhoea-guideline.pdf). It has been suggested that in some regions penicillin may still be considered a treatment option in susceptible populations (4–6). Monitoring of the resistance plasmid also provides some epidemiological information which is useful to trace emerging resistance and multidrug resistance.

The New Zealand Reference Culture Collection is a member of the World Federation for Culture Collections and is held by ESR. It holds approximately 4000 strains and supplies reference cultures for quality control, teaching and research. These cultures include isolates which are the subject of formal publications, the first New Zealand isolate of a species, and strains with particular antimicrobial sensitivity patterns, plasmid profiles or other properties (http://www.esr.cri.nz/competencies/Health/Pages/nzrcc.aspx).

As part of an investigation into the molecular markers of antibiotic resistance in New Zealand isolates of *Neisseria gonorrhoeae*, four isolates from ESR were tested to form suitable controls for diagnostic testing. In addition to culture-based susceptibility testing, three molecular assays were carried out to detect the *gyrA* gene, (associated with ciprofloxacin resistance), the penicillin resistance plasmid found in PPNG, and the mosaic *penA* sequence (associated with reduced ceftriaxone susceptibility).

MATERIALS AND METHODS

Genotypes

DNA Extraction by the Cobas 4800 CTNG Test

A swab of each cultured isolate was taken into Cobas 4800 collection buffer and was tested in the Cobas 4800 system as previously described (7). Residual DNA remaining from the CTNG amplification test was utilised for the three antimicrobial resistance marker molecular assays.

Fluoroquinolone resistance and gyrA

Siedner et al stated that the mutation of importance in determining quinolone resistance is the Ser91 codon →Phe alteration, with over 99% of QRNG shown to have mutations at this site (8). They developed a real time PCR assay for analysis of mutations in the Ser91 region of the *gyrA* gene by amplification and melt curve analysis. PCR and melt curve analysis on DNA showed the presence or absence of the *gyrA*

mutation and ciprofloxacin susceptibility could then be predicted. This previously described assay's primers and probes, with run conditions matched to other APL assays, were further developed and validated at APL and the four culture collection isolates were tested.

*gyr*A-PCR

Briefly, each *gyrA*-PCR mastermix contained 1x FastStart DNA Master (Roche), 0.5U UNG (Roche) 2.5 mM $MgCl_2$, 0.2 mM of primers NGGYRASER91-F and NG-GYRASER91-R) (IDT) and probes *gyrA*-ser-LC and *gyrA*-ser-Flu (TIB MolBiol) (8) as well as 5mL of cobas 4800 residual DNA or control material. Amplification was carried out using a LightCycler 480 (v1.0) with a 10 minute denaturation at 95°C followed by 45 cycles of denaturation at 95°C for 5 s, annealing at 52°C for 5 s, and extension at 72°C for 10 s, with a ramp rate of 20°C/s. Melting-curve analysis was performed using 95°C for 60 s, 40°C for 20s, and heating to 80°C with a ramp rate of 0.03°C/s with continuous fluorescence acquisition.

Penicillin resistance and PPNG

Penicillin resistance in *N. gonorrhoeae* may be due to either mutations in chromosomal genes encoding penicillin-binding proteins (PBPs) and/or affecting outer membrane permeability or by acquisition of plasmids encoding production of a beta lactamase (penicillinase) (12). Goire et al developed a real-time PCR for detection of penicillinase producing *N. gonorrhoeae* using non-cultured clinical samples (9). They selected conserved targets outside of the beta lactamase gene on the gonococcal plasmids to serve as indirect markers of penicillinase activity specific to *N. gonorrhoeae* (pPPNG). This previously described assay's primers and probes, with run conditions matched to other APL assays, were further developed and validated and the four culture collection isolates were tested.

pPPNG-PCR

Briefly, each PPNG-PCR mastermix contained 1x FastStart DNA Master (Roche), 0.5U UNG (Roche), 2.0mM $MgCl_2$, 0.4 mM of primers PPNG-F2 and PPNG-R2 and 0.2 µM of the PPNG TM2 probe (IDT), and 5mL of cobas 4800 residual DNA or control material. Amplification was carried out using a 10 minute denaturation at 95°C followed by 55 cycles of denaturation at 95°C for 15 s, annealing and extension at 60°C for 60s.

Reduced susceptibility to ceftriaxone and mosaic penA

Goire et al (10) and Unemo et al (11) observed that the emergence of extended cephalosporin resistance is preceded by a gradual rise in MICs. Studies have implicated alterations in PBP-2 (encoded by mosaic *penA)* as the primary binding site of β-lactam antibiotics leading to decreased affinity as a key marker or principal 'alteration of interest' (14,15). Therefore the previously described Goire et al (10) assay was developed and validated with APL run conditions and the four culture collection isolates were tested.

Mosaic *penA*-PCR

Briefly, each mosaic *penA*-PCR mastermix contained 1x FastStart DNA Master (Roche), 0.5U UNG (Roche), 2.0 mM $MgCl_2$, 0.4 mM of primers Mosaic F and Mosaic R and 0.16mM of Mosaic probe (IDT), and 5mL of cobas 4800 residual DNA or control material. Amplification was carried out using a 10 minute denaturation at 95°C followed by 55 cycles of denaturation at 95°C for 15s, annealing at 60°C for 10s and extension at 72°C for 12s.

The three molecular predictors of resistance (or reduced susceptibility) assays produced valid results against each of the three ESR culture collection strains. The WHO-K calibrator strain (4543) also gave expected results (11).

Table 1. The phenotypes and genotypes of four *N. gonorrhoeae* isolates from the ESR culture collection

ESR Culture collection number	Cobas NG/CT result	Beta lactamase (cefinase disc)	PEN	pPPNG	CIP	*gyrA* Ser91Phe	CTX MIC mg/L	Mosaic *penA*
2222	Pos	Yes	R	Pos	S	Neg	0.006	Neg
3330	Pos	Yes	R	Pos	S	Neg	0.004	Neg
4033	Pos	No	I	Neg	R	Pos	0.023	Neg
4543*	Pos	No	R (CMRNG)	No	R	Yes	0.064	Yes

Key: Pos = Positive, Neg = Negative, R = resistant, S = susceptible, CMRNG = Chromosomal mediated resistant *N. gonorrhoeae,* pPPNG = plasmid of Penicillin Producing *N. gonorrhoeae*, CTX = ceftriaxone, gyrA ser91Phe = gyrase A mutation, PEN = penicillin; *WHO-K calibrator strain. Colour key: Green = characterisation at APL, Black = Characterisations available from literature or routine antimicrobial testing.

DISCUSSION

As emerging technologies have led to the widespread use of molecular methods for the diagnosis of gonorrhoea, isolates are frequently not available for traditional culture-based antimicrobial susceptibility testing. It is therefore likely that laboratories will employ molecular methods to predict susceptibility to antibiotics even though it must be acknowledged that, in contrast to phenotypic methods, genotypic assays will not detect novel, uncharacterised mechanisms of resistance to antimicrobial agents. This is a major limitation when developing possible molecular solutions to address a lack of antimicrobial susceptibility information. The detection of a single mutation will not usually predict the complex interactions of multiple mutations and there is a need for laboratory tests to be clearly defined and measureable in regard to antibiotic susceptibility outcomes. However, molecular methods remain important technology to further investigate and develop. It is also important to acknowledge the need for ongoing culture of circulating isolates of *N. gonorrhoeae* in New Zealand so that antimicrobial susceptibility testing can continue and new and emerging resistance phenotypes detected.

One of the most challenging obstacles for laboratories when setting up a molecular test is the availability of suitable control material. This study outlines the genotype and phenotype of four *N. gonorrhoeae* isolates available from the New Zealand culture collection with regard to three classes of antimicrobial agents. These isolates are readily available in New Zealand and may therefore be useful to laboratories as they consider how to address the issues around providing susceptibility data on *N. gonorrhoeae*.

The detection of pPPNG in DNA from *N. gonorrhoeae* predicts resistance to penicillin due to plasmid-encoded beta lactamase production. Detection of these plasmids is a useful epidemiological tool and can confirm an isolate as multi drug resistant if other markers are assayed as well. The detection of the gyrA mutation at codon 91, from serine to phenylalanine, has been repeatedly reported in the literature (8,16,17) to predict reduced susceptibility to ciprofloxacin so is useful as a test on *N. gonorrhoeae* DNA from patients who are unable to be treated with ceftriaxone, and for monitoring and epidemiological purposes. A lack of the mutation is a good indication of susceptibility to ciprofloxacin. The detection and monitoring of the mosaic *penA* in New Zealand is useful to map the spread of decreased susceptibility to ceftriaxone (18).

CONCLUSIONS

Four *N. gonorrhoeae* isolates available in the New Zealand culture collection have been characterised for three molecular markers associated with resistance to penicillin, ciprofloxacin and ceftriaxone, thereby making them suitable for use as controls in any new molecular assays being set up by diagnostic laboratories in response to the need for data on resistance to antimicrobial agents in the absence of cultured isolates.

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REVIEW ARTICLE

Breastfeeding reduces procedural pain in infants: A review of the literature

Linda R Appleyard
Middlemore Hospital, Auckland

ABSTRACT

Pain-induced stress in infants undergoing painful procedures, such as heelstick and venepuncture, has been found to cause both short and long term detrimental effects. Because it is not desirable for infants to have potent medicinal analgesia, researchers have sought other methods of pain relief that are effective. It has been found that breastfeeding during heelstick or venepuncture provides significant analgesia for infants. Maternal holding has also been found to offer some pain relief. This review looks at some of the studies that have revealed these findings.

Key words: analgesia, breastfeeding, infants, maternal holding, pain.

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INTRODUCTION

Poorly managed pain which induces stress early in life has been shown to have short and long term detrimental effects. Heelstick and venepuncture are common painful procedures endured by infants. As pharmacological analgesia is not desirable, it is vital that acceptable and effective pain relieving methods are used (1-3). Research has been carried out with both premature and full term infants regarding pain and increased stress. Although premature infants are more likely to undergo repeated painful procedures, this article will focus on near term and full term infants and the analgesic effects of breastfeeding. It is these infants with effective sucking skills who will benefit the most. Breastfeeding during painful procedures, such as heelstick or venepuncture, has a significant analgesic effect. Where breastfeeding cannot take place, maternal holding, though not as effective, will reduce some pain.

DISCUSSION

The studies which were reviewed examined pain management in infants and the analgesic effect breastfeeding has during heelstick or venepuncture. Most of these used randomised controlled groups. Some used controls such as infants swaddled in cots (1,2), while others compared breastfeeding with other forms of possible pain relief, such as oral glucose solution (3,4). Some used maternal holding (4,5), and some used a pacifier; with holding (5), or without holding (2).

The studies used a variety of tools to assess pain in infants. These included the Neonatal Facial Activity Coding System (4), the Neonatal Infant Pain Scale (2,3), crying (1,4,5), grimacing (1), and physiological parameters such as heart rate (1,2,4,5), respiratory rate (2,3), blood pressure and oxygen saturation (5,6). The majority of the studies were performed while infants underwent heelstick procedures (1,2,5,7) while one used venepuncture (3) and one did not stipulate (4). All of these studies demonstrated that infants' pain responses while breastfeeding were reduced significantly compared with the control groups. In some cases pain responses were virtually eliminated completely (1,2). While all studies found that breastfeeding significantly reduced pain compared to no intervention, some studies using glucose in the control groups produced controversial results (2,3). However, as some studies included both term and preterm infants, less efficient breastfeeding skills in the preterm infants could inhibit the pain relieving effects of breastfeeding (2,3). Moreover, for glucose to be effective the dose needs to be large, introducing its own risks. In addition, the possibility was raised that glucose may have a sedative rather than an analgesic effect (2,3). Therefore, glucose as pain relief for mature infants is a less desirable option than breastfeeding. Although pacifiers were used only in control groups, pacifier use for term infants was cautioned against by one set of authors due to the association between early pacifier use and the reduced duration of breastfeeding. The concern was that mothers included in the trial could see pacifiers as a means of comforting her infant, whereas breastfeeding empowers the mother to comfort and calm her infant (5).

It is not known what components of breastfeeding are most responsible for the analgesic effect. Breast milk contains tryptophan, a precursor of melatonin which increases beta endorphins that may procure pain relief. However, simply administering breast milk to the baby does not provide the same analgesic effect as breastfeeding (3). Various authors propose that during breastfeeding, the combination of smell, taste, suck, touch, seeing and hearing, and the closeness of the infant's mother, saturates the senses, thereby reducing pain (2,3,5).

Although pain is a necessary physical warning to preserve life, and crying is an infant's means of communication, pain-induced crying in infants has been linked to many negative physiological effects (2,3,6-8). Crying that has been induced by pain has been shown to have significantly stronger amplitudes than crying induced by fussing or hunger (6). Studies have shown that cardiovascular function, metabolism, and intracranial pressure can all be affected by pain and crying in infants (3,6,7). Short term compromise induced by pain include; increases in heart rate and blood pressure, a drop in pulse pressure which may impair circulation to the brain, a decrease in arterial oxygen levels, changes in blood flow pressure in the brain (3,6,7), and a rise in cortisol levels (6,7). Physiological stress as measured by cortisol will rise and continue to rise as crying time increases (6,7). High levels of cortisol begin to act as an immunosuppressant which may impair the infant's ability to fight infection (6). Pain-induced crying may also activate a negative stress induced biochemical cascade, indicated

by elevated levels of renin and aldosterone. In addition, a temporary but significant rise in the blood white cell count induced by vigorous crying may lead to a false diagnosis of infection, followed by unnecessary antibiotic therapy (6,8). Interestingly, one report has shown that even mild crying increased the white blood cell count substantially (8). Research is increasingly attributing long term adverse effects to stress that occurs early in life, even at low levels. These effects can include an increase in pain sensitivity during further procedures in infancy, and this heightened sensitivity to pain may continue through to adulthood (1-3,6).

Although the option to breastfeed during painful procedures must be the mother's choice, it needs to be an informed choice. The findings that breastfeeding significantly reduces pain should be explained to the mother prior to any painful procedure. However, if this has been given and the mother still prefers not to breastfeed, or the infant is not wanting to breastfeed or is being fed with formula, then being held by the mother will still produce some analgesic effect (5). This may be further enhanced by skin to skin contact where possible, which has also been shown to have some analgesic benefit (9,10). Additionally, if the breastfed infant is held close to the mother's breast, breast milk odour has also been demonstrated to have a calming effect with pain response indices and cortisol levels reduced (5,7). These options reduce or eliminate the physiologically harmful act of crying and at the same time allows the mother to be actively involved in comforting her infant through a procedure that she too may otherwise find distressing.

Despite the large body of evidence recommending breastfeeding for pain relief during heelstick or venepuncture, there still appears to be a gap between awareness of this, and implementation. Although no risks to the infant have been identified with this practice, ongoing fears appear to remain. Fears voiced by health professionals are, a mother may drop her infant, the infant may choke, and the infant may associate pain with breastfeeding. None of these concerns have been substantiated (2,3,6). Others have expressed the belief that the infant is best left in their cot if sleeping as they don't always wake. While this may be true, it is impossible to predict which infants will wake and which will not. However, of very real concern to health professionals involved in collecting blood samples from infants is the risk of harm to themselves. This is due to the often awkward positions required to access the infant's heel when held by the mother. Therefore, it is vital that time is taken prior to the procedure to ensure that any risk that may contribute to gradual process injury of the collector is averted. In a hospital setting the bed can be adjusted to the correct height for the collector, or if the mother is seated in a low chair, could be asked to move from the chair to the bed. In all settings, as mothers are generally well women, instruction can be given to manoeuvre their bodies, and therefore the infants, into a position to allow accessibility to the heel without risk of injury to the collector. Anecdotal evidence suggests that infants that are breastfeeding while undergoing painful procedures bleed more freely, reducing the time required for the collect. Therefore, this may compensate for the time required to reposition the mother and infant for the safety of the collector.

CONCLUSIONS

Crying induced by pain has been shown to have adverse effects on infants, not only in the short term, but in the long term also. Research has clearly shown that breastfeeding is a safe and effective analgesic intervention to reduce pain during painful procedures such as heelstick or venepuncture. If breastfeeding is not possible, then being held by the mother has also been shown to produce some analgesic effect. Mothers should be informed of these options prior to these procedures being performed on their infants.

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CASE STUDY

House Dust Mites in urine. Spurious finding in two cases

Sharda Lallu[1], Sarla Naran[1] and Peter Bethwaite[2]

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ABSTRACT

Urine cytology is usually done for initial evaluation of symptomatic patients, follow-up of patients with tumoral pathology, and for risk population screening. Nevertheless, sometimes elements or structures are observed that initially seem unrelated to what is being looked for. Mites belong to the order Acarina and their presence has been noted in human body fluids, including urine. We report the spurious finding of house dust mites in urine samples from two patients, originally mistaken for pubis lice in the first case. Medical laboratories should be aware of the possibility of house dust mite contamination of urine specimens.
Key words: House dust mites, Papanicolaou stain, urine

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INTRODUCTION

Mites belong to the order Acarina and only a few species are known to affect humans. Mites in sputum specimens were first reported in 1944 by Carter et al. in Ceylon (1). The acaroid mite is a kind of arthropod and its geographic distribution appears to be global and mites can survive in many environments including the storehouse, farmhouse, stored food stuff, various drugs, packing material, household objects, and human and animal bodies. Its infection in human cause acariasis in some organs including the lung, intestines, and the urinary tract by inhalation, ingestion, and transmission through the skin (2-4). House dust mites can also cause asthma and extensive dermatitis to atopic eczema through the allergens that they produce (5). Most adult mites possess the usual arachnoid appendages, jaws, palps at the front end, and four pairs of legs. This report describes the spurious cytologic findings of adult dust mites in urine samples from two patients. With referral from a parasitology laboratory, and experts on house dust mite identification, we concluded that the microscopic objects were most likely dust mites, the first case as being *Euroglyphus maynei* and the second case as being of the *Dermatophagoides* species (6,7).

From the laboratory perspective it may not be possible to decide whether the presence of mites is due to contamination or a true infection. The possibility of infection should only be considered in the presence of a considerable number of adult mites with inflammatory reaction (3) and after repeated identification of mites in consecutive samples from a symptomatic patient, and that the clinical findings are compatible with such an infestation. Mites can be present in cytologic samples as a contaminant from the environment. In this article we present two cases of urine samples in which we observed a single mite. Presence of a single mite without inflammatory reaction and relevant clinical findings led us to consider their presence as a contaminant.

CASE HISTORIES

Case 1: A 30 year old pregnant female presented with chronic haematuria without other symptoms. We received a urine sample from the urologist for cytologic examination in which we found an adult mite, originally mistaken for pubis lice. On two consecutive urine samples from this patient we did not find any adult mites. On examination by her general practitioner no visible opalescent nits or live lice and blue macules at feeding sites were present.

Case 2: A 72 year old female presented with haematuria and dysuria. We received a urine sample for cytologic examination in which we found single adult mite without inflammation. We did not receive any further urine samples from this patient.

MATERIALS AND METHODS

In both cases we received fresh mid-stream urine samples in a summer month from the urologist for cytologic examination. Filter preparations were made on size 5 micron, 25 mm diameter Sartorius AG-cellulose acetate filters using the cytosieve method in which cells are trapped in filters pores and fixed in 95% ethanol. Filters were stained by the Papanicolaou method. The main components of Papanicolaou stain includes basic dye-hematoxylin, which stains the nucleus; and three acid dyes-light green, eosin, and Orange G, which stain the cytoplasm. With the Papanicolaou stain, the nucleus stains deep blue, nuclear details are sharp, the nucleous stains red, and the cytoplasm stains eosinophilic, cyanophilic, or orange (8).

RESULTS

Cytologic findings

Filter preparations of both urine samples demonstrated blood, benign squamous cells, scattered reactive urothelial cells and a single well preserved dust mite, approximately < 0.5 mm in size, pinkish brown in colour with partially folded legs (presumably 4 pairs), jaw, and palps at the front end (Figures 1 and 2). No inflammation was seen in both cases.

DISCUSSION

Mites belong to the order Acarina and are a kind of arthropod with only a few species known to affect humans (5-7). Mites are distributed throughout the world and thrive in warm, moist environments (7). They are tiny creatures less than 1 mm in length, usually invisible to the naked eye. Mites are found almost everywhere in nature, on land and in water, living on organic matter. The body of the mite is divided into two regions; a front part called the cephalothorax and a hind part called the abdomen. Although there is no clear demarcation between these parts, most adult mites possess the usual arachnid appendages, jaw and palps at the front end, and four pairs of legs. Most mites are quite harmless themselves but their fecal

pellets contain digestive enzymes that can cause severe conditions such as asthma, allergic reaction, dermatitis, intestinal and urinary acariasis, and respiratory disorders (2,4,5).

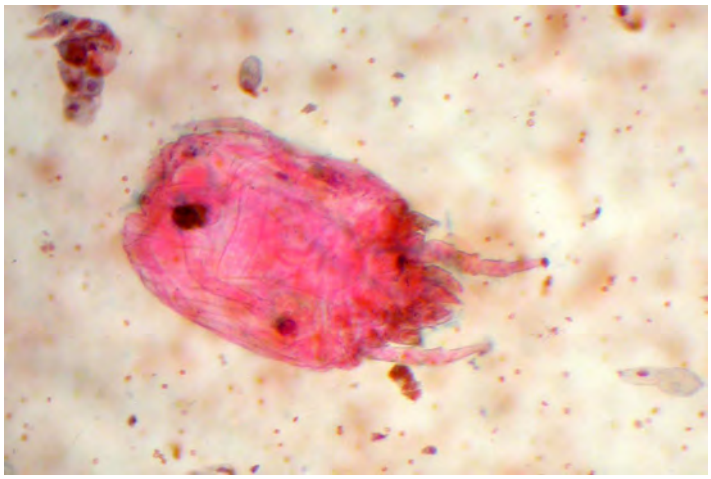

Figure 1. Filter preparation of urine from case one showing blood, benign squamous cells, reactive urothelial cells, and adult mite with one pair of legs, jaw and palps at the front end, and lateral three pairs of legs folded against the body (Papanicolaou stain X 400).

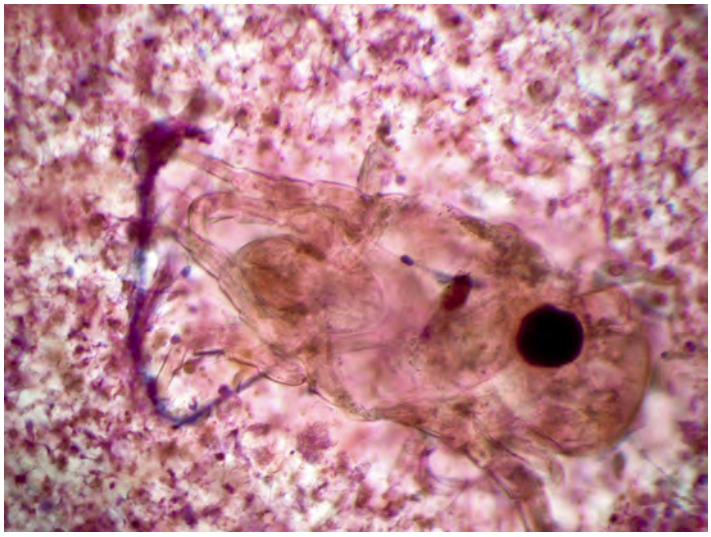

Figure 2. Filter preparation of urine from case 2 showing blood, much debris, benign squamous cells, and adult mite with two pairs of legs, jaw and palps at the front end, and lateral two pairs of legs partially folded against the body (Papanicolaou stain X 400).

A study in China found that the prevalence of human intestinal, respiratory and urinary acariasis (mite infection) was associated with occupation and was higher in individuals working with medicinal herbs, in store houses, in mills, or other sites where the density of mites was high (4). Nevertheless, mites can be found in cytologic samples as a contaminant from the environment, as we have observed in two cases of urine samples. In spite of their relative large size, mites are not always conspicuous because they are often transparent and unstained, and the joined appendages and sac-like bodies cause them to resemble specimen contaminants such as food. In many cases the legs are folded against the body rather than extended making the mites considerably less conspicuous and may be overlooked on routine screening, especially in cases of contaminants.

The differential diagnosis includes *Sarcoptes scabie* which are most commonly associated with humans and cause scabies with pruritus skin manifestations such as papules, blisters and eczematous changes. *Pthirus pubis* has a similar appearances but is normally bigger in size (1-3 mm long) and has broader crab like bodies with three pairs of legs, a small head with short antennae and simple eyes (9), which were absent in both our cases. *Pthirus pubis* infests hair in the pubic area and physical findings include visible opalescent nits or live lice, which were not present in our patients.

We conclude that the microscopic object in each urine sample were house dust mites that were contaminants because consecutive two urine samples from the first patient did not show any dust mite. One reason for house dust mites as a contaminant is the presence of house dust mites on clothing (10) and on skin (11) as evidenced by the presence of house dust mite allergens on these environments and thus may have been transferred into the urine specimens. In New Zealand 98% of house dust mites are *Dermatophagoides pteronyssinus* (12). They were first described in domestic homes in New Zealand in 1971 (13). New Zealand has some of the highest levels of house dust mite allergens in the world and this reflects the very high number of house dust mites in New Zealand domestic dwelling (14). The clinical significance of mites in cytologic samples largely depends on the identification of the mite species.

CONCLUSION

In our study, in the first case the mite was *Euroglyphus maynei* and the second being of the *Dermatophagoides* species (which was identified by an experienced house dust mite expert but he was unable to determine whether it was *D. pteronyssinus* or *D. farina*). To avoid contamination of urine specimens sterile specimen containers should be used when sampling and the container should be kept closed until ready for examination.

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TH PULLAR MEMORIAL ADDRESS

Looking forward with hindsight

Alex Dempster

Southern Community Laboratories, Dunedin

It is a great privilege for me to give the TH Pullar Memorial Address. Thos Pullar was of a previous generation and died just before I started training in pathology. His name and reputation was familiar to me because my teachers spoke of him with respect.

Thos Pullar was born in Auckland, but the latter part of his schooling was in Edinburgh at George Heriot's School. He trained in medicine in Sheffield gaining the gold medal in pathology and was subsequently biochemist at the Royal Hospital Sheffield and assistant pathologist at Sunderland. He gained MRCP London in 1933 and became clinical pathologist to Mt Vernon Hospital. In 1936 he accepted the position of pathologist at Palmerston North Hospital. As such he was one of the early pathologists in New Zealand following Pearson D'Ath and others and was probably the first pathologist in New Zealand with a strong biochemical background. However, at this time sub-specialisation by pathologists was not an option, and judging from the titles of his two published papers he did his share of surgical and autopsy pathology (1,2). He promoted communication between clinicians and pathologists and had a continuing interest in tumour pathology.

Thos Pullar's most notable achievement was his motivation and unceasing efforts in establishing a career path for medical laboratory technologists (3). He encouraged development of appropriate educational activities and organizational oversight with formation of the Medical Laboratory Science Board. These efforts finally resulted in the process of registration that is reflected in the Institute that you have today.

The title of my talk is looking forward with hindsight, although the ancient Andean Indians stated, wisely, that "*the past is in front of you, the future is behind*". This conference's theme is "*focus on the patient*". The subject provides an excellent platform to explore the role of the modern laboratory, present issues and our role as laboratory professionals in improving patient care and management (4).

It is hard for the modern laboratory technology graduate to conceive of the manual input into laboratory work, even in the 1960s and of the extraordinary technological and biomedical advances that have taken place since then. I was personally attracted into pathology through technology some 60 years ago when I spent several school holidays working in the kitchen of the Dunedin laboratory and was introduced by an astute Professor D'Ath into the techniques of tissue block preparation and staining.

Since that time, the introduction of laboratory automation has resulted in greater uniformity and standardisation of testing, with the first Coulter counters and single channel autoanalysers introduced to diagnostic laboratories about 50 years ago. From the time that laboratories had manuals of biochemical methods that involved weighing and measuring of reagents and utilisation of primitive spectrographic techniques, we have seen enormous advances in automation of testing processes and standardisation of commercially supplied reagents. These changes have resulted in vast improvements in reproducibility, inter-laboratory result comparison and the establishment of reliable "normal" analyte ranges.

One of the recent buzzwords is "harmonisation" of laboratory testing that includes not only harmonisation of methods and results, but also includes terminology, units, reference limits, and criteria for result interpretation. (5)

These wide ranging changes through improved test accuracy, and addition of newer and in some cases disease specific diagnostic modalities have greatly influenced clinical diagnosis and patient management. Just one such example has been the use of troponins in the management of ischaemic cardiac disease (6).

Two of the really significant scientific developments, if not the most important, that have resulted in major changes in most areas of laboratory technology began with the discovery of the structure of DNA by Watson, Crick and Wilkins who won the Nobel Prize. Rosalind Franklin who collaborated with important spectrographic work, and ironically died in her early 30s of ovarian cancer, possibly of genetic origin, was not included as an author of the original paper. This discovery was followed by developments in genetic analysis, the development of monoclonal antibodies, and FISH and PCR technologies that reach into most laboratory specialties.

The modern understanding of the human genome has played a critical role, and from this, tests have been developed to identify specific disease related translocations that can be diagnostic for certain tumours or can be used to identify those individuals with an inherited predilection for diseases linked to specific genetic defects. Also the ability to identify certain tumour markers assists in identifying patients who will respond to specific treatments. These developments are all largely beneficial to patients as well as improving the efficiency of health spending.

Can we predict how developments in these areas might result in changes and increasing sophistication of testing? To some extent we can foresee likely developments by reviewing relevant current scientific literature and by following up promising research developments. I'm now going to highlight some general issues that are very relevant to patient benefits from laboratory testing and our profession as a whole and will then conclude with some specific examples from my own specialty areas of cytology and anatomical pathology.

The first issue is that of communication in its widest sense. To the uninitiated clinician or administrator, the modern laboratory is an amazing place, where staff operate complex machines that distribute results, usually electronically, to clinicians and others that require them. At times this results in a lack of understanding of the clinical role of the laboratory professional, both technologist and pathologist in patient care and indirectly causes one of the significant problems we all experience.

The most problematic is the failure of clinicians to provide relevant clinical information when requesting tests. As histologists and cytologists we frequently receive requests lacking critical, and at times, any, clinical information. This can result in the performance of expensive additional testing to answer questions already known, or prevent useful additional tests being added, based on the knowledge and experience of the laboratory professional.

The next problem is that of the inappropriate or unnecessary tests that should be challenged by the laboratory. This requires tact and solid knowledge of the issues on the part of the laboratory professional to challenge a clinical decision. Frequently it will cause conflict and the path of least resistance and to save time is to shut up and do the test. There have been some quite innovative approaches to reduce inappropriate testing.

Infomatics is a rapidly developing area that permits integration of laboratory test results at the user interface. An example is with GP software that matches laboratory records to individual patients, flags those requiring urgent intervention and may provide a historical graph of particular analytes against the expected range. There is also the potential to use similar programmes to incorporate relevant clinical data onto laboratory request forms.

We, clinicians and patients, are now able to access a vast resource of scientific and medical literature online. But even if we consult peer reviewed literature, there can be conflicting evidence and we look for sources to validate the information. These issues need to be resolved when decisions are to be made about test or new technology introduction. Laboratories have always been enthusiastic about introducing the latest technology and are actively encouraged to do so by manufacturers of newer, better, and more expensive equipment. Some technological developments that are already taking place are likely to affect the structure of laboratories as we know them and the range of tests that are performed. With increasing testing complexity there is a gradual move towards consolidation of testing into larger institutions, for a variety of reasons not always with the best outcomes.

There have been the debates about near patient testing with the obvious benefit of diabetics managing their own treatment with great effect. The future prospect is of direct patient monitoring with direct transmission of results to clinical management services. It has been reported recently that the Google Company is sourcing expertise in real time monitoring of health related parameters and is looking with Novartis at a wearable contact lens that could determine glucose levels in tears. Possibly a wearable testing device will soon tell us when we have had one drink too many! This is not a particularly outrageous suggestion as there is already a basic wearable device that can determine alcohol in sweat.

It is still early days in the development of this type of technology and there are sceptics who believe there are enormous scientific and regulatory hurdles to be overcome but predicting the future is not science. It is quite possible that the medical laboratory of the future will, to a much greater extent, confine its activities to sophisticated testing that will be relevant to personalised medicine and there will be less emphasis on routine analyte analysis.

Biological reagents are now widely used across all laboratory disciplines but for the remainder of this presentation my remarks will be confined to my own specialty areas of cytology and surgical pathology. With the development of fluorescence microscopy in the early 1970s, we attempted some in-house methods of virus identification in tissue specimens using indirect immunofluorescence and polyclonal antibodies. The illustration is of Herpes virus in a tissue section from a case of congenital Herpes virus infection and Influenza A virus in tissue culture (Figure 1).

In cytology and anatomical pathology immunohistochemistry has taken much of the guesswork out of difficult tumour diagnosis. The images show cytology membrane and cell block preparations of a non-small cell carcinoma of lung, possibly adenocarcinoma. Immunochemistry showed positive chromogranin and synaptophysin and negative TTF1 staining confirming a diagnosis of neuroendocrine carcinoma (Figure 2).

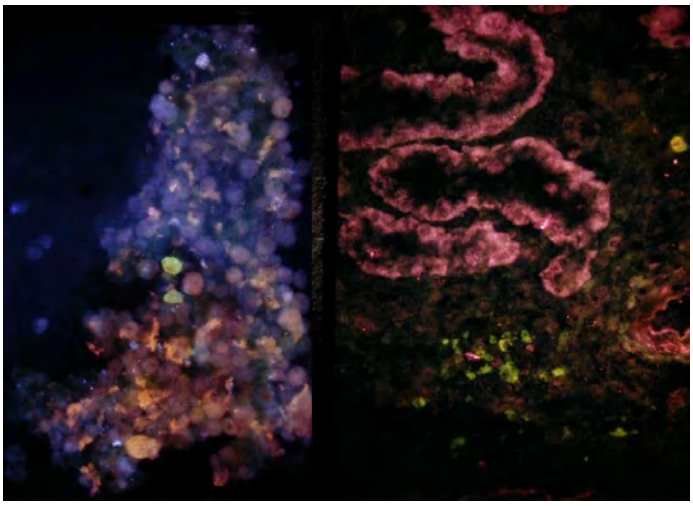

Figure 1. Indirect immunofluorescence from the 1970s using polyclonal antibodies.
Left: Influenza A in tissue culture.
Right: Herpes simplex in tissue in case of congenital herpes.

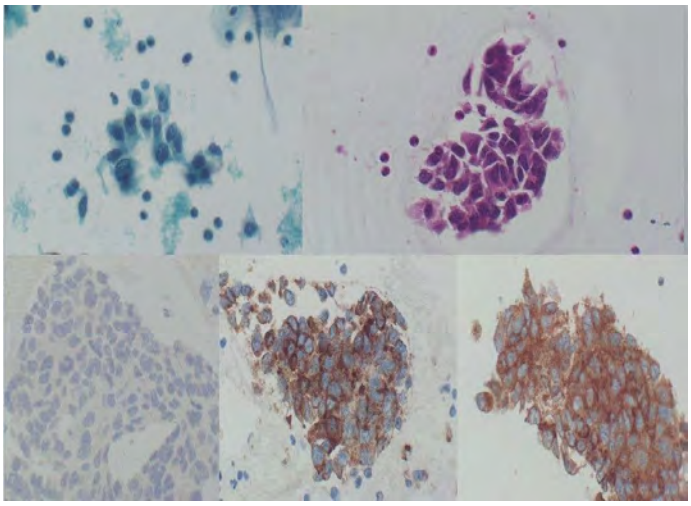

Figure 2. Neuroendocrine carcinoma of lung.
Top left: Surepath preparation, top right cell block (H&E), bottom left TTF1, bottom centre chromogranin, bottom right synaptophysin.

The unravelling of the human genome resulted in the introduction of tests for specific genetic abnormalities that are specific for some tumours, especially some of soft tissue origin as well as identifying individuals with the risk of genetically linked tumour development (7,8). Genetic analysis can provide prognostic information for a variety of tumour types such as ocular melanoma and breast cancer with multi-array gene studies such as Oncotype DX and Mammaprint. These are widely used in North America and to some extent in Europe, but there are alternative opinions that the information provided by these currently costly tests can be acquired by simpler methods (9).

However, introduction of new techniques means that older technology measuring similar parameters may become outdated. Unexpected consequences can also occur. Resistance to change has been encountered when long established tests (ESR, differential counts in bronchial washings, neutrophils in synovial biopsies) are deeply embedded in clinical practice (10).

A current issue is the proposal that antibody testing for high risk HPV (hrHPV) be introduced as the primary screening method for HPV related cervical abnormalities without co-testing by cervical cytology. This development has already been, or is planned to be introduced in several countries including the UK, NZ, and Australia with the potential to cause major changes in cytology services.

There remains controversy as to the desirability of introduction of HPV screening alone as the primary screening method for HPV related cervical abnormalities. There are differences between competing commercial products and not all high risk HPV viruses are included in current tests (11). Some of these issues have been clarified by publications from senior laboratory scientists (12,13).

The main issues can be summarised as follows. HPV testing as a stand-alone screening process presents difficulties in interpreting results in the under 30s as the incidence of transient HPV infection is high. Even infection with hrHPV only results in the development of a high grade lesion in a small proportion of the infected group. The potential demand for colposcopy from such testing would result in a very significant workload increase for colposcopy clinics.

In some countries screening begins at the age of 30. It has been shown in those countries with limited health resources that cannot support a screening programme, a single HPV test at 35 appears to be the most effective method of reducing invasive cervical carcinoma (14). However, in developed countries with a high incidence of HPV infection in the under 30s such as the UK, Australia, and New Zealand it has been shown that slightly over half of those diagnosed with CIN 2/3 were between the ages of 20 and 29 and about 10% of cases of invasive cancers were diagnosed in this group.(14)

Although HPV testing is at least as sensitive as well performed routine cytology, neither process approaches 100% sensitivity or specificity. Positive predictive value (PPV = true + false positives/true positives) is a better assessment of specificity than NPV because the latter is obscured by the large number of negative cases (98%) that inevitably occur in any screening programme. In the ARTISTIC trial in England 10.9% of cases of CIN2 and 4.3% of CIN3 were HPV negative (15). Although almost all CIN2 cases are positive just before biopsy, only 83% were positive three years previously. In Australian data (16) 11% were HPV negative at biopsy and 29% two and a half years previously. This is especially relevant because of the increased screening interval that has been suggested.

Another significant issue is that only about 75% of women with invasive carcinoma are HPV positive one to five years prior to diagnosis (13). One group have shown low virus loads early in invasive cancer when cases may be HPV negative but are PCR positive (17). However, PCR testing is expensive and of low sensitivity and is not useful for screening purposes.

But also as the sensitivity of screening tests are increased so the PPV is decreased. New biomarkers continue to be developed and one, p16ink4a has shown to be applicable for confirmation of high grade lesions in cervical smears. Similarly P16 and Ki67 in histology and as a dual stain procedure in cytology have been proven to be helpful in confirming possible but morphologically inconclusive high grade lesions such as ASH. Where cytology is of a high standard, HPV co-testing alone is of little and at best marginal value in improving detection high grade lesions

Ultimately whatever screening procedures are used will be a trade-off between PPV for high grade lesions and the cost of testing. Co-testing for HPV with cytology is especially useful for test of cure following treatment in women who continue to be HPV positive following treatment of high grade lesions. The 10 year risk of CIN 3 post treatment if HPV negative is 2.1% and 1.4% when combined with cytology. Those who remain HPV positive but do not have a high grade lesion on colposcopy can return to three year screening. Once HPV vaccination is well established and covers a large proportion of the female population, HPV testing will be necessary to determine the frequency of HPV infection and those who will need further testing.

These issues associated with just one diagnostic process are examples of the major sea changes occurring in diagnostic technology. The outcome of decisions regarding changes in primary cervical screening will have significant impacts on the cytology service, cytotechnologist jobs, costs and possibly individual patient outcome. However, it has to be recognised that in any screening process, some patients, depending on the techniques and processes used, will escape the net and develop disease.

It is critical that we use our scientific knowledge to try and identify unintended consequences in advance of significant changes in laboratory methodology. There are those who predict that there will come a time when H&E tissue diagnosis in surgical pathology will no longer be necessary and that genetic and immune technology will achieve diagnosis. The problem is that there is genetic crossover between conditions with widely differing outcomes and that clinical management and therapy is directed towards modified H&E diagnosis aided by genetic and immune information with markers such as EGFR Her-2 and oestrogen receptors, all relevant to tailoring chemotherapy to the patient. Similar and as yet undeveloped markers will also become at least as important in other clinical areas for patient tailored therapy.

It is now impossible to open a surgical pathology journal and find an article without pictures of the brown and red stains of immunohistochemistry. However, morphological observations are still providing new information such as the recent identification that the growth pattern of renal cell carcinoma provides a prognostic parameter independent of traditional tumour grade and stage.

In other disciplines within laboratory technology, new developments also have the potential to change the face of diagnostic processes as we know them. As laboratory professionals, we play an important role in being able to analyse the significance of these developments from peer reviewed literature, to be able to assess the implications in economic terms and patient outcomes and to be able to provide informed opinion as to when, how and where they should or should not be introduced.

Now that we have academic posts in laboratory technology in health science faculties, the opportunity exists for laboratory scientists to have increasing involvement in the scientific assessment of technological and biomedical developments, the application of which will play very significant roles in future patient diagnosis and management.

AUTHOR INFORMATION

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N Z J Med Lab Sci 2014; 68: 94-97.

Journal Reviewers 2013/2014

The listed persons below reviewed articles submitted to the Journal from September 2013 to August 2014, some more than once. All submitted articles undergo peer review in order that the Journal maintains its high standard. Additionally, thoughtful comments and suggestions made by reviewers help authors in ensuring that their articles, if accepted, are put in front of the reader in the best possible light. The Editors cannot be experts in all disciplines of medical laboratory science and thus rely on quality peer review by others. We thank the reviewers for their time and effort.

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Rob Siebers, FNZIMLS FNZIC FSB, Editor
Terry Taylor, BSc DipMLS MNZIMLS, Deputy-Editor

Life Membership

Life Membership was awarded to Ross Hewett, Laboratory Manager LabPlus, Auckland District Health Board, at the Opening Ceremony of the NZIMLS Annual Scientific Meeting in Dunedin on 12 August 2014.

Ross has a distinguished career in Medical Laboratory Science, qualifying in 1977 with a Part 1 and Part 2 Clinical Biochemistry after training at Palmerston North Hospital. He spent the next five years overseas working in London in private pathology and then in Saudi Arabia as Laboratory Manager in a private hospital in Jeddah. On returning to New Zealand, he worked at the Central Institute of Technology in Upper Hutt, teaching Medical Laboratory Scientists before joining the Pathology Lab at Hutt Hospital.

A significant change in career took him and his family to Auckland in 1984 to join Boehringer Mannheim where he stayed until the beginning of 2001. During his time in the industry he progressed from sales to sales management, to marketing to senior management, finishing as Managing Director of Roche Diagnostics Australia. On returning to New Zealand in 2001, Ross joined LabPlus as a Medical Laboratory Scientist, then Business Development Manager and in March 2007, Laboratory Manager of LabPlus.

In his current position of Laboratory Manager, Ross's main area of interest is the changing role of medical laboratories in New Zealand and the professional development of Medical Laboratory Scientists.

He serves the profession in numerous additional roles including:

- Service Manager, National Forensic Pathology Service
- Advisory Group member, National Coronial Pathology Service
- Advisory Group member, National Paediatric and Perinatal Pathology Service
- Advisory Group member, National Newborn Metabolic Screening Programme
- Member of the Auckland Region Joint Advisory Group – Pathology Service
- Member of the NZ Ministry of Health (MOH) Pathology Round Table chaired by MOH Chief Medical Officer.

Ross joined the NZIMLS Council in 2002 and has been Secretary/Treasurer since 2004, where he was instrumental in the restructuring of the NZIMLS Executive Office and the financial accounting systems and governance of the NZIMLS. This has hugely contributed to the strong position the NZIMLS is currently in.

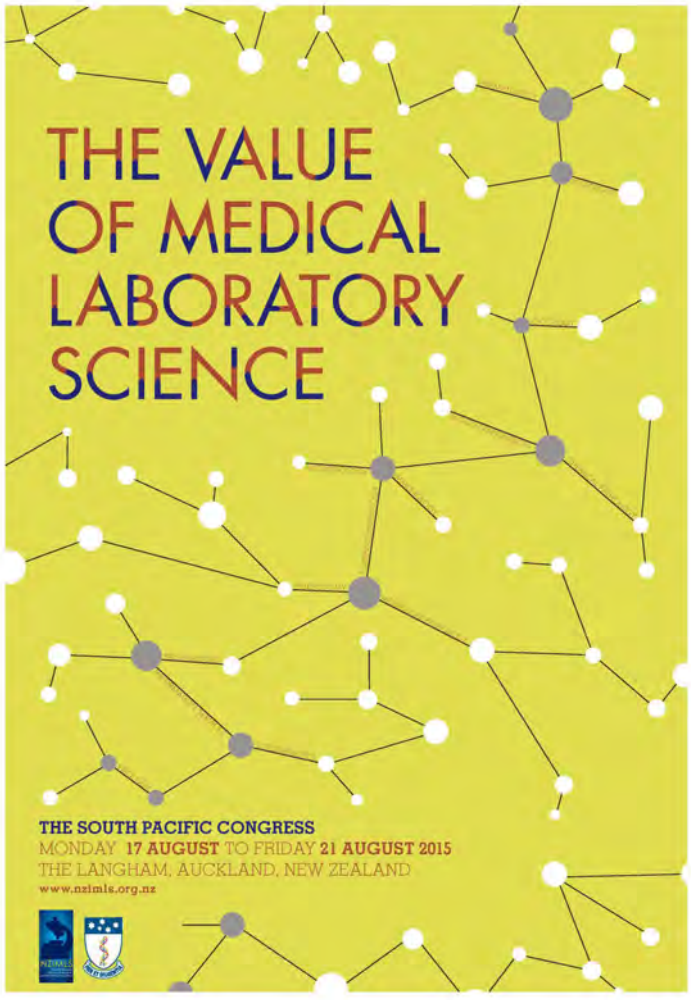
He was convenor of:

- The South Pacific Congress, Auckland 2007
- The NZIMLS Scientific Meeting, Bay of Islands 2010
- The NZIMLS North Island Seminar, Auckland 2013
- He has also organised a number of Biochemistry Special Interest Group Meetings.

Ross was honoured by the NZIMLS when asked to present the TH Pullar Memorial Address in 1998 in Palmerston North.

There can be no more a deserving recipient of the Life Membership award than Ross for his services to the profession and in particular to the NZIMLS.

NZIMLS Immediate Past President, Ken Beechey presenting Life Membership to Ross Hewett at the opening of the NZIMLS Annual Scientific Meeting, August 2014



Abstracts of the NZIMLS ASM, Dunedin, August 2014

Adoptive immunotherapy targeting viral antigens

Prof Helen Heslop, The Methodist Hospital & Texas Children's Hospital, USA

Immunotherapy with antigen-specific T cells has the potential to reconstitute antiviral activity post transplant without inducing Graft vs. Host Disease. Our group has performed a series of clinical studies showing that cytotoxic T lymphocytes (CTLs) specific for Epstein-Barr virus (EBV) provide effective therapy for EBV-related lymphomas post hemopoietic stem cell transplant (HSCT). To extend the approach to additional viruses we developed methodology for using genetically modified antigen presenting cells approach to generate CTL from donor peripheral blood that target CMV, EBV and adenovirus and showed that adoptively transferred donor-derived CTLs can reconstitute antiviral immunity to all three viruses and effectively treat established infections. However, the time taken to prepare patient-specific products and the lack of virus-specific memory T cells in cord blood and seronegative donors restricts application. More recently we have evaluated whether T-cell lines manufactured using methods that exclude viral components and utilize simplified manufacturing technology can be clinically effective. To date we have administered these lines to 10 allogeneic HSCT recipients as treatment for CMV, adenovirus and EBV lymphoma. Eight treated patients, including one with a biopsy-proven EBV lymphoma and 3 patients with double reactivations, had complete clinical responses to rCTLs, which corresponded with an increase in the frequency of virus-specific T-cells detected in peripheral blood. In a follow up study we have simplified the manufacturing further by using overlapping peptide pools and extended the specificity to include HHV6 and BK. Ten patients have been treated on this study with responses seen to infections with all 5 viruses. Another means of avoiding growing CTLs for individual patients is to bank lines that are then available as an 'off the shelf' product of most closely HLA-matched allogeneic cytotoxic T lymphocyte lines (CHM-CTLs). We evaluated this strategy in a multicenter study through the NHLBI Specialized Centers for Cell-Based Therapy (SCCT) program in HSCT recipients who had viral reactivation or infection refractory to standard therapy. The overall cumulative incidence of first CR/PR in 50 patients based on viral load by day 42 was 74.0% (73.9% for CMV, 66.7% for EBV and 77.8% for adenovirus).

Point of Care testing: what's the point?

Linda Grady, ICU Nurse Educator, Dunedin Hospital

Point Of Care (POC) testing devices have the potential to deliver more rapid results for critically ill patients, and results for patients who are in centres without laboratory support. In intensive care departments, a blood gas analyser within the department is part of the minimum standard for modern unit design. Other than their increased per test cost compared to conventional laboratory testing, it would seem that they are an obvious solution and a real advantage in a large number of environments. Why hasn't uptake been universal? POC devices have enjoyed good uptake in several smaller hospital emergency departments, as well as some GP centres. Similarly, POC devices are used in clinical care to rapidly monitor blood sugar, ketone and coagulation profiles in our intensive care - but not much more than that. Even in a retrieval and ambulance environment, where POC devices have the capacity to enhance diagnosis and treatment options at the bedside, their uptake has been limited. Why? Cost and the number of tests likely to be performed in a centre are factors which have limited uptake, as are the capacity to link results of those tests into the rest of the medical record.In resource limited environments (such as transport) the "what can you do anyway" question limits utility. Many clinicians do not trust point of care devices, believing that "bigger must be better" or that results from the laboratory must be more accurate than those perfumed at the bedside. The fact that POC devices are "stand alone" whereas laboratory tests have support of a dedicated lab team also decreases this trust.

The role of laboratory tests in a randomised controlled trial to evaluate safe sleep options for New Zealand babies

Baddock SA[1], Taylor BJ[2], Tipene-Leach DC[2], Williams SM[2], Tangiora AG[2], Jones R[2].
[1]Otago Polytechnic, Dunedin, [2]University of Otago, Dunedin

Purpose: Sudden Death in Infancy (SUDI) remains a significant issue, with the rate among Maori being 5 times that of non Maori, non Pacific (2.34 deaths/1000 live births vs. 0.52). Many deaths are associated with bed-sharing and maternal smoking. The wahakura (flax bassinet) has been developed by Maori as a potentially safer way of bed-sharing. The aim of this study is to assess the risks (e.g. infant head covering or prone sleep position) and benefits (e.g. increased attachment and breastfeeding) of using the wahakura compared to the standard bassinet.
Methods: 200 pregnant women were recruited from Maori communities in areas of high deprivation in NZ, and randomized to receive a wahakura or a bassinet during pregnancy. Investigations included laboratory testing of infant urinary cotinine and maternal salivary oxytocin, questionnaires at baseline (pregnancy), 1, 3 and 6 months, and an overnight sleep study at 1 month with video, oximetry and temperature recordings.
Results: Infant urinary cotinine gives a measure of passive smoke exposure on the sleep study night to validate reported smoking data. Maternal salivary oxytocin levels, in association with the questionnaires, contributes to understanding about maternal parenting factors, including beliefs about infant care, attachment, and parenting adaptation.
Discussion: This laboratory testing has enabled validation of the self-reported smoking data and has contributed a biochemical analysis to complement questionnaire data on infant-mother attachment. Together with parental self-reported data, and objective overnight video and physiological data, it has enabled a comprehensive investigation of the wahakura as a culturally acceptable SUDI intervention.

The critically ill neonate: challenges in laboratory investigation

Assoc Prof David Reith, Dunedin School of Medicine

The critically ill neonate presents challenges to laboratory diagnostics and at the same time laboratory results are important in their management. A range of serious illnesses can present with a similar clinical picture: serious infection, endocrine and metabolic disorders can all masquerade as each other; but all have specific treatments that are life-saving. Sample collection is difficult because of difficult venous access, a reduced total blood volume, and high haematocrit. Hence, individual samples are precious. The laboratory plays a key role in the management of these patients and two-way communication is important.

Stem cell transplantation

Prof Helen Heslop, The Methodist Hospital & Texas Children's Hospital, USA

Hematopoietic stem cell transplantation (HSCT) is an established treatment approach for many malignant and nonmalignant diseases that affect the hematopoietic and immune systems. As transplantation has become safer, it has become used earlier in the course of malignant diseases with improved outcomes. Over the past 15 years indications for HSCT and cellular therapies have broadened, and the future suggests even wider applications, especially in delivering novel treatments for malignancies. A number of key advances have contributed to making HSCT a more commonly available and successful treatment modality. First there was improved understanding of the critical role of histocompatibility in allogeneic HSCT and development of high resolution molecular methods to more accurately type donors and recipients. Additional sources of stem cells were also employed so that bone marrow (BM), peripheral blood (PB), and umbilical cord blood (UCB) are all now widely used in clinical practice to provide long-term hematopoietic reconstitution. These advances along with the increasing numbers of donors in large registries of unrelated donors and cord blood units both expanded access to transplant and allowed recipients to find more closely matched donors. More recently approaches to either deplete T cells ex vivo or deplete alloreactive cells in vivo have resulted in improved outcomes for haploidentical transplant further increasing donor options. Finally there have been improvements in graft versus host disease prophylaxis and supportive care during the period of hematopoietic and immune suppression post transplant. HSCT should therefore be considered for patients in whom this procedure is likely to result in superior long-term disease-free survival (DFS) compared with other therapeutic modalities. Potential candidates must also have a suitable source of hematopoietic stem cells (HSCs) available at an appropriate time in the course of the disease. Current research in HSCT is aimed at improving outcomes and trying to reduce complications of the procedure which include infection, graft failure, regimen related mortality and when undertaken for malignancy relapse. The laboratory plays a key role in the management of transplant patients in performing tissue typing to identify the best donor and in monitoring patients post transplant for engraftment, infections and relapse.

The patient's view of the laboratory in a hospital - what do they want?

Ailsa Bunker, Counties Manakau DHB, Auckland

Often the only direct contact patients have with the laboratory is the phlebotomist. From the patient's view the phlebotomy service and the laboratory are the same. The phlebotomist's skill and behaviour determines the patient's perception of the quality of the entire laboratory. Patients in a public hospital are generally not there by choice. They do not choose the hospital and they definitely do not choose to be sick. Conversely, phlebotomists and laboratory staff have chosen a career in health and have a direct effect on the patient's hospital experience. So what do patients want? The majority of patients focus on relieving symptoms and curing illness. They want care immediately, delivered with kindness. They expect the best treatment, and to know their health workers are highly qualified. How are we going to give patients what they want? We need to begin by selecting staff who value and care for people, and provide those staff with the best possible training. Training needs to include not only technical skills but customer service and cultural competency. We need to aim for the highest quality of care and service by utilising quality assurance programmes, constantly improving our service and responding to customer feedback. Finally, we have a vested interest to ensure we pass on our skills and our caring hearts to the next generation of phlebotomists and laboratorians. They will be our caregivers!

Laboratory testing in reproductive medicine

Dr Wayne Gillett, Dunedin School of Medicine

Laboratory testing is an integral part of managing all aspects of reproductive medicine from puberty to menopause. Diagnosis, monitoring and risk assessment are the three main indications for routine tests. Most are performed in reproductive endocrinology and infertility. In assessing the infertile couple the two main tests are the semen analysis and measurement of ovarian function. Since a normal menstrual cycle is indicative of normal ovulation, ovulation testing is only useful if the cycle is not normal. In primary care there is frequent misuse of tests of reproductive hormones, FSH, LH and progesterone. Interpretation of FSH and LH is best if measured in the basal phase, i.e. early in the cycle when estradiol is low. Progesterone interpretation needs the date of the following menstrual period. Hormone testing is useful for diagnosis of PCOS and ovarian failure but, again, many tests are requested that are not that helpful. Assisted reproductive techniques are dominated by IVF because it is the most effective treatment for infertility. Safety and risk issues require close monitoring.

Development of biomarkers and targeted therapies in Alzheimer's disease

Dr Joanna Williams, University of Otago, Dunedin

Alzheimer's disease (AD) is a neurodegenerative disease, expected to afflict 50 million people worldwide by 2050. Despite this there is no known cure or effective treatment. This is likely because the underlying pathological changes occur as early as 20 years prior to acknowledgement of symptoms meaning that current therapies are given in the late, intractable, stages of the disease. An easily administered predictive test for AD, allowing accurate early diagnosis and intervention to delay onset of the disease, would bring enormous benefits to the health of affected individuals and to the economics of their healthcare. Alongside this it is crucial to develop effective therapies, giving hope to those diagnosed with AD. We aimed to determine if altered levels of microRNA in blood plasma, alongside a specific protein marker, TTR and ApoE 4 might act as a marker of the disease process potentially allowing early detection of Alzheimer's disease. We have profiled the expression of plasma microRNA in Alzheimer's-affected (n=49) and age-matched elderly participants (n=42) using TaqMan Low Density Arrays (TLDAs). Following data normalisation, differentially expressed microRNA were identified using unpaired t-tests. Using Receiver Operating Characteristic Curves we found that the predictive power of our composite signature (3 microRNA, TTR levels and ApoE 4 status) was excellent (multivariate logistic regression: $p < 0.0001$; AUC = 0.89; 95% CI: 0.81-0.95), suggesting that the AD disease process is reflected in altered microRNA levels in plasma. Alongside this we are exploring the neuroprotective potential of a small peptide derived from the amyloid precursor protein. Our preliminary in vitro studies indicate that these molecules may curtail aspects of AD pathology. Supported by grants from the Health Research Council and Royal Society of NZ Marsden Fund.

Human variability: A risk or a defence?

Dr Hillary Bennett, Leading Safety Limited, Auckland

As organisations have attempted to create safer workplaces, there has been a strong focus on understanding human performance in terms of human failure i.e. human errors and noncompliant behaviours. Human actions and judgements are seen to degrade systems and to undermine safety. This failure focus, frames humans as a liability and as ‘villains’. The value of focussing on how people’s erroneous actions and judgements create an unsafe workplace has been questioned. An alternative view is to frame people as ‘potential heroes’ who are adaptive and resourceful. It is this performance variability that creates safe workplaces.

New Zealand health portals coming to a GP practice near you

Graeme Broad, SCL, Invercargill

Around since the 1900s, health portals have been on the NZ health radar since 2001. These are planned to move away from the traditional 'paternalistic' health care system to one that is a patient driven internet system. Originally touted for full implementation by the end of 2014, this target has been revised to a more realistic 50% GP practice implementation. Advantages have been said to be patients can view: their medical history, current medicines, order repeat prescription request, manage appointments, manage guardian/custodial accounts from one origin. Barriers to overcome for the introduction of portals in New Zealand are: sufficient patient/GP education, security and privacy assurances, patient focus rather than a clinician focus, multiple portals for a given patient that might not communicate with each other, GP resistance (practice costs, inconvenience of using emails, charges etc).

Prostate disease and the role of PSA screening

Dr Elspeth Gold, University of Otago, Dunedin

Prostate disease is a significant health issue. The current test for prostate cancer, PSA, has significant limitations, so much so that it is not recommended as a screening tool in most countries. There are, however, some ways in which PSA is effective, one is monitoring disease recurrence after radical prostatectomy and the other is change over time in an individual (PSA velocity).

Metabolic disease, genetics and 'FIZZY' drinks. Sugar -sweetened drinks, genes and metabolic health

Assoc Prof Tony Merriman, University of Otago, Dunedin

Major metabolic diseases are diabetes, gout and kidney and heart disease. Like other common human conditions they are caused by the impact of the environment on an individual who has inherited a set of risk genetic variants. A combination of good understanding of the biochemical (metabolic) effects of the processing of sugar and the interaction of sugar drinks with inherited genetic variants provides strong evidence that sugary drinks are causal of metabolic disease.

A patient's perspective

John McKenzie, Principal, North East Valley High School, Dunedin

John McKenzie takes nine pills every morning as well as two wee yellow Methotrexates on Monday and some Folic Acid on Fridays - Monday for Metho, Friday for Folic.... He had appendicitis when he was six - ten days in Kew Hospital. That meant injections with those huge needles every four hours. However, he did like the hospital school. John was on Zantac in the 1980s for years until his GP tried some super antibiotic which laid him low for days then cured him! He came up with an allergic reaction one night in the early 90s and drank the kids' phenergan to stop it worsening. This ailment progressed and some time later became anaphylaxis. In the early 2000s, John's GP said he had high triglycerides and needed to have a check up at the hospital but he shifted districts and not knowing what that word meant, he didn't take it too seriously until three years later he had a heart attack. They put in a stent. Late in 2012, John started to experience pain in his joints. Next minute he was admitted to Dunedin Hospital with very high levels of inflammation. Polyarthritis they called it. So, nine pills each morning is a pretty small price to pay for such a succession of health hiccups!

Scanning CSF for xanthochromia - the first year

Christian Christian, SCL, Invercargill

Introduction: Cerebrospinal fluid (CSF) scanning for xanthochromia is an important tool in the investigation of possible subarachnoid haemorrhage (SAH). In June 2013, our laboratory started CSF scanning for Southern District Health Board (SDHB) and Nelson & Marlborough DHB. The following report relates to our experiences from the first year of testing.
Methods: Scanning and reporting were carried out according to UK guidelines (1). Data collected included patient demographics, location, requester, clinical findings, CT scan result, time elapsed between ictus and lumbar puncture, and the degree of protection from light afforded the specimen in transit to the laboratory.
Result: In the first year of testing, we received 71 requests for scanning. In general, provision of clinical information was poor. In SDHB, the majority of requests were from Dunedin Hospital. The number of requests in SDHB increased 58% after introduction of the on-site service. Most patients had negative CT scans except for 2 where a CT scan was not done. Furthermore, 17% of CSF specimens received for scanning were not light protected.
Conclusion: Introduction of an on-site service for CSF spectroscopy has been successful and has resulted in a much improved service for laboratory users. There was a significant increase in CSF scanning requests after this test became available on site. We are unable to draw firm conclusions about adherence to specimen collection guidelines due to the general lack of clinical information provided. Adherence to specimen preservation guidelines was poor.
Reference: Cruickshank A, et al. Revised national guidelines for analysis of cerebrospinal fluid for bilirubin in suspected subarachnoid haemorrhage. *Ann Clin Biochem* 2008; 45: 238-244.

Molecular epidemiology of Group A *Streptococcus* from pharyngeal isolates of children in Northland

Noah Mhlanga, Northland DHB

Aims: The aim of the project was to assess the circulating emm types of Group A *Streptococcus* (GAS) amongst Northland school aged children and to attempt to correlate this to the geographic distribution of acute rheumatic fever (ARF) cases in Northland. A second aim was to compare the distribution of emm types covered in the 26-valent experimental vaccine with those circulating in Northland (McNeil et al. *Clinical Infectious Diseases* 2005; 41(8): 1114-1122).
Methods: 197 GAS isolates were collected from Northland Pathology Laboratory, a community laboratory service provider, between March and May 2013. Polymerse Chain Reaction (PCR) analysis and Deoxyribonucleic Acid (DNA) sequencing of the N-terminal portion of the emm gene was performed at the Institute of Environmental Science and Research Limited (ESR) laboratory (Porirua, New Zealand).
Results: A total of 36 different emm types were obtained out of the 197 GAS isolates analyzed. Of these emm 1 was found as the predominant emm type constituting 23.9% (47/197 of the total isolates. The 26-valent experimental vaccine covered 36% (13/36) of the total number of emm types in the study although these 13 emm types represented 117 GAS isolates giving potential vaccine coverage of 59.3% (117/197).
Discussion: Despite a large number of emm types identified in the study only a few of them predominated. emm 1 the predominant emm type in the study has been previously implicated in ARF, invasive GAS infections and acute post streptococcal glomerular nephritis (APSGN). This baseline information is important in GAS vaccine research and development for New Zealand .

Establishing a new QC regime for capillary electrophoresis

Alicia South, SCL, Dunedin

Purpose: In this laboratory capillary electrophoresis (CEP) is used to perform serum protein electrophoresis. A large number of QC error flags led us to question our quality control (QC) procedures and we set out to establish an improved QC program. We describe here the process undertaken to achieve this.
Methods: A pooled 'normal' serum was established as a QC material. Literature data on the allowable limits of performance for each of the electrophoretic fractions was sourced. Using this information with means and standard deviations for each fraction using the QC pool, capability (CI) scores were calculated.
Results: We were able to demonstrate that pooled patient serum can be used (with appropriate precautions) to create a suitable CEP control material. Data generated using this control showed that all electrophoretic fractions, except beta-2, were considered 'well performing assays' (CI <4) with beta-2 being classed as an 'average performer' (CI 4-6). Appropriate QC ranges and QC rules were able to be established using this information. Establishing a 'performance-based' QC procedure (rather than accepting the manufacturer's recommended regimen) allowed a more accurate assessment of laboratory performance.
Conclusion: The newly established QC regimen is performing well with fewer QC 'false alarms'. The QC pool is run on all capillaries for every run prior to patient samples, and allows easy troubleshooting without having to repeat batches. The new QC protocol allows more effective assessment of CEP performance and shows that the CEP system as we use it performs well.

Editor's note: This presentation was the winner of the Hugh Bloore Memorial Poster Prize.

Targeted immunotherapy in haematological disorders

Prof Helen Heslop, The Methodist Hospital & Texas Children's Hospital

A major focus of cancer research is to develop targeted small-molecule or biological therapies that have greater efficacy and lower toxicity than conventional chemoradiotherapy. Emerging information from genetic studies has led to the clinical testing of a number of small molecules targeting specific pathways in hematologic malignancies. This effort has produced several small molecule drugs that have shown impressive clinical activity and have progressed to become part of the standard of care for certain malignancies. The first example of such targeting was the use of the tryrosine kinase inhibitor Imatinib to target the bcr-abl fusion in chronic myeloid leukemia, a therapy which has transformed the therapy of this disease. More recently targeting the B cell receptor has shown considerable activity in B cell CLL and some types of lymphoma. However other therapies show only temporary beneficial effects. The human immune system also has immense potential to act as a highly targeted oncolytic system. Monoclonal antibodies (MAb) have been the most widely adopted form of immunotherapy for hematologic malignancies, and these targeted agents have contributed to the treatment both of Hodgkin and non-Hodgkin lymphoma and of chronic lymphocytic leukemia. While targeted small molecule and monoclonal antibodies have indeed had a major impact on cancer care, the ability to exploit the T cell immune response for this application may have still greater potential. Over the past decade, several studies have illustrated the potential of T cells to have sustained efficacy, even in patients with advanced cancer. For example, treatment of melanoma with expanded tumor-infiltrating T cells produces durable responses in subjects with stage IV melanoma. Similar benefits have been observed in the treatment of Epstein -Barr virus (EBV)+ post-transplant lymphoma, in which EBV-specific T cells induced CRs in more than 70% of the patients with no recurrences up to 12 years of follow up. More recently, several studies of T cells engineered to express a chimeric antigen receptor (CAR) targeting the CD19 molecule on B cell acute lymphoblastic leukemia elicited rapid and sustained responses in over 70% of patients. However, this therapy was associated with cytokine storm-like toxicity. The laboratory is critical in defining targets in individual patient's tumors, monitoring therapy and monitoring complications such as cytokine storm.

Molecular detection of diarrhoeagenic *Escherichia coli* in stool samples

Rowan Thomas, University of Otago, Dunedin

Background: Shiga toxin-producing and enteropathogenic strains of *Escherichia coli* (STEC and EPEC respectively) are endemic in New Zealand (1,2). At Southern Community Laboratories (Dunedin Hospital) as with many diagnostic laboratories, O157:H7 strains are the only serotype of STEC routinely detected in stool samples based on the well-known sorbitol-fermenting reaction in plate media. However, this approach has a low sensitivity and provides no information on other Shiga-toxin producing serotypes of *E. coli*. These "non-O157" serotypes are increasingly recognised to produce a significant proportion of diarrhoea, haemorrhagic colitis, and haemolytic uraemic syndrome (HUS) cases in other countries (3,4). In the last two decades, significant advances have been made in molecular techniques for the detection of diarrhoeagenic *E. coli* in stool samples. These methods rely on the detection of key virulence genes that are not present in commensal *E. coli* such as the shiga toxin genes (stx1, stx2 and variants) and the attaching and effacing gene (eae), which is present on the locus of enterocyte effacement (5). STEC encode one or more stx, while the presence of eae is believed to be necessary for the infection process. The intent of my MSc study is to examine the prevalence of STEC in diarrhoeal samples using TaqMan RT-PCR analysis. Only one previous study, which found an incidence of STEC in stool samples of 10%, has been carried out on faecal STEC in Dunedin and did not use molecular techniques (6). It is anticipated that the molecular techniques proposed will be much more sensitive.

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Epigenetic biomarkers and leukaemia

Dr Ian Morison, SCL, Dunedin

Recent studies of myeloid cancers have brought together two inter-related themes on the causes of these diseases. It has been known that many different mutations contribute to AML and MDS. In addition it is known that aberrant epigenetic markers, such as abnormal DNA methylation, are common in myeloid cancers. Genome-wide sequencing studies have now revealed numerous recurrent mutations of which a substantial proportion disrupt genes that are involved in establishing and maintaining the epigenetic pattern of the cell. Some of these mutations are predicted to cause widespread gene silencing, whereas others might cause gene activation.

Cervical screening and HPV

Assoc Prof Peter Sykes, University of Otago, Dunedin

Human papilloma viruses (HPV) are common causes of anogenital infections. A large number of sub types have been identified. A number of these subtypes have specific cancer causing properties and are classified as high risk. Infection with high risk HPV is identifiable in almost all cased of cervical cancer. HPV infection is normally acquired through sexual contact and active infection is very common in sexually active young women. Most HPV infections resolve as a result of the host's immune response. For a proportion of women however, infection does not resolve. Persistent infection is associated with an increased risk of cervical cancer which may be potentiated by other factors such as smoking. There is a range of well described morphological pre-cancerous changes demonstrated in cervical cells. These range from CIN1 (normally associated with acute HPV infection of either low or high risk types) through CIN3, (more frequently associated with persistent high risk HPV infection), to cancer (almost always associated with persistent infection with high risk HPV). Vaccination against high risk HPV prior to the onset of sexual activity has a large potential role in the prevention of cervical cancer and its precursors. The backbone of prevention of cervical cancer is the screening for cytological abnormalities caused by HPV. While our screening program is currently very successful, cytological screening is limited by a number of sensitivity and specificity related issues. There is a range of tests available for the detection of HPV. These are largely, but not exclusively, PCR- like tests for capsid protein HPV DNA. Detection of high risk HPV DNA is currently used to triage women with mild cytological abnormalities and in follow up after treatment. PCR based techniques are normally highly sensitive; HPV as a primary screening test has the potential therefore, to increase the sensitivity of the cervical screening program. The increased cost may be offset by increasing the screening interval and raising the age of the first screen. A number of screening programs are planning to change to 1º HPV screening, and the NZ screening program is also due to consider this issue.

Sexually transmitted infections: New Zealand's challenges

Dr Jill McIlraith, Aurora Heath Centre, Dunedin

New Zealand has one of the highest rates of Chlamydia and gonorrhoea in the developed world, with those under 25, and Maori and Pacific Islanders bearing the greatest disease burden. Chlamydia remains by far the most common sexually transmitted disease in New Zealand, with more than 25 000 confirmed cases in 2012. As in the rest of the world, syphilis is undergoing a resurgence in New Zealand and presents unique difficulties in diagnosis and follow-up. Reasons for these trends are complex, as is the challenge to reverse them. A combined approach by clinicians, laboratory staff, community educators and health managers, backed by the political will, is needed.

Mycobacterium tuberculosis - the ongoing scourge of consumption

Dr James Ussher, University of Otago, Dunedin

Despite huge advances in medicine in the 132 years since Robert Koch described *Mycobacterium tuberculosis* as the cause of consumption, *M. tuberculosis* remains the 8th leading cause of death worldwide. Nine million people become infected with *M. tuberculosis* each year. Coupled with the emergence of multi-drug resistant and extensively drug resistant (XDR) *M. tuberculosis*, "consumption" remains a major public health problem in the 21st century .

Surgery at sea and medical glamping: the New Zealand Defence Force's developing role and capabilities in the Pacific

Lt. Greg Tuck, NZ Defence Force

Deployable healthcare is seen as a contribution the New Zealand Defence Force (NZDF) can provide to maintain stability and security within the Pacific region. This is through aiding in times of disaster, boosting day-to-day healthcare, and providing trauma surgery support to military operations such as peacekeeping and the making safe of unexploded ammunition. NZDF capabilities are being upgraded including the regeneration of a tented surgical facility and the establishment of a surgical hospital on board the Royal New Zealand Navy vessel HMNZS Canterbury. The medical scientific officers of the New Zealand Army contribute to these projects. Staffing for these facilities will come from full and part time Army staff, and civilian volunteers. When active, these deployable facilities will contribute to the security and health of Pacific nations.

Interaction of Health Services with Maori 'Hononga'

Carl Te Ahuru, Kaumatua Hata, Southern DHB, Dunedin

The name of our presentation "Hononga" speaks of human connection through toto (blood) and in Te Āo Māori (the Māori world), whakapapa. Blood ties human experience to the past, present and future, and as such is regarded as sacred due to its' life giving properties. The divide between Te Āo Kōhatu (traditional times) and Te Āo Hurihuri (the changing world) presents challenges for health professionals working with the diverse needs of Māori. The role of "Kaitiakitanga" (Guardianship) is significant in the context of Blood Banks when ensuring that their services are "culturally safe" and observant of cultural consideration.

Childhood pneumonia in Nepal - the journey towards routine pneumococcal vaccination

Prof David Murdoch, University of Otago, Christchurch

Pneumonia is the leading single cause of childhood mortality globally, with over 1.4 million deaths per year. Of the estimated 156 million cases of childhood pneumonia that occur each year, 97% are from developing countries, such as Nepal. Early case-finding and treatment, and vaccination have the potential to markedly reduce pneumonia mortality and morbidity. The pneumococcal conjugate vaccine will be introduced into the routine immunisation schedule in Nepal later this year. This important decision was informed by a collaborative programme of research involving clinicians, laboratory scientists, academics, the Nepal Ministry of Health, and the World Health Organization. This research defined the burden of pneumococcal disease, pneumococcal serotype distribution and carriage rates, and pneumococcal conjugate vaccine effectiveness in local communities.

Understanding immunohistochemistry: pitfalls and their solutions

Prof Jane Dahlstrom, ACT Pathology and ANU Medical School, Canberra

Immunohistochemistry is routine in surgical pathology and is commonly requested to diagnose a cell type or organism. It is also used to direct further treatment, and in some malignancies, has a role as a prognostic marker. Pathologists and scientists must therefore be familiar with the potential technical and interpretive pitfalls that can occur. These can be divided into pre -analytical and analytical. Pre-analytical variables that affect immunostaining include tissue type, tissue fixation, type of fixative used, duration, temperature, and pH of fixation, tissue processing, tissue necrosis/preservation, and levels of antigen expression in the tissue. Analytical factors relate to the immunolabeling procedure itself and the pathologists interpretation of the staining characteristics. Even with the introduction of semi automation immunolabeling procedure can be capricious. There can be variability of the result related to the antibody clone purchased, the dilution of the antibody, the pH of the retrieval solution used and the antigen retrieval method used. Pathologists and scientists need to be familiar with the diagnostic location of immunolabelling for the particular antibody purchased for the particular tissue being assessed. This means being familiar with its cross-reactivity and also the thresholds used for immunoreactivity in tumoural pathology where interpretation will determine whether a patient is eligible for specific hormone treatment or chemotherapy. Understanding the limitations of immunohistochemistry, and the causes of false positives and false negative results, is essential to ensure high quality service provision to patients.

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Comparison of processing methods for FFPE FISH testing: a comprehensive review of manual and automated processing at Canterbury Health Laboratories

Rebecca Day, Canterbury Health Laboratories, Christchurch

Objectives: To use mobile laboratory testing to provide LDL/HDL cholesterol ratios to enable instant feedback for participants in a work and community based health and wellness program.

Methods: Pre and post program lipid panel testing was carried out on participants of a 12-week health and wellness program using the mobile laboratory testing unit COBAS b101. The results of the lipid panel tests were then incorporated into the advice and strategies given to the participants starting the program. At the end of the program the test results were used to clearly identify gains from the lifestyle changes and provide individual goal adjustments beyond the guided program.

Results: Blood cholesterol levels are seen as a key indicator of a lifestyle risk factor. The lipid panel test, as part of the initial health screen, can assist to identify modifiable diet and lifestyle changes. The mobile testing enabled the program to give instant personalised feedback, and rationalise goals based on actual data within the single consultation. The ability to do this onsite also saved participants a significant amount of time and removed the clinical aspect of obtaining a blood sample from a commercial laboratory via venipuncture.

Conclusion: Mobile testing offers the ease of instant results, which can be explained and clarified there and then.

Synthetic cannabinoids – a recent history in New Zealand

Dr Leo Schep, University of Otago, Dunedin

The term synthetic cannabinoids describes a range of chemicals that bind to cannabinoid receptors within the brain and mimic the effects of tetrahydrocannabinol. In the last 3 years, a large number of marketed products were legally sold throughout New Zealand. Consequently there were increasing numbers of patients attending emergency departments and medical centres, with symptoms ranging from agitation and tachycardia to seizures, paranoia and violence. Added burdens were placed on other social services as well as the police, as growing numbers of users were suffering adverse mental health issues. The Government responded by passing the Psychoactive Substance Act (PSA), which requires manufacturers of these drugs to prove low risk of harm, in a manner similar to that required for pharmaceutical drugs, before they could be registered for legal sale. Manufacturers would need to show evidence of safety following preclinical animal studies and clinical investigations with human volunteers before they could be legally sold. However, the accompanying safety testing regime for the PSA had not been finalised and a number of products were granted temporary sale licences. Due to growing public alarm, all products were withdrawn from the market and animal testing was removed from the regime. Given this amendment to the PSA, it becomes difficult to establish evidence of low risk for these chemicals and there is now a danger these psychoactive drugs may yet again become legally available in New Zealand .

Infectious diseases

Dr Jill Wolfgang, University of Otago, Dunedin

Fever in the returning traveller can be a diagnostic dilemma. The fever may represent infections acquired abroad and not familiar to the physician. Often the list of potential diagnoses is long and overwhelming. Plus, a large proportion of illnesses in returned travelers is caused by common non-tropical infections (such as bacterial pneumonia or pyelonephritis). To narrow the differential diagnosis, it is important to ascertain the geographic area of travel, the time spent in the area, activities performed (i.e. freshwater exposure, animal bites, and mosquito exposure). Travel to developing countries can lead to a myriad of possible infections not normally encountered in one's daily practice. Limited resources do not allow for all inclusive testing to narrow the diagnosis. Laboratory confirmation of diseases is essential to direct therapy.

Home is where the staph is

Rebecca Busch, Canterbury Health Laboratories, Christchurch

Two siblings presented to their GP multiple times over a two year period for recurrent skin infections and abscesses. The abscesses required incision/surgical drainage and despite prolonged antibiotics still reoccurred. Multiple investigations were carried out to discover what was causing the abscesses and why the infections were so severe. It was proposed that the patients may be immunocompromised in some way. Swabs were often taken and *Staphylococcus aureus* was the only organism isolated. A biopsy was carried out and bacteria were noted to be present right down to the fat layer which is unusual. Isolates were referred to ESR for investigation and the *Staph aureus* was found to be Panton-Valentin Leukocidin (PVL) positive. PVL is a cytotoxin that can destroy white blood cells and cause extensive tissue necrosis and severe infection. The children were given a combination of oral and topical antibiotics and Bactroban to eradicate the PVL positive *Staph aureus* and a household decontamination was also undertaken. PVL is not routinely screened for but should be considered if a patient has recurrent abscesses.

Genetic profiling of South Island malignant melanoma cases

Ahn A[1], Gardner J[2], Ferguson P[3], Kenwright D[3], Fitzgerald P[4], Eccles MR[1]
[1]Department of Pathology, University of Otago, Dunedin;
[2]Anatomical Pathology, Christchurch Hospital, Christchurch;
[3]Department of Pathology, University of Otago, Wellington;
[4]Southern Community Laboratory, Dunedin

Oncogenic mutations in BRAF and NRAS genes have been well described in melanoma in the USA and European population. With advances in therapeutic drugs targeting these mutations, melanoma is now believed to be at the forefront of personalised medicine. However, the frequency of BRAF and NRAS mutations in the New Zealand population has not been investigated. Recently other recurrent mutations in melanoma, indicative of potential drivers mutations have been discovered in the exon of RAC1 (1,2) and in the promoter of TERT (3,4). The aim of this study was to find a preliminary prevalence of recurrent mutations in the BRAF, NRAS and RAC1 genes and the promoter of TERT in melanomas from the New Zealand South Island population. Formalin Fixed Paraffin Embedded (FFPE) tissues, consisting of 50 primary and 37 metastatic melanomas, from 87 melanoma patients were collected from South Island patients. Mutations were analysed in exon 15 of the BRAF gene, exon 2 of the NRAS gene, the RAC1 gene and the TERT promoter by polymerase chain reaction amplification and Sanger sequencing. Overall, the incidence of NRAS mutations was 26% (23/87). This was slightly higher than the incidence of BRAF mutations, which were found in 24% (21/87) of the tissue samples. The relatively high prevalence of NRAS mutations, when compared with the number of BRAF mutations, is an unexpected result and is not consistent with published data from other parts of the world. The RAC1 mutation was identified in 2% (2/87) of cases and TERT promoter mutations were found in 72% (62/86) of our tissue samples. Interestingly the incidence of TERT mutations in our primary melanoma cohort was 74% (37/50), which is greater than that previously found in the literature of (33% to 37.9% (3,5)). These preliminary results suggest that New Zealand has a distinctive pattern of oncogenic mutations in melanoma with a higher proportion of NRAS and TERT mutations. This may be due to the strong ultraviolet light exposure in New Zealand.

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Movement disorders, Parkinson's disease and brain research

Dr Timothy Anderson, University of Otago, Christchurch

Most movement disorders can be described in terms of too much (hyperkinetic) or too little (hypokinetic). A number of conditions can have mixtures of both, so that in Parkinson's disease (PD) there is frequently co-existent rest tremor and bradykinesia. Diagnosis of most movement disorders, including PD, is still clinical, but laboratory testing, especially genetics and immunology, is becoming increasingly valuable in establishing aetiology. In PD, we have become more aware over the last decade of the importance of non-motor symptoms (e.g. dysautonomia, sleep disorders, pain, anxiety) and in particular cognitive impairment, to the extent that we now know that 70-85% of patients will ultimately develop dementia (PDD), distinct from Alzheimer's dementia. Research at the New Zealand Brain Research Institute (NZBRI) in Christchurch has been particularly focused on identifying objective biomarkers, especially neuroimaging markers, that reflect and predict significant cognitive decline in PD.

Alicia South, SCL Dunedin, winner of the 2014 Hugh Bloore Memorial Poster Prize, pictured with Immediate Past President, Ken Beechey

Editor's note
Only abstracts that are informative have been included. Any references to 'results will be discussed and/or presented' have been excluded.

MINUTES OF THE 70TH ANNUAL GENERAL MEETING HELT AT THE DUNEDIN CENTRE ON WEDNESDAY 13 AUGUST 2014 COMMENCING AT 12.30PM

PRESENT:
The President and Secretary/Treasurer presided over approximately 60 members.

APOLOGIES:
Apologies were received from:
Mike Legge, Kevin Tebbutt and Kirsten Beynon

Motion:
Moved R Hewett, seconded T Barnett
That the above apologies be accepted.
Carried

PROXIES
That the following proxies were received:
Bettina Heaton - 6
Kevin Tebbutt - 1
Monica Hubbard - 1

MINUTES OF THE PREVIOUS ANNUAL GENERAL MEETING
Motion:
Moved R Hewett, seconded R Siebers
That the minutes of the previous Annual General Meeting held on 22 August 2013 be received.

Motion:
Moved R Hewett, seconded T Taylor
That the minutes of the previous Annual General Meeting held on 22 August 2013 be accepted.
Carried

BUSINESS ARISING FROM THE MINUTES
Nil

REMITS AS CIRCULATED

Motion:
Moved R Hewett, seconded R Siebers
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."*
Carried

Motion:
Moved R Hewett, seconded R Siebers
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 T Rollinson
That the President's Report be received.
Carried

ANNUAL REPORT
Motion:
Moved R Hewett, seconded T Rollinson
That the Annual Report be received.
Carried

FINANCIAL REPORT
Motion:
Moved R Hewett, seconded B Heaton
That the Financial Report be received.
Carried

Discussion:

L Dent commented that the NZIMLS bank balance seems to be very high and questioned if this should be the case. Could some of these funds go towards offering more scholarships.

R Hewett explained that the NZIMLS has encountered some bad years. Therefore, there is a need to have a contingency in hand. Reserve funds are there to cover any unexpected events and it is prudent that there are sufficient funds to carry the NZIMLS over in any hardship years. With the profits that have been secured over the past couple of years, Council will consider offering a second scholarship again.

ELECTION OF OFFICERS

The following members of Council were elected unopposed:

President:	R Hewett
Secretary/Treasurer:	T Barnett
Region 2 Representative:	M Janssen
Region 3 Representative:	C Bromhead
Region 5 Representative:	T Taylor

Motion:
Moved R Hewett, seconded R Siebers
That the election of officers elected unopposed be approved.
Carried

The results of the elections for Region 1 are as follows:

Ailsa Bunker - 67
Kevin Tebbutt - 55

Motion:
Moved R Hewett, seconded A Calvert
That the election of A Bunker to the position of Region 1 Representative be accepted.
Carried

HONORARIA
Motion:
Moved R Siebers, seconded R Hewett
That no honoraria be paid.
Carried

AUDITOR
Motion:
Moved R Hewett, seconded T Barnett
That Hilson Fagerlund Keyse be reaffirmed as the NZIMLS Auditors.
Carried

GENERAL BUSINESS
On behalf of the PPTC, R Siebers thanked the NZIMLS for their generous donation which goes towards the South Pacific programme that the PPTC runs.

2015 CONFERENCE
South Pacific Congress is to be held in Auckland at the Langham Hotel, 17 – 21 August 2015. The theme for this SPC is "Value of Medical Laboratory Science".

2016 CONFERENCE
No offers were received to organise the 2016 conference.

There being no further business, the meeting closed at 1.04pm

SCHOLARSHIP REPORT

Barrie Edwards & Rod Kennedy Scholarship Report

Julie Creighton

Canterbury Health Laboratories, Christchurch

I was thrilled and delighted to be this year's recipient of the Barrie Edwards and Rod Kennedy Scholarship Award. The conference I elected to attend was the Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) 2014, held in Washington, DC. ICAAC is the American Society of Microbiology (ASM) premier conference on antimicrobial agents and infectious diseases. The meeting is widely attended and highly regarded by scientists, clinicians, pharmacologists and research scientists. The conference is run over 5 days and attracts thousands of delegates, nearly 50% of them from outside of America, so there is a real global feel to the meeting. There were many internationally acclaimed researchers presenting at the meeting and it is an awesome feeling to be sitting in the crowd listening to the professors and clinicians whose many papers you have read over the years. Of course, some of them make better writers than they do presenters, but overall the standard of speakers was excellent. A wide variety of topics was on offer, but the main focus for me was on antimicrobial resistance, rapid laboratory diagnostics and sexually transmitted diseases.

One of the first plenary sessions was on the urgent need to fast track new antimicrobial agents. John Rex, from AstraZeneca, reminded us about how truly amazing antibiotics are in that they significantly reduce mortality and morbidity. You can't do heart surgery, treat premature babies, perform transplants without antibiotics. In a way their power has made things too easy in that antibiotics were given instead of thinking about clean water, preventing infection and immunisation. The rising tide of antimicrobial resistance threatens public health worldwide and there are few new drugs in the pipeline – mainly due to costs involved in developing, trialling and bringing to market these agents. John revealed new incentives from the US government including the GAIN act in 2012 and DRIVE-AB, which is a huge collaborative approach between companies and countries. One solution is to get the government to agree to purchase a certain amount of drug, whether it's used or not, then the companies can have guaranteed profit up front. Alternative products can include vaccinations, monoclonal antibodies, and probiotics.

Patrice Nordmann (internationally renowned researcher and publisher of 100's of papers on MDR-Gram Negatives and the inventor of the CarbaNP test) spoke on the problem of global epidemics caused by carbapenemase producing *Kleb.pneumoniae* clone ST258 and how the situation has worsened over the last three years, with 17 countries now elevated to endemic status. The virulence of ST258 may be due to capsular polysaccharides. Another worry is the international spread of oxa48 in Enterobacteriaceae. Prof Nordmann recommended the EUCAST algorithm for detection, CarbaNP and Cepheid Xpert Carba-R. It was interesting to see the growing presence of EUCAST in the USA, with CLSI trying to emulate EUCAST with harmonising clinical breakpoints, introduction of epidemiological cut-offs and having smaller select committee groups.

There was a two hour session looking at the most important and popular papers from 2014. Many of the papers were Virology based and discussed the recent Ebola outbreak; Chikungunya virus and the potential for it to spread or be imported into other countries (due to global warming, could come into USA). MERS-CoV was also discussed with a warning to check for the disease in people returning from Saudi Arabia. Definite links supporting camel to human spread. There was talk of a Dengue vaccine which looks as though it's effective, but needs vaccinations at 0, 6 and 12 months. David Paterson, Australia, was one of the guest speakers. He discussed papers relating to antimicrobial resistance. He said that although antibiotics increase the human life span by 2-10 years, there are now many concerns around too much use. Over 51 tons of antibiotics are used in the US/year; 80% of which is used in agriculture. There is a direct link between the use of Ceftiofur in chickens and increasing Salmonella resistance and the use of azoles in agriculture leading to fungal resistance. For a copy of the handouts, go to: http://static.coreapps.net/tristar-icaac14/handouts/cfb798819342bb56ba8b48329a642f84_1.pdf

There was a really good session on sexually transmitted diseases, with a particular emphasis on one of CDC's most urgent threats i.e. *N.gonorrhoeae* antibiotic resistance. The rate of *N.gonorrhoeae* infections has increased in recent years, as has the prevalence of resistant isolates, with up to 50% resistance to ciprofloxacin, 10% plasmid penicillin resistance, 5% azithromycin and 5% reduced ceftriaxone MICs. *N.gonorrhoeae* accumulates resistance mechanisms without any apparent cost to fitness. However recent data is suggesting a slight improvement in resistance rates due to the introduction of combination ceftriaxone (IM) and azithromycin therapy. New novel antimicrobials are still needed. Unfortunately there is no single detection method for NAAT resistance testing and culture is still encouraged. Researches are now looking at whole genome sequencing in order to find specific resistance mechanisms. [N.B. Whole genome sequencing is being talked about as almost routine! So much more work being done in this area to understand antimicrobial resistance, organism virulence and functioning.]

On a personal note, I presented a poster at ICAAC titled: Detection of *Staphylococcus saprophyticus* hyper β-lactamase producers. I hope to publish this work in the near future. I did factor in some time to do tourist activities. Washington is such a fabulous city to visit, with all the iconic attractions (Capitol Hill, Washington Monument, Lincoln Memorial, The White House and of course all the glorious Smithsonian museums) in such a small, walkable, area. Put it on your bucket list. Although it was autumn, I happened to arrive at the beginning of a week long heat wave, with temperatures up to 36^{o}C! Within a short time I had various foot blisters and rather pink shoulders – all worth it!

From 2016, the ASM and ICAAC will have joint meetings – which will be a huge meeting, well worth consideration of attendance. The inaugural meeting will be Boston, 2016. For anyone wanting further information on any of the above, please contact me by email julie.creighton@cdhb.health.nz

Sincere and grateful thanks to NZIMLS Council and the families of Barrie Edwards and Rod Kennedy for selecting me as the recipient of this scholarship and to Fran van Til for her organisational help.

QUESTIONS WE'VE BEEN ASKED

When will I get my exam results back?

This is a question the NZIMLS Executive Office receives regularly. Here we endeavour to explain the marking process and when you can expect your results.

All QMLT and QSST examinations are sat on November 5th. Every year there are a large number of candidates writing each exam.

Papers are collated by the Exam Supervisors and sent to the Markers, who are from various laboratories all around New Zealand and there are different Markers for each discipline. Once received, the markers check each document to ensure the information on the front sheet is correct and each candidate can be identified. After marking, the papers are then sent to a Moderator, whose job it is to ensure consistency of marking. The marked papers are then sent to the Executive Office, where marks are recorded and results letters are then produced and sent to candidates. This process usually takes four-six weeks and we endeavour to have results letters to you by mid-December.

Certificates are then printed for those candidates who are successful in passing their exams. During the first Council meeting of the New Year, the examination results are ratified, and the Certificates signed. The timing of this part of the process depends on when Council first meets for the year. All successful candidates should receive their certificates and badges mid-end March the year following the writing of their examination.

SPECIAL INTEREST GROUP REPORT

Microbiology Special Interest Group 2014

The 2014 Microbiology SIG meeting was held at the Château on the Park, in Christchurch, on Saturday 7th June. The full day consisted of 15 excellent talks on many aspects of microbiology. Best Overall Speaker went to Melanie Cottle with her case history presentation of a young male, recently arrived from India, who had contracted a multiple-drug resistant TB infection. Best First Time Speaker award went to Coco Leung, who presented a case history of a domestically acquired Cyclospora parasite infection. The meeting was attended by over 100 delegates who enjoyed the cabaret style table seating and fabulous food provided by the Château. Special thanks to the sponsors, including Canterbury Health Laboratories, IMMUNZ, Ngaio Diagnostics, Roche and ThermoFisher.

EUCAST, what, why, how?

Julie Creighton, Canterbury Health Laboratories

Antimicrobial susceptibility testing is one of the most critical areas of microbiology and helps to determine patient therapy and to monitor for antimicrobial resistance. Standardised guidelines set by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) have been adopted widely across Europe and lately by many Australian laboratories. CHL is the first laboratory in New Zealand to change from CLSI to EUCAST. Disk diffusion methodology is similar to CLSI, but only one type of media is required for fastidious organisms such as *Strep.pneumoniae* and *H.influenzae*. EUCAST is independent from the influence of drug companies and FDA when setting break points – which are based on PK/PD, MIC distributions, clinical trials and medical experience. When changing to EUCAST, a careful plan must be put in place to determine who's in charge (scientist(s) and clinician), a suitable time frame (need at least six months), method comparison, documentation, what drug/bugs still need CLSI, preparation/ ordering new media & antibiotics, validation/ QC, any comment code changes, education, staff training and communication with all relevant parties. A wealth of information including methods, reading guide, rationale for decisions and expert rules is available on the EUCAST web site www.eucast.org. For further information contact Julie by email julie.creighton@cdhb.health.nz .

Gonorrhoea – what crisis?

Julie Creighton, Canterbury Health Laboratories

Gonorrhoea is acquired mostly by sexual contact. Prevalence rates have increased in recent years; with the WHO estimating over 100 million adults are newly infected annually, with a high percentage of these infections occuring in the Asia Pacific Region. According to ESR statistics, New Zealand has also seen increasing prevalence from 2011 to 2012; most strikingly in young females in the 15–24 year age group. Prevalence rates in males aged 15-29 have also increased. Local CHL data shows a predominance of positive samples from MSM, with more than 50% of positive sites being from the rectum or pharynx. Higher prevalence rates are partly reflected in the escalating use of NAAT technology and increased testing of non-genital sites. High risk factors continue to be MSM, multiple partners, and no condom use. Historically, treatment was non specific and has included various tree barks, mercury, and heating chambers or elements! Antibiotics, namely penicillin in the 1940's, were set to revolutionise treatment. However, since this time *N.gonorrhoeae* has proved itself accomplished at acquiring antimicrobial resistance (mainly from horizontal gene transfer from commensal Neisseria species) with each new class of antibiotic introduced, including penicllin, tetracycline, ciprofloxacin, azithromycin and most alarmingly, in third generation cephalosporins. Globally, decreased susceptibility to ceftriaxone and even resistance is a disturbing concern. Locally we have seen a ceftriaxone MIC 'creep'. Until new antibiotics can be found, dual therapy consisting of IM ceftriaxone and oral azithromycin is recommended for empirical treatment.

Borderline oxacillin resistant *Staph aureus* (BORSA) – a case study

Liz Frater, Capital Coast Health, Wellington

In April 2014, a patient who transferred to our hospital developed persistent *Staphylococcus aureus* bacteraemia despite being on treatment with adequate doses of intravenous flucloxacillin. He had a complicated infection involving bone and prosthetic material. During the laboratory work up of his blood and tissue isolates, he was found to have borderline oxacillin resistant *Staphylococcus aureus* (BORSA). Here I present the clinical case, the mechanisms of resistance and the laboratory work up required to identify BORSA. BORSA is an uncommon phenotype in New Zealand, but one that is easily missed if both cefoxitin screens and oxacillin MIC determination are not performed by diagnostic laboratories. Identification is important particularly in complex infections where source control is difficult as alternative antibiotic therapy may be required to avoid development of further complications.

Comparison of methods for the detection of *Clostridium difficile* toxin

Tina Littlejohn, MedLab Central

Introduction: Toxigenic *Clostridium difficile* is a major cause of antibiotic associated diarrhoea and is the causative agent for virtually all cases of pseudomembranous colitis. Although about 2% of normal healthy adults are colonized with *C.difficile* many patients acquire this organism through nosocomial infection. Two toxin proteins (tcdA) and (tcdB) are thought to be the primary virulence factors of *C.difficile*.
Methods: From 27/09/2012 to 05/10/2012 31 faecal samples were tested using the Ngaio Diagnostics EIA kit (already in-use at Medlab Central), the Immunz Meridian GDH kit, and the Ngaio Diagnostics Coris and Prolab GDH kits.
Results: Of the 31 samples, six were positive by EIA, nine were positive by Meridian GDH, and eight were positive by both Coris GDH and Prolab GDH. To confirm that the GDH positive samples were toxin-producing *C.difficile*, all positive samples were tested by the Immunz Illumigene technology and the Ngaio Diagnostics Great Basin technology. Eight of the nine samples tested were positive by both technologies. One sample that tested positive by Meridian GDH was negative by the Illumigene and Great Basin tests. All kits had good sensitivity and specificity reports. Price for test was comparable.
Conclusions: The final decision as to what kits to use came down to ease of use and set up space. The Ngaio Coris GDH test was quick and simple and was similar to other kits already being used in the department. The Ngaio Great Basin toxin kit is a one-step method with the ability to walk away and retrieve the result when finished. The Illumigene system involved more process steps and required greater set-up space. In addition, weekly bench rotations meant that the simple-to-use Great Basin technology was more suitable for implementation and training purposes.

It's not always norovirus

Mary Stevens, Canterbury Health Laboratories (CHL)

In 2012 a multiplex real time PCR to detect norovirus (GI and GII), rotavirus, adenovirus and astrovirus was implemented at Canterbury Health Laboratories. This replaced less sensitive and specific methods. In August 2013 sapovirus was added to the PCR and we have since found several small local outbreaks of this virus, although norovirus remains the most frequently detected gastroenteric virus. Of 2054 samples tested between 21 August 2013 and 26 May 2014, 333 (16.2%) were positive for norovirus, 61 (2.9%) positive for sapovirus, 50 (2.4%) each for rotavirus and adenovirus and we obtained 31 (1.5%) astrovirus positive samples. Symptoms of all the gastroenteric viruses are similar, and all can affect people of any age. Epidemiologically it is important to identify the causative agent of viral gastroenteritis, particularly in an outbreak situation, multiplex PCR is an effective way to do this quickly and reliably.

Dunedin's poo journey so far

Ricci Bergin, SCL, Dunedin

In Dunedin we have been comparing traditional methods of faecal pathogen identification with molecular methods. This began with a student project comparing traditional faecal parasite identification using trichrome and modified Zn staining, with the Aus Diagnostics platform that uses nested PCR. Following this we also looked at a Roche platform that uses the Light Cycler 480 for amplification, and a Genetic Signatures platform that uses their Hamilton machine for extraction. For these we also identified bacterial pathogens and Genetic Signatures also had targets we tried for viruses. We found detection of bacterial pathogens was relatively similar between current methods and the molecular methods, but the parasite identification had some differences. Traditional methods identified fewer cases of *D. fragilis* – due to its fragility - and more cases of *E.histolytica*, probably due to the inability to differentiate between *E.histolytica* and *E.dispar* under the microscope.

Just another alpha-haem strep?

Emma Cochrane, West Coast Health, Greymouth

Streptococcus gallolyticus subsp *gallolyticus* (formerly referred to as *Streptococcus bovis* biotype I) is a rare coloniser of the healthy human gastrointestinal tract, but it has an association with premalignant colonic lesions and colon cancer in humans. The ability of *S. gallolyticus* to bind to collagen type IV present in the basement membranes of polyps and early colorectal tumours is believed to be a contributing factor. As a result of its association with colon cancer a full bowel examination is recommended for patients who are found to have an infection caused by S.*gallolyticus*. Neoplasia of the colon has not appeared until years following S.*gallolyticus* infection in some cases, therefore surveillance bowel examinations are recommended for patients with a normal initial bowel examination. *S. gallolyticus* also has an association with liver disease and is a causative organism of bacteraemia and endocarditis. For an organism present in the gastrointestinal tract to cause endocarditis it must adhere to the gastrointestinal epithelium or the extracellular matrix, then cross the epithelium, evade the immune system in the lamina propria, survive in the blood stream and finally establish a site of infection on a heart valve. A number of studies have reconstructed the host interactions with *S.gallolyticus in vitro*, the results support *S.gallolyticus* possessing a number of virulence factors which allow it to cause endocarditis originating from the gastrointestinal tract. The earlier colorectal cancer is detected the better the prognosis; however, a large number of colorectal cancer cases are diagnosed during the advanced stages. Premalignant colonic lesions are usually asymptomatic and do not usually lead to a positive occult blood test, the currently used screening test for colon cancer. The isolation rate of *S.gallolyticus* has been found to be up to five times higher in patients with colorectal cancer compared with healthy controls. Increased levels of serum *S.gallolyticus* IgG antibodies have also been found in patients with colorectal cancer compared with healthy controls. So could a *S.gallolyticus* faecal antigen test or serology be utilised as a diagnostic tool in the early detection of colorectal cancer?

"A resistant problem" - a case of multi drug resistant tuberculosis

Melanie Cottle, Capital Coast Health, Wellington

A young male who arrived in New Zealand from India in 2008 was started on standard quadruple TB therapy on the basis of an abnormal chest x-ray combined with clinical presentation. A number of samples sent to the laboratory saw the isolation of Acid Fast bacilli (AFB) from the Bactec MGIT 960 broth (Mycobacteria Growth Indicator tube) 7H9 liquid culture medium. A MPT64 antigen test performed on the positive MGIT Broth confirmed the growth of *Mycobacterium tuberculosis* Complex in 15 minutes. Phenotypic susceptibility testing, performed using the Bactec 960 SIREO (streptomycin, isoniazid, rifampicin, and ethambutol) kit (Becton Dickinson), indicated growth in four out of five of the antibiotic containing tubes 4-5 days after incubation; including three antibiotics the patient was receiving. With worsening patient condition and the unusual phenotypic susceptibility results, further testing was urgently required. The HAIN Life Sciences genotype strips (Fort Richard) allowed rapid confirmation of resistance to high level isoniazid and rifampicin using the MTBDR plus strip and resistance to fluoroquinolones and ethambutol using the MTBDRsl strip. Referral to LabPlus, Auckland confirmed the susceptibility results. However, susceptibility to moxifloxacin classified the isolate as MDRTB, - but "within a whisker of XDRTB" (extensively drug resistant TB). The emergence and spread of MDRTB is a major global health problem. Fast, reliable testing methods in the laboratory are extremely important for early diagnosis, so appropriate antibiotic therapy is provided for the best outcome of the patient, and to limit the spread of disease. After multi-disciplinary involvement between Capital and Coast Health Respiratory Laboratory, microbiology consultants, respiratory physicians, infectious diseases and public health teams regionally, and with support from experts in Auckland and Australia the patient did well on a six drug regimen, was discharged and continues to receive treatment under the drug observed therapy system.

Black- but not the ace of spades

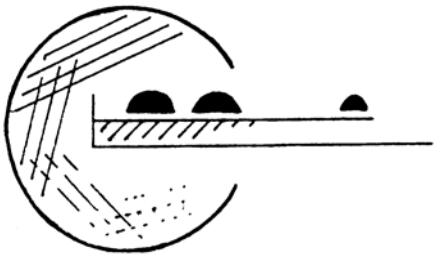
Lois Seaward, Canterbury Health Laboratories

A case history is presented from a 66 year old compromised male patient, who had a mass excised from his left elbow in February 2014. The direct Gram stain , KOH and methenamine silver stains all showed numerous fungal hyphae, many showing a bulbous tendency. After 3 days incubation at 36^{o}C, a fine black growth was just visible. This later became a carpet of black, raised, moist fungus, with tufts of aerial hyphae. A flag mount showed rocket-shaped conidiogenous ellipsoidal cells with yeast-like budding. This, together with its colonial appearance, was highly suggestive of a *Exophiala* spp. MALDI-TOF failed to identify the fungus (both direct and by extraction). Best alignment on the ITS2 data base from the DNA sequencing of the PCR product was *Exophiala* spp. (The patient was later discovered to have had *Exophiala jeanselmei* identified by previously referred cultures from us to LabPlus, Auckland Hospital, in 2003 and 2007). Susceptibility testing results, using Sensititre YeastOne, revealed itraconazole as the antifungal of choice. Itraconazole was subsequently administered for the next six months for this chromoblastomycosis infection caused by *Exophila jeanselmei*. (It should be noted that there are no standardised MIC interpretation guidelines for this fungus).

EUCAST - Our community lab perspective

Catherine Gordon, Southern Community Laboratories, Christchurch

Canterbury SCL recently completed the switchover to EUCAST guidelines for antimicrobial susceptibility testing and methodology. All our sensitivity testing is manual and the majority is disc diffusion. This simplified the changeover, and providing only community services meant there wasn't an extensive range of antibiotics to compare and review. After initially comparing the zone differences, what to do with any 'gaps' with the new guidelines was decided on in conjunction with the microbiologist. Staff were educated, QC performed and the system was implemented. However, we did complicate the process by changing the brand of discs being used and reviewing all our antibiotic profiles and reporting orders. This was where we face the biggest challenges; the actual switchover was relatively straight forward. If anyone is planning on switching and wants to discuss anything feel free to contact me.



THE Pacific WAY

GREETINGS FROM THE PPTC

Laboratories are an essential component of public health systems, particularly for disease surveillance, diagnosis, prevention and treatment. Health laboratories in Pacific Island Countries and Territories (PICTs) have identified multiple challenges to effective performance, including financing, qualified and skilled workforce, information, medical products and technologies, service delivery and leadership and governance.

The PPTC is recognised internationally as a 'Centre of Excellence' in terms of teaching and training programmes provided to National Health Laboratories of Pacific Island Countries. The PPTC is a World Health Organization (WHO) Collaborating centre. It offers excellent training programmes both in New Zealand and Pacific Island settings. These short term in-country teaching workshops have proven extremely valuable and have made an immediate and significant impact in terms of capacity expansion and up skilling personnel, however on-going consolidation programmes are essential if such a difference in the development or enhancement of skill is to be further advanced and maintained.

The goal of the PPTC is "to assist national health laboratories of the Pacific region to develop a laboratory service that is appropriate, affordable and sustainable and will provide immediate benefits to the healthcare settings in which they are used".

New Zealand based courses provided by the PPTC at the Centre this year were as follows:

Haematology and Blood Film examination 4th August – 29th August

Haematology continues to be weak in performance in Pacific Island Laboratories and this is due to a devastating lack of expertise in "Blood film examination and interpretation" throughout the region. The PPTC offered a 4 week training course in August of this year at its Centre in Wellington and four students attended: June Teiti from the Cook Islands, Nerisa Faumuina from American Samoa, and Bridget Kavana and Niam Pokale both from Papua New Guinea. The course was a great success and the students gained a great deal of knowledge and skill over the 4 week duration.

Microbiology 1st – 26th September

The PPTC also offered a 4 week training course in Microbiology in September at its Centre in Wellington and three students attended : Senisaleti Pasikala from Tonga, Felix Kokoa from Tuvalu, and Bernard Tatireta from Kiribati.

This was also a great success in terms of the learning experience the students received, and a big thankyou to Russell for the excellent teaching and training that he provided.

Laboratory Quality Management 29th - 24th October

The third course offered for this year is the Laboratory Quality Management course and this currently is in session at this moment. Three students are attending this course and they are Ravendra Prasad and Asena, Bukadua both from Fiji, and Tekaibeti Taratake from Kiribati.

Blood Transfusion Science 3rd – 28th November 2014

This will be the final course in Wellington for this year and we are pleased that the New Zealand Blood Service will once again be offering their expertise in terms of teaching and training to our nominated students.

For further information contact:

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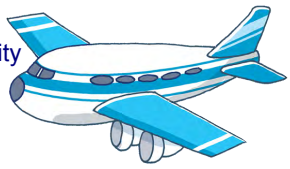
Telephone: +64 4 389-6294, Fax: +64 4 389-6295,
Email: pptc@pptc.org.nz Website: www.pptc.org.nz

Overseas Travel:



In July of this year, the implementation of Laboratory Quality Management Systems (LQMS) continued with visits carried out in Tonga (Navin Karan), Kiribati (Russell Cole) and Samoa (Filipo Faiga).

Navin then travelled to the four Federated States of Micronesia in the northern region of the Pacific and delivered teaching and training in Microbiology as a commitment to our in-country teaching programme.

Associate Professor Rob Siebers visited Samoa in September to assess progress in LQMS as did Clare Murphy in Vanuatu.

Phil Wakem travelled to the Cook Islands in late September to meet with the staff and to assess LQMS, and in October, Phil Navin and Rob will travel to Fiji to attend the Fiji Medical Laboratory Science Conference which is to be held on the 9-11th of the month.

Navin will then continue on to Kiribati and later to American Samoa to complete his LQMS visits for this year. Towards the end of October, Rob is scheduled to visit Tonga, and Russell will visit Samoa which will also complete their travel for this year.

Phil returns to Manila in November to attend an international forum of World Health Organisation Collaborating Centres. The PPTC is a registered Collaborating Centre of WHO, and Phil will attend this forum along with 200 participants from 124 WHO Collaborating Centres located in the Western Pacific Region.

Contact Us

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NZIMLS

BARRIE EDWARDS & ROD KENNEDY SCHOLARSHIP

The Barrie Edwards & Rod Kennedy scholarship is one of the most significant awards offered by the NZIMLS. The scholarship provides the winner with support to attend an international or national scientific meeting up to a maximum value of $7,500.

Application for this prestigious scholarship is 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 is one scholarship awarded in each calendar year. Closing date is 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.

Barrie Edwards

Rod Kennedy

NZIMLS Presents the

SOUTH ISLAND SEMINAR

2015

Saturday

7 March

Oamaru

Opera House

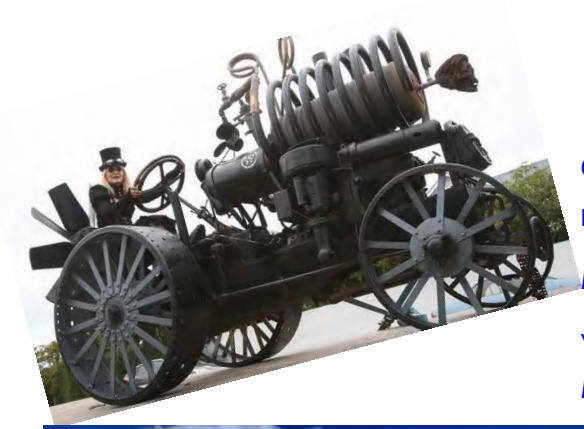
Join us at the end of the seminar and catch up with colleagues over drinks and nibbles

PRESENTERS WANTED!

Contact Erolia Rooney

erlia.rooney@nzblood.co.nz

Registration will be available in the New Year at www.nzimls.org.nz



Come and visit amazing Oamaru—where past meets present and punk becomes futuristic!

Make time to wander through the old buildings;

visit the Steampunk Museum;

or stay the week-end and visit the Moeraki Boulders

Journal questionnaire

Below are 10 questions based on articles in the November 2014 Journal issue. Read the articles carefully as 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 cannot then claim additional CPD points for reading the articles from which the questions were derived.**

The site will remain open until Friday 27th February, 2015. You must get a minimum of 8 questions right to obtain 5 CPD points.

The Editor sets the questions but the CPD Co-ordinator, Jillian Broadbent, marks the answers. Please direct any queries to her at cpd@nzimls.org.nz.

NOVEMBER 2014 JOURNAL QUESTIONS

1. What is the empirical treatment and alternative treatment of gonorrhoea in New Zealand?
2. Penicillin resistance of *N. gonorrhoea* may be due to what?
3. What is the major limitation when developing possible molecular solutions to address a lack of antimicrobial susceptibility information?
4. What has been reported to predict reduced susceptibility to ciprofloxacin in the treatment of *N. gonorrhoea* infected patients?
5. What fears have been voiced by health professionals regarding breast feeding for pain relief in infants undergoing heelstick or venepuncture?
6. What substance in breast milk may procure pain relief in infants and what does this substance increase?
7. Der p 1 is the major group one allergen of which mite species, what does it induce, and what does it contribute to?
8. Acaroid mites can survive in many environments. Name six such environments.
9. The possibility of a true mite infection should only be considered when?
10. Which immunochemistry test confirms diagnosis of neuroendocrine carcinoma?

AUGUST 2014 JOURNAL QUESTIONS AND ANSWERS

1. Extended spectrum β-lactamase-producing organisms have the ability to hydrolyse which β-lactam antibiotics?
   Ceftazidine, ceftriaxone, cefotaxime, and aztreonam
2. What was the main conclusion of the study by Lippi and Ippolito?
   Results of PT, APTT and fibrinogen in patient samples containing up to 3.6 g/L of cell-free haemoglobin are reliable.
3. What was the limitation of the study by Lippi and Ippolito, and what do the authors recommend to overcome this limitation?
   Limitation that it was a pilot study. Findings to be confirmed using a larger sample size, and in patients taking heparin, or oral anticoagulants such as dabigatron, rivaroxaban or edoxaban.
4. What constitutes the most important route of HIV, and hepatitis B and C virus infection in health care professionals?
   Accidental needle-stick or sharps injuries caused by hollow bore needles or other objects.
5. What has been shown to significantly reduce HIV transmission between sero-discordant couples?
   Early commencement of highly active anti-retroviral therapy (HAART) for HIV-infected patients.
6. In difficult cases of chromophobe renal cell carcinoma (ChRCC) what features establishes the correct diagnosis?
   A positive Hale's colloidal iron stain and ultrastructural demonstrations of numerous oval cytoplasmic microvesicles.
7. What has been associated with poor prognosis of ChRCC?
   Presence of sarcomatoid elements, tumour size >80 mm, tumour necrosis, and vascular invasion.
8. If untreated, patients with heparin-induced thrombocytopenia (HIT) can develop which thrombotic problems?
   Skin necrosis, venous gangrene, limb complications, and even death.
9. What is the treatment for HIT?
   Stop heparin and use alternative anticoagulants such as direct thrombin inhibitors or direct Xa inhibitors.
10. What are the current functional laboratory tests to demonstrate platelet activation by the HIT antibody?
    Serotonin release assay, heparin-induced platelet aggretation test using platelet-rich plasma, and whole blood platelet aggregometry.

2014 NZIMLS CALENDAR *Dates maybe subject to change*		
Date	**Seminars**	**Contact**
08 November 2014	Immunology SIG Seminar, Tauranga	tim.taylor@pathlab.co.nz
29 November 2014	Mortuary SIG Seminar, Rotorua	jason.sayers@lakesdhb.govt.nz
Date	**NZIMLS Examinations**	**Contact**
05 November 2014	QMLT and QSST Examinations	fran@nzimls.org.nz
11 – 12 November 2014	Fellowship Examinations	fran@nzimls.org.nz
Date	**Council**	**Contact**
27-28 November 2014	Council Meeting	fran@nzimls.org.nz
24 December 2014	Executive Office Closed for Holiday period	fran@nzimls.org.nz sharon@nzimls.org.nz
2015 NZIMLS CALENDAR *Dates maybe subject to change*		
Date	**Council**	**Contact**
12 January 2015	Executive Office re-opens	fran@nzimls.org.nz sharon@nzimls.org.nz
Date	**Seminars**	**Contact**
07 March 2015	South Island Seminar Oamaru	erolia.rooney@nzblood.co.nz
Date	**Events**	**Contact**
18 – 21 August	NZIMLS / AIMS South Pacific Congress The Langham, Auckland	rossh@adhb.govt.nz

Please Note: The NZIMLS Executive Office will be closed for the holiday period from 24 December 2014, re-opening on 12 January 2015.

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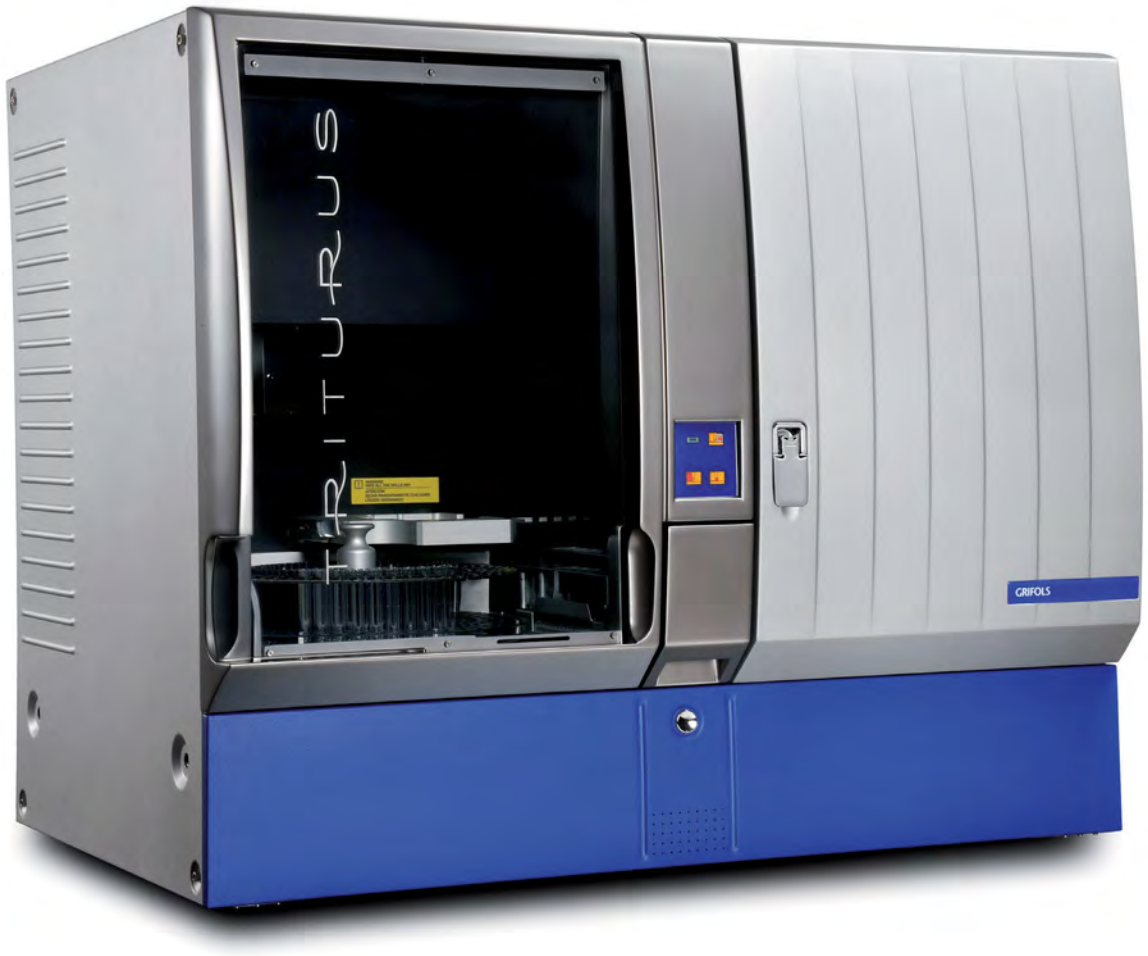

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