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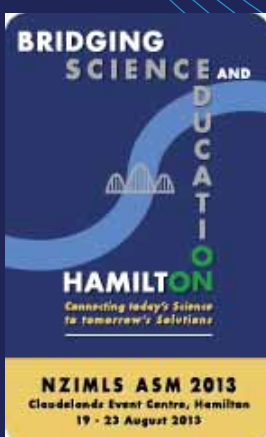
ISSN 1171-0195

Volume 66 Number 3 November 2012



# New Zealand Journal of Medical Laboratory Science

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New Zealand Journal of

# Medical Laboratory Science

Volume 66

November 2012

ISSN 1171-0195

Number 3

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Each year the NZIMLS Council invites a prominent medical laboratory scientist or pathologist to deliver the TH Pullar Memorial Address at the Annual Scientific Meeting. Dr TH (Thos) Pullar, a pathologist, was for many years involved in building up laboratory standards, and with the training and welfare of medical laboratory scientists. This year the TH Pullar Memorial Address was given by Robin Frazer, Emeritus Professor at the University of Otago Christchurch. His address "Pathology: the study of structure and function in health and diseases" is in this issue.

Bernard Chambers from Middlemore Hospital, Auckland was a past recipient of the NZIMLS Barry Edwards and Rod Kennedy Scholarship and attended the Institute of Biomedical Sciences Congress in the UK in 2011 where he presented a study "Evaluation of the new red cell research parameters on the Sysmex XE-5000" which is published in this issue. The Sysmex XE-5000 analyser includes four new red cell research parameters. The aim of his study was, among other, to establish reference intervals for these four parameters and look at their values in different anaemic populations. He found that these new parameters correlated better with MCV and MCH results from the analyser than CellaVision estimates. He concluded that the %LScRBC and %Micro R were useful for predicating restricted erythropoiesis in iron deficiency and thalassaemia and that the %LScRBC may provide extra information for clinicians in determining renal patients with functional iron deficiency.

In this issue are two case studies. The first one from Sharda Lallu and colleagues from Wellington Hospital reports a case of primitive neuroectodermal tumour of the tongue. Histologic appearance, and ultrastructural and immunohistochemical findings confirmed the diagnosis.

The second case study, by Aus Molan from Palmerston North Hospital, was a case of bacterial meningitis in which conventional Gram stain and culture methods failed to identify the causative agent (*Neisseria meningitides*) that was subsequently identified by a PCR method. This illustrates the importance of molecular methods for the rapid diagnosis of bacterial meningitis.

There is often a lot of confusion between registration and membership, and renewing your Annual Practising Certificate (APC) and renewing your membership and/or CPD enrolment with the NZIMLS. In this issue Sharon Tozer from the NZIMLS Executive Office clarifies that the Medical Sciences Council of New Zealand (MSCNZ), not the NZIMLS, registers medical laboratory scientists and technicians and issues the APC; while the NZIMLS provides the CPD programme and offers membership. She also provides a chart setting out the main functions of the MSCNZ and NZIMLS and what benefits membership of the NZIMLS provides.

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# T.H. Pullar Memorial Address. Pathology: the study of structure and function in health and diseases

*Robin Fraser*

Dr T.H. "Thos" Pullar, the champion and friend of New Zealand medical laboratory scientists and technologists would no doubt have received great support from Christchurch Pathology, which is celebrating its 100<sup>th</sup> Anniversary. Because of earth-quake-munted venues we are so grateful for your invitation to celebrate in Wellington.

Pullar's idea of teamwork, in my opinion, has so enhanced New Zealand pathology.

Our Christchurch pathology began in 1912 with the appointment of Dr. AB Pearson from Edinburgh. His first autopsy report (No.1 Christchurch) was dated September of that year. The following year Pearson appointed Mr. T Ross (bacteriologist). Christchurch soon built up a collegiate of scientists, technicians and medical pathologists, so making a huge contribution to patient care, diagnosis and inevitably to medical research.

Pathology rapidly expanded and WW2 saw Pearson's assistant pathologist, Dr. Denis Stewart in the Middle East fighting yellow jaundice (hepatitis A) with occasional cases of fulminant hepatitis and death of several of our troops. Denis returned to take over the Christchurch department, while Pearson joined his son Colin in his pioneering private pathology practice.

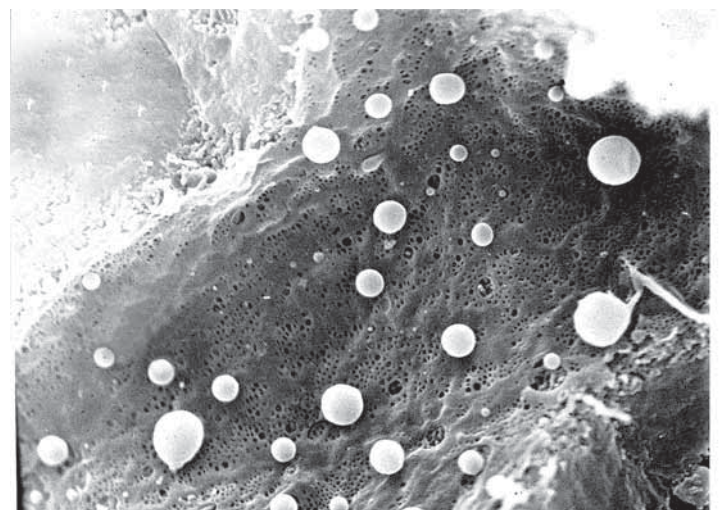
Dr. Edgar Thomson (RPAHospital) and Dr. Fred Gunz,(Sydney Hospital), both having worked previously in Christchurch, encouraged me in 1974 to become senior lecturer in Professor Roy McGiven's new academic-hospital pathology group ( Christchurch School of Medicine, now University of Otago, Christchurch ). I was stunned with the depth and beauty of our discipline this side of the "ditch." Please let me explain why I believe pathology is team-dependent and so important for our nation's health.

Pathology, or the study of disease, is central to the endeavours of clinicians and biomedical scientists. However, the normal (anatomy and physiology) must first be understood (1). Changes in structure and function of the body, arising from either environmental or genetic defects, lead to physiological compensation. If compensation fails, then disease or even death occurs. Pathology is therefore concerned both with the pathogenesis or the events leading to the disease, as well as the disease itself. For these reasons, pathology, as well as medicine and surgery, have been traditionally the three major departments in the clinical training of medical students.

Our discipline permeates all aspects of endeavor in our medical schools, hospitals and community. The study of abnormal structure and function occurs at the gross level where the coroners' pathologist dissects a body to determine the cause of death following an accident, disease or homicide. This is the setting in which students learn of morbid conditions within the community or hospital, and audit clinical treatment. Structure and function is also important at the microscopic level, where the hospital histopathologists, clinical lecturers and surgeons discuss biopsies with the aid of the light microscope, giving clues as to diagnosis, treatment and prognosis of various diseases.

Normal and abnormal structure and function extend to the

ultrastructure, as determined by electron microscopy. For example, abnormalities of the fenestrated endothelium lining of the liver sinusoids or "liver sieve" (Figure 1) affect lipoprotein metabolism, so playing a role in the pathogenesis of diseases as diverse as atherosclerosis, hepatitis, cirrhosis and even cancer. Our own experimental work gives explanation to public health findings on dangerous life-shortening habits, such as smoking, excess alcohol intake and some diets on the prevalence of atherosclerosis, the trigger to so many sudden deaths we see as pathologists in the mortuary (2-6).



**Figure 1.** Liver sinusoidal endothelium of a corn-oil cholesterol gavaged rabbit. Note the large chylomicrons unable to penetrate the fenestrated hepatic sinusoidal endothelium (original magnification x 20,000).

But structure, function and their abnormalities extend way beyond those elucidated by electron microscopy. Molecular changes alter the trafficking of messages within the cell, to and from its nuclear DNA and cytoplasmic RNA synthesising (rogue) proteins. Cytokines and hormones are messengers to surrounding cells or distant organs. All these pathways may involve specialised disciplines of pathology. Avogadro's number allows the structure of lipoproteins to be calculated from their size (electron microscopy) and composition (lipid chemistry), so important in cholesterol metabolism (7,8).

At the other end of the scale, the changing structure of the universe may influence disease. A lack of sunspots may lead to a mini-ice age, the retreat of citrus trees and the scourge of scurvy, deforestation of Prague and the Thirty Years War (9). An asteroid strike may kill the dinosaurs or may bring new forms of life to earth. The greenhouse effect may alter the distribution of mosquitoes and malaria.

Our Christchurch department includes biomedical researchers, such as the protein group, seeking mutants of serum proteins leading to haemorrhage, thrombosis, infarction, emphysema, dementia and

death. Mutant proteins named by the group read like a page from Thomas Cook, since abnormal proteins tend to be named after the town or region in which the patient lives (specimens came from all over the world).

The original leader of our protein group was Emeritus Professor Robin Carrell, now of Cambridge, U.K. Continuing with his innovative work, our scientists in Christchurch have discovered several protein vectors of similar configuration transporting enzymes and hormones to specific sites of activity. These transporters have been named "serpins." Mutant serpins, mostly synthesized by hepatocytes in the liver, but also by neurons, because of their abnormal dimensions may be trapped in the cells of origin, leading to inclusions which eventually result in necrosis, hepatitis and cirrhosis or, when synthesized in the brain, dementia (10-12).

Because of the research activities of hospital scientists, technologists and their postgraduate students, Christchurch pathology is capable, within weeks of a new test being described in an overseas journal (such as mutant DNA for the diagnosis of haemochromatosis, cystic fibrosis or Huntington's chorea), of having the test up and running for the benefit of those in Canterbury and beyond.

Blood cells are examined by hospital and university haematologists, scientists, students and technicians for the diagnosis, treatment, prognosis and understanding of haematological and other diseases. A major research effort concerned the dendritic cell. This cell presents foreign antigens to lymphocytes, so the body can reject non-self. The aim is to lead the body to regard cancer as non-self. There is also research into the problem of patients with bone marrow transplants being susceptible to fungal infection due to immune depression. Haematologists, microbiologists and virologists are improving techniques for diagnosing fungi, bacteria and viruses from their DNA foot prints.

The microbiologists of the clinical school and hospital laboratories research bacteria in the kidney, protected by chemical osmolites. There is a real tapestry of endeavours in Christchurch, with a geology student from the University of Canterbury liaising with urologists and hospital scientists into the structure of kidney stones and their shattering by ultrasound. The microbiologists also join in world wide crusades against the pneumococcus, bird flu, HIV and have interests in ultraviolet exposure.

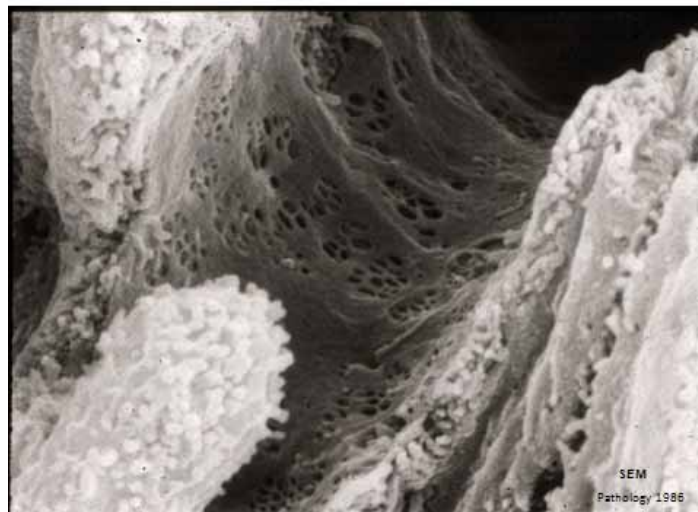
The manner in which white blood cells kill bacteria with the release of oxygen radicals again links biomedical research with microbiology, respiratory pathology and the health of premature babies. Thus our free-radical group meshes nicely with hospital health efforts and extends into the community, advising on the place of foods and vitamins protective against free radical damage.

Throw some students into this tapestry of knowledge, jumble of clinicians, scientists, researchers, technologists and administrators and it makes the curriculum committee wince as to what is our core teaching. It is not just laboratory diagnosis, it is not just biomedical research, it is not just haematology, microbiology, virology, immunology, cytogenetics or forensic pathology. It is indeed the study of disease and health, abnormal and normal structure and function. To our students, both undergraduate and postgraduate in a wide spectrum of health and medical pursuits, one of our major resources is the museum. Not only are there macroscopic specimens of diseased organs, but also an enormous collection of slides and power-points for projection of specimens and their histopathology (13).

More recently genomics and epigenetics have become tools to alleviate familial diseases such as hyperlipoproteinaemias, amyloidosis, haemophilia and even tumours by inserting DNA to replace mutant genes or siRNA to inhibit rogue proteins. Suitable vectors carry the genetic material to reach the appropriate organ (most often the liver). The size and composition of these vectors is all important, since to reach the hepatocytes they are first filtered by the liver's fenestrated sinusoidal endothelium sinusoids (capillaries) (14-16).

In the future, I predict that the porosity of the liver sieve will be recognised of importance not only in the pathogenesis of atherosclerosis, from both environmental and familial hazards, but also in diseases related to immunity and inflammation. I believe our champion, Dr Pullar would have approved of my request for your scientific input into our Australasian Liver Sieve Research Group's recent dreams or hypotheses. These are:

1. To develop a simple clinical liver function test for liver sieve porosity, for example:
  - i. BSP test for albumin uptake, a common LFT from 50 years ago (17).
  - ii. A cholesterol C<sup>13</sup> breath test (18).
  - iii. Imaging of filtration of suitably labelled nano-spheres, as by a spectral CT device (19).We urgently need a safe test to translate this experimental work to the bedside.
2. The role of immune tolerance, related to hepatocytes presenting their proteins as antigens to circulating T cells by contacting them through fenestrae, (a process called trans-endothelial hepatocyte lymphocyte interaction, TEHLI) which depends on a porous liver sieve (20) (Figure 2). We hypothesise that hypo-fenestration brought about by alcoholism (4), nicotine (5) and sedentary old age (2) leads to lack of immune-tolerance, immune hepatitis, active chronic hepatitis and cirrhosis. For example, the carrier state of hepatitis B (derived from being born of an infected mother) may become active hepatitis when defenestration occurs, so leading to T cells without tolerance.



**Figure 2.** A lymphocyte traversing through a rat's sinusoid. Note its stubby microvilli of diameter suitable to insert through fenestrae to contact hepatocyte-microvilli, leading to trans-endothelial hepatocyte lymphocyte interaction (TEHLI).

3. The sieve's place in the treatment of septic shock syndrome (due to TNF alpha and other inflammatory cytokines) from endotoxin activation of the reticulo-endothelial system, especially the liver macrophages (Kupffer cells) being negated by infusion of chylomicrons (21). These lipoproteins which adsorb endotoxins, when small enough pass through the fenestrae (Figure 1) to contact hepatocytes. Their adherent endotoxins are detoxified by the liver and excreted in the bile (21). Artificial fat emulsions (eg Intralipid) may act similarly (22). The latter, however has variable results, which might reflect the use of rabbits as experimental animals (with smaller fenestrae) rather than rats (23). Another factor maybe that TNF alpha decreases the sieve's porosity (24). Sepsis has been shown to correlate with decreased sieve porosity and hyperlipidaemia (25). We also wonder if the saturation of

triglycerides, by changing the proportion of free cholesterol to cholesteryl ester may alter the adsorption of endotoxins by chylomicrons (6,26). One must get in early with treatment.

4. Chylomicrons from the jejunum may lead to endotoxins from within the gut lumen being transported up the thoracic duct to the neck veins to reach the lungs as their first organ of call. If the endotoxins activated the alveolar macrophages might this lead to the shocked lung syndrome? (Fortunately the small gut is usually relatively free of gram-negative bacteria; however, Dr Bruce Dobbs, the CDHB hospital surgical scientist who for thirty years has researched chylomicrons and the liver-sieve with me, points out that colonic lymph mixes with chylomicron-rich lymph in the thoracic duct, where gut endotoxin-chylomicron complexes may occur.) A fascinating editorial raises these possibilities (27). The pathogenesis of diabetes may also be affected by endotoxin-bearing chylomicrons from the gut (28), the excretion of which may be inhibited by our previous findings of less porous liver sieve in diabetes (29).

I am proud to have been associated with the discipline of pathology within our hospital-university environment, which despite financial restraints, clashes over funding, recognition and scientific philosophy, still delivers research-based training to our students and a high standard of scientific laboratory diagnoses to our clinicians and patients and our ethos of translational medical research. The collegiality of New Zealand pathology, with our various national specialist meetings are tribute to Dr. T.H. Pullar's vision of teamwork.

**Keywords:** atherosclerosis, chylomicron remnant, dietary fat, epigenetics, endotoxin, immune-tolerance, inflammation, liver sieve, molecular pathology, toxic shock.

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# Evaluation of the new red cell research parameters on the Sysmex XE-5000

Bernard Chambers

## Abstract

**Background:** The Sysmex XE-5000 analyser includes four new red cell research parameters, namely the percentages of microcytic (%Micro R), macrocytic (%Macro R), hypochromic (%LScRBC) and hyperchromic (%HScRBC) red cells. The aim of this study was to establish reference intervals for these four parameters and look at their values in different anaemic populations. They were also compared with estimates of microcytic, macrocytic and hypochromic red cells obtained from the CellaVision DM96.

**Methods:** 405 samples were analysed in reticulocyte mode for the full study. Also 112 macrocytic sample results were obtained retrospectively to compare with the DM96, along with 82 stained slides from the full study. Results were compared statistically using the Kolmogorov-Smirnov test, independent t-test, Pearson correlation and receiver-operating characteristic (ROC).

**Results:** The values for the four studied parameters were not normally distributed so percentile analysis was used to determine reference intervals. The values were statistically different in each anaemic population except for the iron deficient and thalassaemic group. These parameters proved to be reproducible and stable for at least 16 hours at room temperature.

**Conclusions:** These new parameters correlate better with MCV and MCH results from the analyser than CellaVision estimates. The %LScRBC and %Micro R are useful for predicating restricted erythropoiesis in iron deficiency and thalassaemia. The %LScRBC may provide extra information for clinicians in determining renal patients with functional iron deficiency

**Key words:** Hypochromia, microcytosis, macrocytosis, restricted erythropoiesis.

*N Z J Med Lab Sci 2012; 66: 70-72.*

## Introduction

All modern haematology analysers produce values for mean cell volume (MCV) and mean cell haemoglobin (MCH). These represent the average size and haemoglobin content of red cells produced in the bone marrow over the last 120 days. Until recently, ADVIA instruments (Siemens, Tarrytown, USA) were the only analysers to use flow cytometry to quantify red cell sub-populations. The Sysmex XE-5000 analyser (Sysmex Corporation, Kobe, Japan) is now capable of estimating percentages of microcytic, macrocytic, hypochromic and hyperchromic red cells.

The proportions of hypochromic and microcytic red cells reflect the body's iron status over the previous couple of months. These parameters have been shown to be a useful indicator of functional iron deficiency (1) and disrupted haemoglobin synthesis in thalassaemias (2).

In our laboratory we routinely use the CellaVision DM96 automated microscopy analyser (CellaVision AB, Lund, Sweden). This instrument performs a white cell differential and presents a composite picture of the red cells taken from the stained blood film. It also displays an estimate of percentages of microcytic,

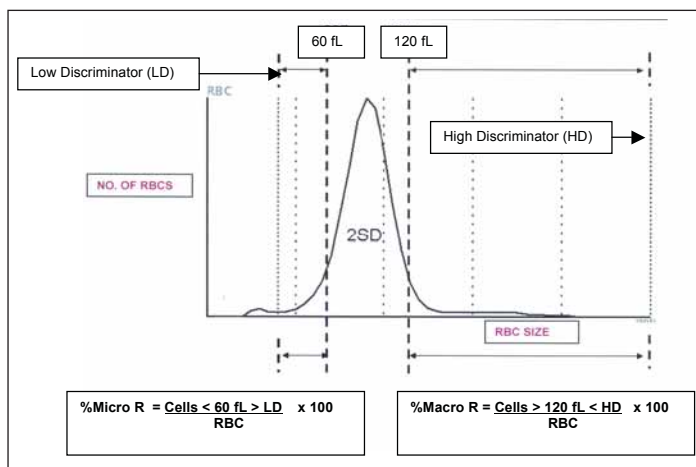
macrocytic and hypochromic red cells. These estimates were also compared with those obtained from XE-5000.

The aim of this study was to evaluate these new parameters, establish reference intervals for a healthy population and investigate their diagnostic performance in different types of anaemia.

## Derivation of the new parameters

Red blood cells (RBCs) and platelets are counted by a Sheath Flow DC detection method. As the cells pass through an aperture, the change in electrical resistance between two electrodes allows precise size distribution of the RBC population. The percentage of microcytic red cells is calculated from the number of cells between 60 fL and the low discriminator for the red cell population (Figure 1). The percentage of macrocytic red cells is calculated from the number of cells between 120 fL and the high discriminator for the red cell population.

**Figure 1.** RBC Distribution Curve showing derivation of % Micro R and % Macro R.

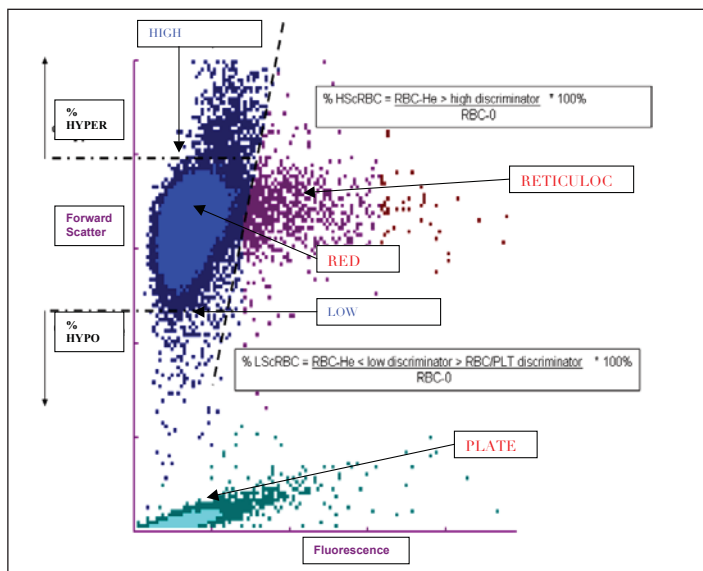


%Micro R: % of microcytic RBCs < 60 fL. %Macro R: % of macrocytic RBCs > 120 fL.

These two new parameters are available on all full blood counts. The other two new parameters are measured in the reticulocyte channel of the XE-5000. In the reticulocyte mode a portion of the sample is stained with a polymethine dye that is specific for the RNA/DNA in the reticulocytes. The cells are then analysed by flow cytometry to produce a scattergram of forward scattered laser light and fluorescence. Forward scatter correlates with the red cell haemoglobin content (RBC-He), so the proportion of low forward scattered red cells (LScRBC) and high forward scattered %LScRBC: % of hypochromic RBCs < 17 pg. %HScRBC: % of hyperchromic RBCs > 49 pg.



**Figure 2.** Reticulocyte scatter showing derivation of %LScRBC and %HScRBC.



## Materials and methods

During a 4-month period, samples were selected from the routine workload at Middlemore Hospital Laboratory (Auckland, New Zealand). The “healthy” population” (N=148) were selected from patients in the Emergency Department, with no clinical disease history and a normal full blood count and biochemical profile.

Three “non-healthy” patients groups were selected for the full study. The chronic kidney disease group (CKD; N=99) were selected from routine monthly bloods sent from the Dialysis Unit.

The iron deficiency anaemia group (IDA; N=100) were selected from samples where iron studies had previously been performed and serum ferritin levels were <20 µg/L.

The Thalassaemic group (THAL; N=58) were selected from samples where haemoglobinopathy screens had been previously performed. There were 31 alpha and 27 beta thalassaemia traits in this group.

Each sample was analysed in the reticulocyte mode of the Sysmex XE-5000, within 12 hours of collection. The new parameter results were obtained from the XE-5000 Research (R) screen.

At the end of the study, an additional “non-healthy” macrocytic population was also included. Only retrospective % Macro R results were obtained from the XE-5000 data base (MACRO N=112) from patients with an MCV >103 fL.

For the comparison between the CellaVision DM96 and XE-5000, a selection of 82 stained blood films from the four “non-healthy” populations were put back on the DM96 analyser for red cell characterization. These values are not stored in the database if red cell characterization is not being routinely reported.

For the reproducibility study, an iron deficient and a normal sample were sampled 10 times in the reticulocyte mode. For the stability study, a thalassaemic sample, kept at room temperature, was sampled every two hours. This was used as it could potentially have to most unstable red cell population.

Statistical analysis was by the Kolmogorov-Smirnoff test, T-test, variance, pearson correlation and receiver operation curves using the statistics package SPSS v13.0 (SPSS, Chicago, USA).

## Results

### Kolmogorov- Smirnoff test

In the “healthy” population the distribution of values for the four parameters were found not to be normal with a right hand skew to the data. P values for %Micro R, %LScRBC and %HscRBC were <0.001 and 0.021 for %Macro R.

### Independent T-Test

In each of the 4 groups sampled in reticulocyte mode, the means for %Micro R, %Macro R, %LScRBC and %HScRBC were significantly different from each other (p<0.001). The only exception was the THAL and IDA group, where the means for %Micro R (p=0.891), %Macro R (p=0.116) and %HScRBC (p=0.393) were not significantly different. However, the %LScRBC was significantly different (p<0.001) between these two groups. The mean %Macro R was also significantly different in the MACRO group compared with the other 4 groups (p<0.001)

### Variance

The means and standard deviations (in brackets) of each population group are displayed in the table below. As the values were not normally distributed, standard deviations were not used to calculate the reference intervals from the “healthy” population. Instead, these were derived by calculating the 2.5% and 97.5% distribution quantiles using the statistical programme R (Bell Laboratories, New Jersey, USA).

	Healthy (N=149)	CKD (N=99)	THAL (N=58)	IDA (N=100)	MACRO (N=112)	Reference interval
%Micro R	1.4 (0.9)	2.6 (0.8)	27.9 (14.0)	28.2 (14.0)	-	0.5 – 4.6
%Macro R	8.6 (2.4)	11.9 (6.7)	4.1 (1.2)	3.7 (1.2)	33.1 (9.0)	6.1 – 13.4
%LScRBC	0.5 (0.5)	3.1 (4.5)	15.9 (11.2)	32.3 (22.9)	-	0 – 1.7
%HScRBC	1.0 (0.2)	0.8 (0.4)	0.2 (0.2)	0.2 (0.2)	-	0.7 – 1.2

### Pearson correlation coefficients

The table below shows the correlation coefficients for the comparison of %Micro R and MCV, %Macro R and MCV and %LScRBC and MCH for each population group.

	Total (N=512)	Healthy (N=149)	CKD (N=99)	THAL (N=58)	IDA (N=100)	MACRO (N=112)
%Micro R vs MCV	r = -0.90	r = -0.78	r = -0.74	r = -0.95	r = -0.95	-
%Macro R vs MCV	r = 0.84	r = 0.86	r = 0.82	r = 0.88	r = 0.83	r = 0.93
%LScRBC vs MCH	r = -0.82	r = -0.49	r = -0.74	r = -0.76	r = -0.93	-

The table below shows the correlation coefficients as above for the 82 slides analysed on the CellaVision DM96 compared with the XE-5000.

%Micro R vs MCV	r = -0.87	%Macro R vs MCV	r = 0.90
Cellavision % MICRO vs MCV	r = -0.55	Cellavision % Macro vs MCV	r = 0.70
Cellavision % MICRO vs %MICRO R	r = 0.69	Cellavision % Macro vs %MACRO R	r = 0.80
%LScRBC vs MCH	r = -0.78	Cellavision % HYPO vs MCH	r = -0.50
Cellavision % HYPO vs %LScRBC	r = -0.40		

## Receiver operating characteristics (ROC)

The reticulocyte haemoglobin concentration (Ret-He) has been shown to be a useful parameter to indicate restricted erythropoiesis in various studies (3). A Ret-He level of 28.5 pg was chosen as a cutoff in the ROC analysis. The area under the curve (AUC) for %LScRBC was 0.978 and for %Micro R was 0.983.

## Reproducibility and stability

Reproducibility testing showed coefficients of variation (CV) between 0.01 and 0.05 for the four new red cell parameters. All parameters remained stable for 16 hours at room temperature before the % LScRBC value started to decrease

## Discussion

The means for each new parameter were shown to be significantly different in each of the four population groups studied, except for the IDA and THAL group where the percentages of microcytic, macrocytic and hyperchromic cells were very similar. These findings agree fairly well with a Spanish study (4). However, those authors found no significant difference between the %LScRBC in these two populations with restricted erythropoiesis. This was probably due to the fact that the criteria for their iron deficient population included many borderline and mild iron deficiencies. They also found the values for their "healthy" population were normally distributed and used two standard deviations for their reference intervals. The reference intervals they established (%Micro R 0.2-1.9, %MacroR 5.0-12.0, %LScRBC 0-0.6 and %HScRBC 0.5-1.1) were similar to those found in the present study using quantile analysis.

There was a strong overall correlation between the MCV and the %Micro R and %Macro R and between MCH and %LScRBC in the total samples tested. This was also so in each population group with the exception of the "healthy" group where the correlation coefficient between MCH and %LScRBC was only -0.49. The MCV correlation would be expected to be good as the values are determined from the red cell distribution plot. The cut off values (60 fL and 120 fL) are fixed by the manufacturer but it would be useful if these could be changed by the operator.

The CellaVision DM96 estimates percentages of microcytic, macrocytic and hypochromic red cells from the stained blood film. During our initial evaluation of the DM96 we decided these estimates did not always correlate with the film and indices and so we do not report them. The correlations between the new XE-5000 parameters and the MCV and MCH were certainly much better than those for the DM96. In our laboratory we use IT3000 Middleware (Roche, Basel, Switzerland). This software runs our film making rules and we also use it for entering blood film comments and manual differentials. IT3000 has the ability to display these new parameters on our enquiry screen and so we can see the percentages of microcytes and macrocytes on every sample. This has become a very useful tool in helping to decide about red cells in the blood film, especially where there is an increased red cell distribution width or dimorphic population.

The AUCs were both close to 1.0 for %LScRBC and %Micro R indicating low false positive predictions for determining restricted erythropoiesis in both thalassaemias and iron deficiencies. The %LScRBC may also prove to be a useful parameter in helping to decide if a patient has functional iron deficiency. This is a common occurrence in CKD where dialysis patients may have adequate iron stores yet cannot utilise this iron to support erythropoiesis when given erythropoietin. These patients typically have normal or high serum ferritin levels but low transferrin saturation and require parenteral iron infusions. The % hypochromic red cells from ADVIA instruments have been demonstrated to be a good predictor of iron deficiency; however this parameter has been shown to be unstable as the sample ages. An Italian study found the %LScRBC to be a better predictor of iron responsiveness than baseline serum ferritin or transferrin saturation in dialysis patients (5). The AUC in that study was 0.72 with a best cut-off value of 2.7%.

Our protocol at Middlemore is to maintain a saturation of 0.2 – 0.4 and ferritin >200 µg/L in dialysis patients. In the CKD population that was sampled, 12% had ferritins <200, 16% RET-He <28.5, 14% saturations <0.2 and 32% with %LScRBC <2.7. A %LScRBC cut-off of 5% may be a better indicator, equating to 16% of these patients.

## Conflicts of interest

The author declares no conflicts of interest.

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# Fine needle aspiration cytology of unsuspected metastatic primitive neuroectodermal tumour (PNET): a case report

*Sharda Lallu, Sarla Naran, Diane Kenwright and Peter Bethwaite*

## Abstract

We report a case of primitive neuroectodermal tumour (PNET) of the tongue that metastasized to a left cervical lymph node in a 47 year old female with a short history of sore throat and swelling in the left upper neck. At presentation a left hypoglossal nerve palsy was evident along with masses in the posterior third of her tongue and the upper region of the sternocleidomastoid muscle. Fine needle aspiration (FNA) of the neck mass revealed a cellular population of spindle cells arranged as syncytial aggregates with indistinct cell borders. Tumour cells were oval, polygonal and spindled in appearance with scant fragile cytoplasm, a high nuclear/cytoplasmic ratios, nuclear hyperchromasia, irregular and molded nuclei, granular chromatin and inconspicuous nucleoli. Histologic appearance, ultrastructural and immunohistochemical findings confirmed the diagnosis of PNET.

**Key words:** fine needle aspiration cytology, metastasis, left neck, peripheral primitive neuroectodermal tumour (PNET), tongue

*N Z J Med Lab Sci 2012; 66: 74-77*

## Introduction

Peripheral primitive neuroectodermal tumour (PNET) is a rare malignant small round cell tumour of neuroectodermal origin with variable cellular differentiation (1,2). The term was first used for a group of embryonal tumours located in the central nervous system (cPNET) and then expanded to include similar peripherally located tumours (pPNET) (3). Peripheral PNETs affect mainly children and young adults, commonly involving the thoracopulmonary region (Askin tumour), pelvis, abdominal region and extremities. These tumours are aggressive, with a tendency to recur and to metastasize especially to bone marrow, brain, lungs and lymph nodes (4).

FNA cytology of PNET in various locations has been reported sporadically (5). The occurrence of these tumours in the head and neck is rare (6,7) and we report the fine needle aspiration [FNA] cytology of a PNET arising in the posterior tongue, that had metastasized to cervical lymph nodes in a 47 year old woman, initially mistaken for a poorly differentiated non-keratinizing squamous cell carcinoma.

## Case report

The patient was a 47 year old woman with a four months history of a left sided sore throat and swelling of the left upper neck region combined with a dysphagia and recent weight loss. At presentation there was a left hypoglossal nerve palsy and although difficult to examine, appeared to have a mass at the posterior third of her tongue. Palpation of the neck revealed a 40 x 20 mm mass in the upper aspect of the sternocleidomastoid muscle. A fine needle aspiration was performed of the neck mass and the initial cytologic interpretation suggested a poorly differentiated non-keratinizing squamous cell carcinoma due to the predominance of spindled cells population and a failure to recognise the "neuroendocrine" nuclear features of the cells present. After the reported cytologic findings of metastatic carcinoma, biopsy of the tongue lesion was performed and demonstrated chronic inflammation only.

Nasendoscopy detected a 37mm x 44 mm mass in the left tongue which was re-biopsied. The findings were of a "small round blue cell" tumour showing mesenchymal differentiation and immunohistochemical positivity for CD99, vimentin, Bcl-2, focal positivity for NSE together with glycogen found within the cytoplasm. FNA of the neck node was repeated and sent for cytogenetic analysis and electron microscopy.

The patient was treated with combined radiotherapy and chemotherapy. At follow up examination 18 months later the patient had dysphagia with evidence of relapse in the posterior tongue with a 60 mm mass in the base of tongue on CT examination, with evidence of multiple pulmonary metastases. The patient died due to the progression of distant metastasis.

## Material and methods

FNA of the left neck mass was performed with a 25 gauge needle and smears were prepared on site and fixed in 95% ethanol and stained with Papanicolaou stain. The remaining material from the needle was washed in 30% ethyl alcohol in physiologic saline. From half of this material a filter preparation was made on size 5 µm Sartorius AG-Cellulose Acetate filter (Germany) using the cytosieve method and stained by Papanicolaou method. The remainder of the aspirate sample was spun down and from the sediment a cell block was made and fixed in 10% formalin, routinely processed and stained with Hematoxylin-Eosin (H & E). A portion of the repeat FNA sample of the neck mass was sent for electron microscopy which was fixed in phosphate-buffered glutaraldehyde, postfixed in osmium tetroxide, embedded in Epon and sections were cut and stained with uranyl acetate / lead citrate. For cytogenetic analysis the part of sample was fixed in cytogenetic transport medium.

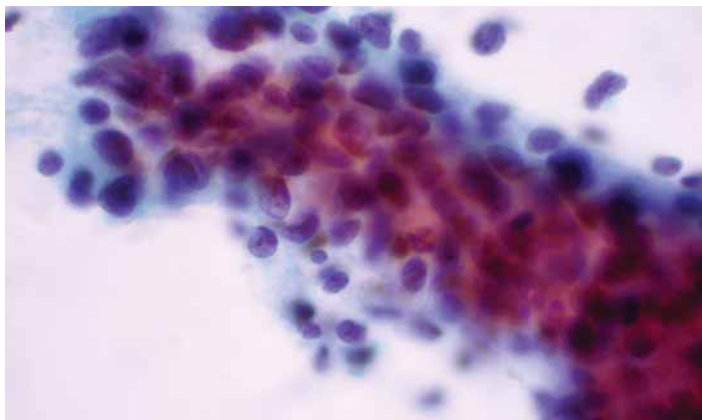
Immunohistochemistry was undertaken using the Strep-Avidin Biotin method (Ventana ES). Sections from the cell block of FNA neck and tongue biopsy were stained with Vimentin (1:4000 Dako), CD99 (1:100 Dako), Bcl-2 (1:30 Dako), NSE (1:2000 Dako), Cytokeratin (AE1/AE3) [1:1000 Dakocytomation], CAM 5.2 (1:100 Dickinson), EMA (1:750 Dako), LCA (1:300 Dako), S100 (1:4000 Dako), HMB 45 (1:500 Dako), Synaptophysin (1:80 Dakocytomation), Actin (1:2500 Dako), Desmin (1:200 Dako) and Myoglobin (1:8000 Dakocytomation). PAS histochemical staining was also performed on cell block and biopsy sections.

## Results

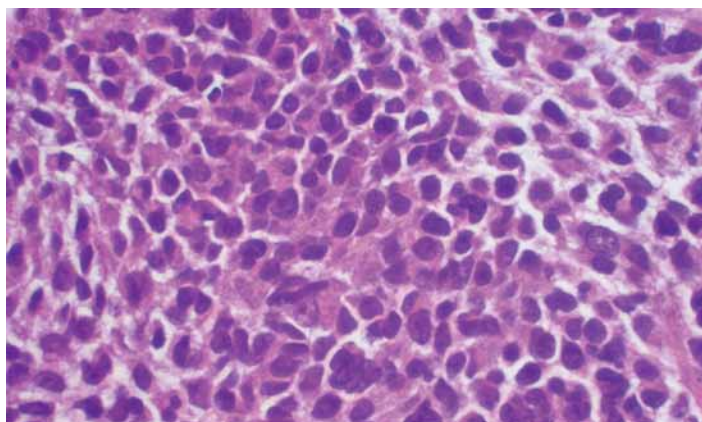
### Cytologic findings

FNA cytology smears (Figure 1) and clot preparations (Figure 2A) were highly cellular and composed of syncytial aggregates of tumour cells with indistinct cell borders and scanty stroma. The tumour cells were oval, polygonal and spindled in appearances. The cells ranged in size with scant and fragile cytoplasm, high nuclear/cytoplasmic ratios, hyperchromatic, angulated nuclei showing nuclear molding, focal pseudorosette formations, granular chromatin and inconspicuous nucleoli and some mitotic figures. The background contained free lying nuclei, blood, apoptotic bodies and necrotic debris.

**Figure 1.** Filter preparations from FNA showing syncytial aggregates of tumour cells with oval to polygonal and spindly appearances, hyperchromatic nuclei, high N/C ratio and indistinct cell border (Papanicolaou stain X 400).



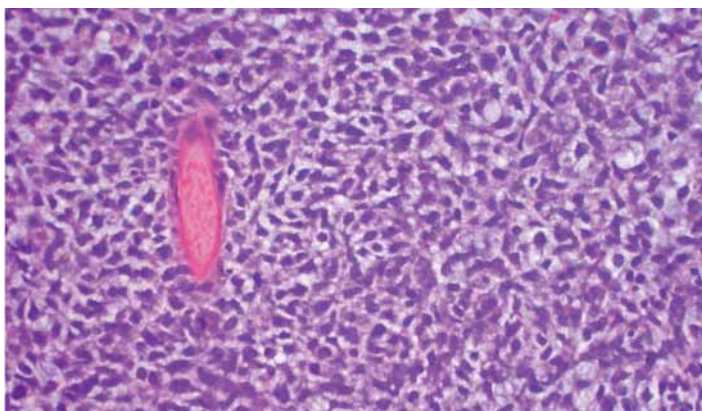
**Figure 2A.** Cell block preparations of FNA showing syncytial aggregates of tumour cells with oval, polygonal, spindly appearances, very high N/C ratio, hyperchromatic, angulated nuclei with scant cytoplasm (Hematoxylin-eosin stained X 400).



#### Histologic findings of the tongue biopsy

The tumour comprised sheets of tumour cells surviving around delicate blood vessels. The tumour cells contained small mildly hyperchromatic angulated nuclei together with a small amount of eosinophilic to clear cytoplasm (Figure 2B). There was a suggestion of a myxoid quality to the background stroma and ill-defined rosette formations. Numerous mitotic figures were identified including abnormal figures and necrotic tumour debris.

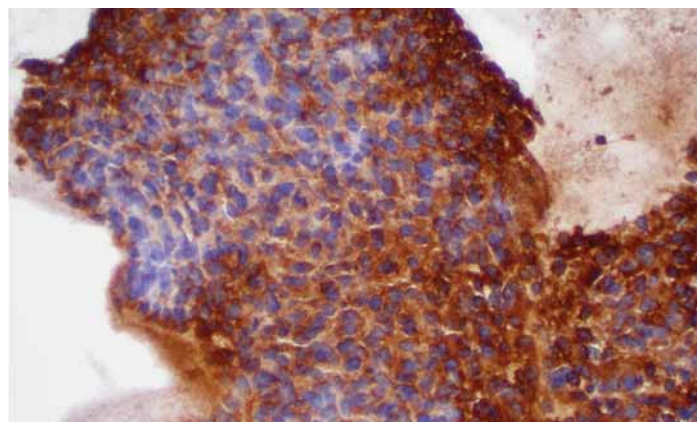
**Figure 2B.** Tongue biopsy section showing sheets of tumour cells contained mildly hyperchromatic, angulated nuclei, high N/C ratio together with a small amount of eosinophilic to clear cytoplasm (Hematoxylin-eosin Stain X 400).



#### Immunohistochemical findings

Immunohistochemical staining on cell block from FNA neck and histologic sections of tongue biopsy showed positive membranous staining within tumour cells for CD99 (Figure 3), Vimentin, Bcl-2 and focal positive staining was seen with NSE. Immunohistochemical stains for Cytokeratin AE1/AE3, CAM 5.2, EMA, LCA, S100, HMB45, Chromogranin, Synaptophysin, Smooth Muscle Actin, Desmin and Myoglobin were all negative. The PAS stain demonstrated moderate amounts of glycogen within the cytoplasm of the tumour cells.

**Figure 3.** Immunohistochemical stained on cell block section showing strong positivity for CD99 (CD 99 Stain X 400).



#### Electron microscopy

Electron microscopy showed primitive, undifferentiated cells with few cytoplasmic organelles but abundant glycogen. Non-specific intermediate filaments were present but no cytokeratin filaments or myofilaments. Cell junctions were infrequent and rudimentary. Occasional small, dense core granules were noted, but interdigitating cell processes were absent.

#### Cytogenetic analysis

Cytogenetic analysis failed to demonstrate metaphases for analysis. Paraffin sections analysed with Fluorescence In situ Hybridization (FISH) studies of the EWS gene showed a normal signal pattern (two yellow signals) with EWSR1 (Zymed laboratories locus 22q12/q13) break apart probe in the majority of sites examined consistent with a normal result.

#### Discussion

Primitive neuroectodermal tumours are members of the Ewing's sarcoma family composed of small round cells normally lacking morphologic evidence of neuroblastic differentiation in the form of neuropil or ganglion cell formation. PNET's account for 1% of soft tissue tumours most commonly involving the thoracopulmonary region (Askin tumour), pelvis, abdominal region and extremities; its presence in the chest wall, posterior mediastinum, myocardium, kidney, vagina, bladder, parotid and orbit has been reported (8). There is propensity for rapid metastatic spread to the distal sites especially the lung, liver, bone marrow, lymph node, pleura and diaphragm. Primary lesions are rare in the head and neck region. The literature reports 43 patients with PNET in the head and neck region, with a mean age of 21 years (9). The prognosis of PNET in this site is also generally poor.

PNET, Ewing's sarcoma, and Askin tumour of the thoracopulmonary region are now considered to be part of the PNET-Ewing's sarcoma family as cytogenetic studies show similar abnormalities; namely the t(11;22) (q24;q12) translocation. The EWS-FLI1 fusion transcript can be detected in 80-90% of the PNET-Ewing's sarcoma family by reverse transcriptase polymerase chain reaction (RT-PCR) (8). FISH did not show EWS gene rearrangement in our case. A few isolated cases have been reported of Ewing's sarcoma with no detectable rearrangement using an EWSR1 break apart probe. Abnormalities were subsequently detected in these cases using FISH probes for

the specific fusion product (10). Therefore, in some rare cases, even if a normal result is reported, a diagnosis of Ewing sarcoma or PNET cannot be completely excluded. In 5 to 10 per cent of EWS primitive neuroectodermal tumours, it is not possible to demonstrate rearrangements of EWS on 22q12 and ETS related oncogenes. Some studies suggest that the type of EWS chimeric fusion transcript has prognostic importance (11).

The cytologic diagnosis of PNET poses a diagnostic challenge due to overlapping cytomorphologic features with those of other small round cell tumours. The potential for misclassification is accentuated when PNETs occur in unusual locations and in an adult group, as demonstrated in our case. The diagnosis of PNET requires a combination of ancillary studies such as immunocytochemistry, cytogenetic, molecular genetics and electron microscopy.

Immunohistochemical staining shows strong dot like or perinuclear vimentin staining and diffuse membranous staining for CD99 in all members of the Ewing/PNET group, although weaker CD99 staining may be seen in other "round blue cell tumours" including rhabdomyosarcoma, T cell lymphomas, synovial sarcoma and small cell neuroendocrine tumours (11). There is variable expression of other neuroectodermal antigens including NSE (positive in this case), synaptophysin, neurofilament, GFAP and PGP9.5. Although not evident in the current case, 20% of cases may show dot-like cytokeratin positivity (11). In most cases the combination of vimentin and strong membranous CD99 and NSE positivity with negative expression of cytokeratins, muscle and haematologic antibodies should exclude neuroblastoma, rhabdomyosarcoma, desmoplastic round cell tumour and leukaemia-lymphoma (12). Ultrastructural features vary depending on the degree of differentiation along the Ewing/PNET spectrum.

The cytologic differential diagnosis of PNET includes lymphoma, neuroblastoma, embryonal rhabdomyosarcoma, small cell carcinoma, synovial sarcoma, small cell variant of melanoma, basaloid squamous cell carcinoma and poorly differentiated non keratinized squamous cell carcinoma (13-18). In this case the absence of lymphoglandular bodies and the presence of large clusters of cohesive cells and a negative stain for LCA ruled out a lymphoma. The presence of neurophil matrix in the background, unipolar cytoplasmic tags (neurites) of the cells forming frequent Homer-Wright rosettes and ganglion cells seen in neuroblastoma were not identified. In addition, neuroblastomas are uniformly negative for CD99 and vimentin.

Rhabdomyosarcoma often shows cellular aggregates, single dispersed cells varying in size and shape, prominent nucleoli, dense chromatin, multinucleation and cytoplasmic vacuoles that were not seen in this material. Rhabdomyosarcomas are positive for desmin, actin and myoglobin. Small cell carcinoma usually shows smearing artefacts, nuclear molding, stippled chromatin with inconspicuous nucleoli, necrotic debris and karyorrhexis. These features are also seen in PNET but negative staining with AE1/AE3, EMA and CD56 normally exclude small cell carcinoma.

Poorly differentiated synovial sarcoma can have the morphologic appearance of a "small round blue cell tumour" and overlapping cytologic features with PNET. The cytologic mimicry makes them unlikely to be diagnosed solely on morphologic grounds. The immunohistochemical markers CD99, Bcl-2, AE1/AE3, cytokeratin and EMA markers are normally positive in synovial sarcoma. In this case, EMA, AE1/AE3 and CAM 5.2 were negative. Bcl-2, although usually positive in synovial sarcoma, is not a very helpful marker in the differential diagnosis as it is positive in other soft tissue tumours (15), and was positive in our case. The small cell variant of melanoma consists of dissociate cells with spindly appearances, prominent nucleoli and intranuclear inclusions, which were not seen in our case; negative immunohistochemistry for HMB 45 also helped ruled out this lesion. The basaloid squamous cell carcinoma consists of small crowded cells with hyperchromatic nuclei, scant cytoplasm, small cystic spaces, necrosis and prominent hyalinoses and are positive for CAM 5.2 and AE1/AE3. Non keratinizing

squamous cell carcinoma consists of oval or polygonal, syncytial aggregates of tumour cells with indistinct cell borders, scanty cytoplasm, hyperchromatic nuclei, irregularly distributed coarse chromatin, mitoses and necrosis. Immunohistochemical staining may be helpful as these tumours lacks immunoreactivity for CD99, NSE and are positive with epithelial markers (13-18).

In summary, FNA cytology along with the ancillary studies such as immunohistochemistry, molecular analysis, cytogenetics, FISH and EM on the aspirated material, will enable a correct diagnosis of primary or metastatic PNET and exclude the other small round cell malignancies that enter into the differential diagnosis as we have experienced in this case.

### Acknowledgments

The authors acknowledge Louise Goossens for her photographic assistance and also David Palmer and Rose Miller for their contribution towards this case.

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# Laboratory detection of *Neisseria meningitidis* – a case study

Aus Molan

## Abstract

The diagnosis of bacterial meningitis remains a challenge to the clinician because of its rapid and lethal course lacking the consistency to particular clinical signs and symptoms. Currently, the diagnosis of bacterial meningitis is mostly done by Gram stain and culture. However, in many clinical settings, the use of rampant and short course antibiotic therapy prior to lumbar puncture reduces the chance of isolation of bacteria in cerebrospinal fluid culture making the diagnosis difficult. The present report examines a case in which conventional Gram stain and culture methods failed to identify the causative agent of bacterial meningitis that was subsequently identified by a Polymerase Chain Reaction (PCR) method. The importance of molecular methods for the rapid diagnosis of bacterial meningitis is also discussed. In a clinical setting, Gram stain and bacterial culture still remains the cornerstones of bacterial meningitis diagnosis.

**Key words:** *Neisseria meningitidis*, Polymerase Chain Reaction, CSF, bacterial meningitis, culture, tissue and organ procurement

*N Z J Med Lab Sci 2012; 66: 78-80*

## Introduction

Invasive bacterial meningitis is a serious disease which can rapidly progress from a mild flu-like illness to death (1). In 2011, a total of 119 cases of meningococcal disease were notified in New Zealand, which equates to a rate of 2.7 per 100 000 population (1). Invasive meningococcal cases with fatality rates of 10 % to 15% have been previously reported and about 20% of the survivors suffer from a number of significant sequelae (2,3). Delays in diagnosis and treatment of meningococcal disease may contribute to its high morbidity and mortality (4). For this reason, administration of preadmission antibiotics to patients with suspected invasive meningococcal disease has been supported by some (5,6). However, after antimicrobial treatment is started, the rate of isolation of bacteria is strikingly reduced (7). In fact, prior antibiotic therapy 12 h or more before lumbar puncture can sterilize the cerebrospinal fluid (CSF) (8).

Once there is a suspicion of acute bacterial meningitis, blood samples must be taken for culture in addition to an immediate lumbar puncture to determine whether the CSF finding is consistent with the clinical diagnosis. The diagnosis is subsequently confirmed by microscopic detection and/or culture of the organism from the CSF (9). Diagnosis of bacterial meningitis based on direct microscopy is quick but lacking in sensitivity while the culture of CSF and blood takes at least 24 h and very often yields a negative result due to prior treatment with antibiotics (10).

In recent years, Polymerase Chain Reaction (PCR) based techniques have increasingly been used to amplify and detect microbial and viral deoxyribonucleic acid (DNA) in clinical samples. The use of PCR for rapid diagnosis of bacterial meningitis has the potential to overcome the poor sensitivity of culture when antibiotics have already been administered (10). The use of broad-range bacterial primers in the diagnosis of bacterial meningitis has been reported in earlier studies (9-11). At present, there is no definitive test that can confirm or exclude bacterial meningitis in patients with CSF findings that are consistent with a diagnosis of bacterial meningitis,

but in whom the CSF Gram stain and culture results are negative. However, a combination of test results may permit an accurate prediction of the likelihood of bacterial versus viral meningitis.

The following case study reports the shortcomings of the Gram stain and culture methods in a bacterial meningitis case caused by *Neisseria meningitidis* that was subsequently identified using a PCR method. The advantages of applying PCR-based methods for the detection of bacterial meningitis, especially in post antibiotic samples, are also discussed.

## Case report

An 18 years old female with no previous significant medical history was admitted to the intensive care unit (ICU) with a three day history of headaches, confusion, agitation, and vomiting. The illness started with a sore throat three days prior to hospital admission. The patient presented to the GP with aches and pains in her arms and legs a day prior to admission, and was given painkillers assuming a viral illness diagnosis. No skin rash was present.

Upon examination at the emergency department, the patient had cerebral irritation with a fluctuating Glasgow Coma Scale (GCS). Impressions of viral meningitis, encephalitis, or other intracranial pathology were suspected. Empirical treatment with IV ceftriaxone (2g) was administered and the patient was intubated to facilitate a computerised tomography head examination. Blood was collected and sent to the laboratory for analysis and culture before admission as an inpatient to ICU.

Blood tests showed a raised white cell count ( $16.6 \times 10^9/L$ ), a high neutrophil count ( $14.8 \times 10^9/L$ ), and elevated inflammatory marker level (CRP: 316mg/L). Additionally, the neutrophils displayed a left shift with toxic vacuolation. Two hours post initial CT head scan, the patient was noted to have fixed, dilated pupils. An urgent follow up CT scan showed significant diffuse cerebral oedema. A lumbar puncture (LP) had not been done at this point and was deferred given the signs of intracranial hypertension.

A LP was eventually performed later in the day (more than 8 h post antibiotic administration) at the request of the Transplant Coordinator to clarify the diagnosis (in particular, to rule out a viral illness). The LP recovered 4 mL of turbid CSF. Analysis performed on the fourth tube showed a white cell and red cell counts of  $1,080 \times 10^6/L$  and  $290 \times 10^6/L$  respectively. Laboratory standard operating procedures for the analysis of CSF require a white cell differential and Gram stain to be performed on samples with a white cell count of  $\geq 5 \times 10^6/L$ . The slides for these tests are prepared using a cytospin technique. No additional centrifugation is performed for any microbiological test regardless of CSF volume. The white cell differential revealed a neutrophil predominance (91%) and no organisms were seen upon examination of the Gram stain. Additionally, the protein level was elevated (4.80g/L) while glucose was significantly below the reference range (0.4mmol/L). The sample was inoculated onto Columbia agar with 5% horse blood and supplemented chocolate agar (Fort Richard, Auckland) and examined at 24 and 48 hours post incubation (5% CO<sub>2</sub> at 37°C). No growth was observed after 48 hours of incubation.

Intravenous ceftriaxone (2g) and vancomycin (1g) were administered together with the treatment of the cerebral oedema



with no subsequent neurologic improvement. The patient was confirmed brain dead after one day of admission into ICU. A family meeting of the patient agreed on organ donation with organs harvested the following day.

Consequently, the CSF sample was sent to LabPlus (Auckland) for PCR testing of: Herpes Simplex Virus, Varicella Zoster Virus, Enterovirus, Parechovirus, *N. meningitidis*, and *Streptococcus pneumoniae*. Using an in-house molecular diagnostics CSF PCR panel, the sample tested positive for *N. meningitidis*. Follow up results from ESR (Porirua) confirmed it as a group C *N. meningitidis* (*siaD* PCR test), subtype (PorA type) P1.5-1,10-8 (PorA type determined by DNA sequence analysis of the *porA* gene).

## Discussion

The present case highlights the value of applying molecular-based methods in confirming the diagnosis of meningococcal disease, especially in post-antibiotic CSF samples. As stated in the Communicable Disease Control Manual (1), a positive nucleic acid test using PCR on CSF samples is an acceptable confirmatory test for the diagnosis of bacterial meningitis. In 2011, 28% (30/108) of meningococcal disease cases reported to the Ministry of Health were laboratory confirmed by the detection of meningococcal DNA by PCR (12). Therefore, culture-negative, PCR-positive cases deserve the same recognition as full culture positive cases.

From a clinical standpoint, this case displayed the classical signs and symptoms of a bacterial meningococcal disease with the exception of the negative Gram stain and culture results. Possible explanations for the observed differences in the detection rate between the Gram stain/culture method and the PCR assay could be: i) bacteria being below the limit of detection (bacterial load) of Gram stain and culture and/or ii) the ability of the PCR method to detect dead organisms. Both reasons are attributable to the effect of the antibiotic treatment, which inhibits the growth of *N. meningitidis* but does not interfere with PCR amplification of the organism's DNA.

Gram stain examination of CSF permits a rapid, inexpensive, and accurate identification of the causative bacterium in 60-90% of patients with community acquired bacterial meningitis, and has a specificity of  $\geq 97\%$  (13). However, the likelihood of visualising the bacterium on the Gram stain relates to the concentration of bacteria in the CSF - concentrations of  $\leq 10^3$  colony-forming units (CFU)/mL are associated with a positive Gram stain result 25% of the time; 103 to 105 CFU/ mL yields a positive Gram stain result in 60% of patients, and CSF concentrations of 1,105 CFU/mL lead to positive microscopy results in 97% of cases (14). However, the yield of CSF Gram stain maybe 20% lower in patients who have received prior antimicrobial therapy (15). In addition, the likelihood of having a positive Gram stain result also depends on the specific bacterial pathogen causing meningitis (16): 90% of cases caused by *S. pneumoniae*, 86% of cases caused by *Haemophilus influenzae*, 75% of cases caused by *N. meningitidis*, and 50% of cases caused by other gram-negative bacilli.

PCR based assays, on the other hand, have consistently shown high sensitivities and specificities (>90%) in comparison to Gram stain and culture (4, 17-19). PCR methods have been utilised to amplify bacterial DNA from patients with meningitis caused by the common meningeal pathogens (*N. meningitidis*, *S. pneumoniae*, *H. influenzae* type b, *Streptococcus agalactiae*, and *Listeria monocytogenes*) (13). Investigators in the United Kingdom have dramatically increased the sensitivity of diagnosis with the routine use of a PCR based assay (5). They have been able to confirm 56% more cases of invasive meningococcal disease with PCR than with culture. Moreover, Richardson and colleagues (4) compared the results of Gram staining and culture of CSF to results obtained with a rapid PCR based assay for the diagnosis of meningococcal meningitis in 281 cases of suspected bacterial meningitis. They reported sensitivity and specificity values of 97% and 99.6% respectively for the PCR based assay compared to a sensitivity of 55% for culture.

The increase in sensitivity of PCR-based assays can be linked to ability of these techniques in the detection of dead bacteria (20). PCR methods are able to detect the presence of organisms as long as the target DNA sequence is not injured, no matter whether the cell is viable, inactive or dead (21). Consequently, PCR techniques are evidently more sensitive than culture; nonetheless, they lack the ability to distinguish active cells from dead cells unless supplementary methods, such as viability assays, are used (22). Hence, given the use of IV ceftriaxone treatment in the present case, it should be no surprise that the Gram stain and subsequent culture were both negative. It is important to note that even if organisms were seen in the Gram stain, the culture may not yield bacterial growth due to the inhibitory effect of the antimicrobial agent.

A recommendation for improved laboratory diagnosis of bacterial meningitis is high speed centrifugation (1000 x g for 10 minutes). While the probability of visualising bacteria on a Gram stain can be increased up to 100-fold by using cytopspin techniques (23), high speed centrifugation of the CSF, if a volume of more than 1mL is available, and using the pellet for microscopic examination and culture increases the bacterial load for both Gram stain, culture, and PCR methods (4,24).

In regards to organ donation, while a donor with bacterial meningitis is often considered to be controversial for organ retrieval; many high quality published studies have established that organ transplantation using donors with bacterial meningitis is an acceptable strategy as long as proper antimicrobial treatment of the donor and the recipient is done (25,26). Authors of a single center 20 year follow up study concluded that given the shortage of organs, the use of grafts from donors with bacterial meningitis (*N. meningitidis*, *S. pneumoniae*, and *H. influenzae*) for heart-lung transplantation seems appropriate if sufficient antibiotic therapy and careful clinical management is instituted for both the donors and the recipient (25).

It is important that clinicians applying PCR-based assays be fully aware of the practical aspects involving the diagnosis of central nervous system infections. If bacterial meningitis is suspected in a patient, antimicrobial therapy should be commenced rapidly. Therefore, decisions regarding the initial treatment in these patients must always be made before obtaining the results of the PCR assay. For the time being, Gram staining and bacterial culture remain the cornerstones of bacterial meningitis diagnosis in a clinical setting.

## Conclusion

This case demonstrates that routine microbiological Gram stain and culture methods can occasionally be substandard in the detection of *N. meningitidis* and potentially other causative agents of bacterial meningitis due to low bacterial load and/or non-viable organisms as a result of antimicrobial treatment prior to CSF collection. For these reasons, it is wise to introduce PCR-based assays as adjuncts to conventional bacterial culture methods in establishing the bacterial aetiology in meningitis. For the time being, Gram stain and culture remain the cornerstones of laboratory detection of the organism causing bacterial meningitis. Additionally, the inclusion of a high speed centrifugation step before performing the Gram stain and culture maybe of diagnostic value. In this particular clinical case, no difference in clinical outcome would have resulted if the isolate was seen in the Gram stain and/or isolated in culture; however, the accurate and timely detection of the causative agent is paramount in any clinical case.

## Acknowledgements

Dr Sam Chan, Clinical Microbiologist for his time and help in preparing a summary of the patient's medical notes and reviewing the manuscript. Dr Daniel Nistor, ICU Consultant for reviewing the manuscript. This case study was presented at the Roche Molecular Users Group, Taupo, September 2012. The author declares no conflict of interest.

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# Registration/APC vs NZIMLS/CPD

Sharon Tozer

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There is often a lot of confusion between registration and membership, and renewing your Annual Practising Certificate and renewing your membership and/or CPD enrolment with the NZIMLS.

## Registration with the Medical Sciences Council New Zealand

It is a requirement of the Health Practitioners Competence Assurance Act 2003 that all persons working in a New Zealand diagnostic medical laboratory in the scopes of practice of a medical laboratory scientist or a medical laboratory technician must be registered with the Medical Sciences Council of New Zealand (MSCNZ).

The MSCNZ is one of sixteen New Zealand health registration authorities appointed by the Minister of Health under the Health Practitioners Competence Assurance Act 2003 (the Act). The MSCNZ is responsible for the administration of the Act in regard to the profession of medical laboratory science.

The primary responsibility of the MSCNZ is to protect the health and safety of the New Zealand public by ensuring practitioners registered in the profession of medical laboratory science are competent and fit to practice.

More information on registration is available at: <http://www.msccouncil.org.nz/registration-information>.

## Annual Practising Certificate

Practitioners must hold an Annual Practising Certificate (APC) issued by the MSCNZ and this must be renewed **annually** prior to 31 March in any given year. In order for an APC to be renewed, practitioners must be enrolled in, and have met the criteria of, a recertification programme which has first been approved by the Council.

More information on the Council's recertification programmes is available at: <http://www.msccouncil.org.nz/recertification-cpd-programmes>

Source: Medical Sciences Council of New Zealand website [www.msccouncil.org.nz](http://www.msccouncil.org.nz).

## NZIMLS membership and CPD enrolment

Membership of your professional association is your first step toward your identity as both a health-care and laboratory professional. Membership is open to those engaged in, or training in the profession of medical laboratory science and/or related fields under the following categories:

- **Member:** Scientists registered with the Medical Sciences Council of New Zealand, including Fellow and Life Members.

- **Associate:** Any person(s) not eligible for any other class of membership, including technicians and non-vocationally qualified persons associated with the profession.
- **Student:** Any person(s) currently enrolled in the third or fourth years of a BMLSc degree taught at a New Zealand University.

Membership of the NZIMLS provides the following benefits:

- Preferential access to continuing educational activities organised by the NZIMLS.
- A sense of professional belonging for MLS students and practitioners.
- Decreased registration costs for attendance and/or participation in NZIMLS CE activities such as seminars, scientific meetings and workshops.
- Access to Fellowship and Technician examinations.
- Three issues of the NZ Journal of Medical Laboratory Science per year.
- Opportunities to participate in the promotion and administration of the profession.
- Discounted membership of the NZIMLS CPD programme.
- Voting rights to elect the Council of the NZIMLS (restrictions apply to some forms of membership).
- Awards and Scholarships available to members only.

## NZIMLS Competence and Professional Development recertification programme (CPD)

The NZIMLS CPD programme is available to all NZ registered medical laboratory scientists, scientific officers, and technicians.

The programme allows participants to maintain a record of laboratory competencies and continuing education and allocated points for activities related to the practise of medical laboratory science. Practitioners should aim to accumulate approximately 100 points per year with a minimum of 300 points required for any three-year period. There are 18 categories of activity that have been selected for their relevance to the profession. There is a single compulsory section (1) that requires you to undergo a yearly peer review of your laboratory competencies. This accounts for 60 points toward the target of 100 points per year. The remaining 40 points can be accrued from any of the other categories.

Approximately 10% of all participants enrolled in the NZIMLS CPD programme will be audited each year. Membership and/or CPD enrolment with NZIMLS must be renewed **annually** at the beginning of each calendar year.

More information on enrolling in the NZIMLS CPD programme is available at: <http://www.nzimls.org.nz/cpd-enrolment.html>

Source: NZIMLS website: [www.nzimls.org.nz](http://www.nzimls.org.nz); NZIMLS Competence and Professional Development Recertification Programme for 2010-2012 ©

**Following is a chart setting out the main functions of both bodies**

NZIMLS	MSCNZ
<b>Council:</b> <ul style="list-style-type: none"> <li>Elected by NZIMLS members</li> </ul>	<b>Board:</b> <ul style="list-style-type: none"> <li>Membership by Minister of Health appointment</li> </ul>
<b>Membership:</b>	
<ul style="list-style-type: none"> <li>Voluntary - open to laboratory personnel and others involved in the profession</li> </ul>	<ul style="list-style-type: none"> <li>Compulsory annual certificate for practising medical laboratory scientists in New Zealand.</li> </ul>
<b>Purpose:</b>	
<ul style="list-style-type: none"> <li>To promote continuing education and professional excellence in medical laboratory science</li> </ul>	<ul style="list-style-type: none"> <li>To protect the public from harm resulting from the actions of medical laboratory scientists through the provision of regulation governing the practice of MLS</li> </ul>
<b>Main Functions:</b>	
<ul style="list-style-type: none"> <li>Represent and act in the interests of the profession and its members</li> <li>Provide opportunities for Continuing Professional Development through:                             <ul style="list-style-type: none"> <li>Competency &amp; Professional Development (CPD) SIG workshops / seminars</li> <li>Annual Scientific Meeting</li> <li>South Pacific Congress</li> </ul> </li> <li>Publish a scientific journal / newsletter</li> <li>Conduct professional examinations for:                             <ul style="list-style-type: none"> <li>Fellowship</li> <li>Qualified Medical Laboratory Technicians &amp; Qualified Specimen Services Technicians (QMLT &amp; QSST)</li> </ul> </li> <li>Develop and maintain contacts with kindred societies overseas</li> <li>Support of the Pacific Paramedical Training Center</li> </ul>	<ul style="list-style-type: none"> <li>Maintain the register of medical laboratory scientists</li> <li>Issue an annual practising certificate</li> <li>Establish and maintain competencies required for registration</li> <li>Consider applications for registration in New Zealand</li> <li>Provide a disciplinary review process as described in the legislation</li> <li>Act in the interest of the public and patients</li> </ul>
<b>Responsible to:</b>	
<ul style="list-style-type: none"> <li>Membership of the Institute</li> </ul>	<ul style="list-style-type: none"> <li>The Minister of Health</li> </ul>

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# Abstracts of oral and poster presentations at the Annual Scientific Meeting of the NZIMLS, Wellington, August 2012

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## **TH Pullar Memorial Address. Pathology: the study of structure and function in health and disease**

*Prof Robin Frazer, University of Otago Christchurch*

Even Dr TH Pullar, the champion and friend of New Zealand medical laboratory scientists and technologists, might have been in awe of the extent to which pathology has expanded since his crusade. In our present understanding of the pathogenesis of malady we need molecular pathologists and protein chemists who understand shapes of molecules altered by the charge of a particle as small as an electron, to astrophysicists who can predict climate change from an increase or decrease in sun spots or other factors to alter climate. An increase in spots might widen the habitat of mosquitoes and so malaria, while a decrease might lessen ultraviolet radiation, good to prevent skin cancer, but a disaster for physiological processes requiring vitamin D. Thus the pathologies of soft bones, altered brain function (including depression or multiple sclerosis), more tuberculosis and common colds. Dinosaur health plummeted eons ago from an asteroid collision. Are some viruses from outer space? Dr Pullar's call for team-work in our laboratories has led me to an exciting lifetime as a pathologist (both experimental and anatomical) since I crossed the ditch (in 1974) from Australia. I have witnessed or experienced personally in Christchurch the team-work enhancing diagnosis of disease and expanding research. These advances cement my belief in the role of structure and function in health and disease.

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## **Economics of healthcare**

*Geoff Simmons, Gareth Morgan Investments*

Is our health system world's best practice, average, or a croc? With this question began two years of study into the health system from economists Gareth Morgan and Geoff Simmons. What they found was startling. Our local health system scrubbed up surprisingly well globally, but it's clear that there is a substantial mismatch between the public's expectations and what the health system actually delivers. Some hard calls need to be made. In 2009 they published Health Cheque, the truth we should all know about NZ's public health system. Due to the feedback of Health Cheque they published a follow up; *A Prescription for Change*. Health Cheque looked inside the issues of our public health system but *A Prescription for Change* went a step further and explored the changes that need to be made to improve our current system, namely: a greater investment in prevention, independent prioritisation of health spending as happens with Pharmac, and improved efficacy and efficiency.

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## **The leader as a systems thinker**

*Prof Jeffrey Braithwaite, Australian Institute of Health Innovation*

Leadership is relatively easy to describe but extremely challenging to enact. Leaders, amongst other things, have to be good managers. They also have to be motivators, change agents, good colleagues and financial engineers. They have to be able to

work in complex cultures and ambiguous political environments and achieve multiple goals, factoring in the needs, demands and requirements of many stakeholder groups. Effective leaders must manage up, down, laterally and with external bodies and groups and they must have at their disposal a wide range of tools, techniques and strategies by which to accomplish their objectives. Few people find this easy and few leaders are effective in their roles without experience and training. One way to accomplish leadership is to be an effective systems thinker. This involves appreciating the whole system and understanding the sub-systems and their interfaces. To be an effective systems thinker the leader will need four demonstrable skills; to apply diffusion of innovation methods to create a tipping point for change; to be persistent in the face of challenging circumstances; to negotiate with multiple stakeholders constantly; and to navigate through uncertainty and complexity. In health care there is too much management and not enough leadership and people much more readily take a structural view than a systems view. This needs to change.

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## **Evolution, revolution, science changing life (CML)**

*Dr Peter Ganly, Canterbury Health Laboratories, Christchurch*

Although chronic myeloid leukaemia is a rare disorder, it has achieved many 'firsts' on the road to a better understanding of malignant disease. Such understanding has underpinned the development of the first and best example of a medical treatment targeted specifically at neoplastic disease which effectively controls the leukaemia without the 'off target' adverse effects commonly seen with conventional chemotherapy. The study of chronic myeloid leukaemia has played a central role in driving the evolution of knowledge, gained over more than one hundred years, which now culminates in today's revolution in the therapy of cancer.

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## **Towards targeted therapy in multiple myeloma**

*Dr Ken Romeril, Wellington Hospital*

Multiple myeloma (MM) accounts for 10% of all haematologic malignancies. The annual age-adjusted incidence in the United States has remained stable for decades at around four per 100,000. Local data would suggest that there is apparent increase in incidence. The median age of diagnosis is about 65 years. It is a genetically complex disease and recent research has shown that there is intraclonal heterogeneity of myeloma -propagating cells. There are various clinical phases which include monoclonal gammopathy of undetermined significance (MGUS) and smouldering MM (SMM; also known as asymptomatic MM). Symptomatic MM is defined by clinical symptoms and evidence of organ damage. The condition has moved from one with a short survival of 2 to 3 years to one where the average survival is now around 7 years. Clinical progress has come about through the use of novel agents such as thalidomide and the increased use of proteasome inhibitors such as bortezomib. There has been an increased understanding of the genetic architecture. Genetic expression profiling (GEP) can now identify most groups of molecular subtypes of MM and

their clinical application continues to be developed. The immunomodulatory drugs such as thalidomide and lenalidomide are very effective in the low-risk groups. Patients with high-risk disease such as 17p deletion do not benefit as much from the use of even bortezomib. Genome sequencing has identified BRAF mutations in 4% of MM patients and this may be the first example of specific targeted therapy. The ultimate goal should be personalized cancer care for myeloma patients.

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## Synthetic cannabinoids in New Zealand; a sequel to benzylpiperazine

*Dr Leo Schep, University of Otago, Dunedin*

Benzylpiperazine (BZP) remained legally available in New Zealand for approximately 8 years. Despite growing evidence of its adverse clinical effects, predominantly associated with its sympathomimetic action, attitudes in some sectors of society changed, leading to a normalising of drug behaviour. Thereafter, BZP was replaced by other classes of drugs, particularly the synthetic cannabinoids. Although these cannabinoids bind to the same receptors as marijuana, presenting patients have differing signs and symptoms to marijuana; additionally, there is evidence of adverse psychological effects, a distinct withdrawal syndrome, and users have the added risk of serotonin syndrome. Despite substantial differences in the pharmacological action of these two classes of drugs, public exposure to and use of these synthetic cannabinoids were similar to those of BZP. Both were sold in an unregulated market and widely promoted as safe alternatives to other drugs, such as methamphetamine, despite a lack of knowledge of their respective toxicities. There were also no quality controls in their manufacture and because of their legal status they were both perceived as 'safe' leading to increased use and more frequent incidents of toxicity. Mounting public concern about these products finally led the Government to ban synthetic cannabinoids in 2011, pending new legislation. Based on recommendation from the New Zealand Law Commission, the future legal status of all recreational drugs will depend on their being proved safe by the importers and suppliers. Such legislation will help minimise the harm to users and the wider community; most incidents of future toxicities associated with recreational drugs will most likely be associated with use of those that are illegal.

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## Culture changes vs. restructuring

*Prof Jeffrey Braithwaite, Australian Institute of Health Innovation*

Health systems are constantly undergoing change. Often, however, there are feelings that the types of change being sponsored and the outcomes that change programs realise are less than envisaged by those sponsoring the change. One reason for this sad state of affairs is that people are spending inordinate amounts of time reorganising, restructuring and reshuffling the organisation or services. The metaphor that comes to mind is 'changing the deck chairs on the Titanic.' There is strong suggestion that despite its popularity reorganising as a change strategy is a blunt tool at best and a disaster at worst. An alternative instead of reorganising the boxes on the organisational chart is to undergo transformational culture change. This involves much more deep and profound alterations to the way people behave and inter-relate, and to the collective attitudes, beliefs and values of workplace groups. Many theorists believe that this can lead to much more sustainable and productive change but it is much harder to achieve and requires longer term investments than a restructuring exercise.

Discovery of JAK2 and other mutations that have improved our understanding of myeloproliferative neoplasms  
Dr Peter Ganly, Canterbury Health Laboratories, Christchurch

In addition to chronic myeloid leukaemia, a number of other conditions are recognised which are classified under the heading of myeloproliferative neoplasms. Polycythaemia vera (PV) and essential thrombocytosis (ET) are the commonest of these and are closely related clinically. It was a great advance to find that both of these nearly always (PV) or often (ET) share a common mutation in JAK2, a step in a signal transduction pathway controlling haematopoietic cell proliferation. Primary myelofibrosis has some resemblances to PV and ET, may arise from each of these diseases, and also often has acquired this mutation. Other mutations in signal transduction elements or transcription factors have been found in a minority of these diseases, either with or as an alternative to JAK2 mutations. Study of mutations can provide information on how these disorders develop and how normal cellular control mechanisms are subverted. They may also simplify diagnosis and classification of the myeloproliferative neoplasms and they suggest 'druggable' targets for therapy.

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## Thyroid tumor markers - new challenges and solutions

*Prof Stefan Grebe, Mayo Clinic, USA*

**Background and purpose:** In the USA, thyroid cancer yearly incidence has grown from 7800 cases in 1974 to 56400 for 2012, while 10 year mortality rates have declined from ~15% to <4%. Thyroid cancer will be the 3rd most common diagnosis in living cancer patients by 2020, just behind prostate and breast. Since recurrence rates exceed death rates 2-5 fold, these patients continue to require follow-up, a key part of which is serum thyroglobulin (Tg) measurement. However, the reliability of Tg immunoassay (IA) measurements is compromised in the ~25% and ~10% of patients with anti-Tg autoantibodies (TgAB) and large remnants, respectively. These problems will increase, as less radical treatment is becoming more common due to declining mortality rates. These issues can be addressed through molecular tumor markers and Tg measurement by mass spectrometry (MS) instead of IA. **Methods:** Measurement of circulating Tg and TSRH mRNA has been one molecular marker approach, while the other has been testing for circulating thyroid cancer-associated nucleic acid alterations. We have studied circulating BRAFV600E extensively, and more recently miRNA. Several Tg MS assays have been developed. **Results:** Tg and TSRH mRNA measurement is of marginal value. Detection of circulating BRAFV600E correlates with disease status, and might be useful in some patients. No definitive conclusions can be drawn yet on miRNAs. Tg by MS overcomes the problems of TgAB, but its analytical sensitivity needs to improve. MS methods that can distinguish iodinated Tg from non-iodinated Tg may offer further improvements in the future. **Conclusions:** Alternative methods to IA Tg are being developed and Tg by MS seems to be the current front runner for a clinically useful method.

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## Free radicals and biomarkers of oxidative stress in disease

*Prof Christine Winterbourne, University of Otago, Christchurch*

Free radicals and other reactive oxidants are produced in all our cells as a consequence of breathing oxygen. They are also generated by cells of the innate immune system for fighting infections. They are potentially damaging but kept in check by antioxidant defences. However, there is increased production in a number of inflammatory and degenerative diseases, including cancer, cardiovascular disease, inflammatory lung diseases and neurodegeneration. Key questions are how important is oxidative injury in the disease pathology and can antioxidant intervention be beneficial. Free radicals are short lived and cannot be measured in the body directly. We are therefore reliant on biomarkers or

footprints of their reactions with biological molecules to detect them. Using this approach, associations between elevated biomarker levels and disease severity have been seen for a number of conditions.

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## Why should clinicians care about MRSA and VRE?

**Anja Werno, Canterbury Health Laboratories, Christchurch**

Methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *enterococcus* (VRE) are well recognised human pathogens as well as colonisers of human skin, mucous membranes and other sites. The introduction of antibiotics has been one of the major advances in medicine in the last century, yet, it has come at a price. Antimicrobial pressure has caused the microorganisms to adapt and develop resistance mechanisms. Looking back over the last few decades it is astounding and scary to observe the speed and success of these adaptation processes. The challenge in the health care system is to have a well-functioning screening strategy and monitor health care workers for the presence of certain colonising organisms without spoiling the exercise by creating a witch-hunt. The balance will lie in the process that encourages screening for the benefit of the patient and is in the interest of the health care dollar without penalising health care professionals in form of fiscal disadvantages or by ways of stigmatisation.

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## Role of the laboratory in the discovery of antibiotics

**John Aitken, Otakaro Pathways Ltd, Christchurch**

The discovery of penicillin by Sir Alexander Fleming in 1929 opened the doors for effective treatment of systemic infections using antibiotics. The precise circumstances surrounding the original observations are the stuff of myths. There is the legend, but the truth is somewhat more instructive. In 1944, streptomycin was discovered by a group under the direction of Dr Selman Waksman. Like Fleming before him, Waksman was awarded the Nobel Prize. Like Fleming, there are two versions, the myth and the truth. In 2012, we are entering the post-antibiotic era. New discoveries are rare, and the inclination to further develop potential candidates even rarer. In Canterbury, a small group of scientists has carried out bio-prospecting on the New Zealand bush to find novel antibacterial innovations. The lessons of penicillin and streptomycin are still relevant today.

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## Multiple endocrine neoplasia (MEN1) - a case study

**Sujata Hemmady, LabPlus, Auckland DHB**

**Introduction:** Multiple endocrine neoplasia type 1 (MEN1) is a rare hereditary endocrine cancer syndrome characterized primarily by tumors of the parathyroid glands, endocrine gastroenteropancreatic (GEP) tract and anterior pituitary. Other endocrine and non-endocrine neoplasms including adrenocortical and thyroid tumors, meningiomas, thymic, gastric, and bronchial carcinoids also occur. MEN1 patients usually have a family history as inheritance is autosomal dominant. Entero-pancreatic gastrinomas and thymic and bronchial carcinoids are the leading cause of morbidity and mortality. **Methods:** A young Caucasian female presented with recurrent asymptomatic hyperparathyroidism and non-insulin-dependent diabetes with occasional spontaneous hypoglycaemia. Family history revealed that the patient's great grandfather had died at age 45 of severe diarrhoea and had a pancreatic tumour. Her grandfather had type 2 diabetes and hepatic metastases and father had been recently diagnosed with an insulinoma. **Results:** The patient had MEN 1- like symptoms with abnormally high levels of serum prolactin, calcium, parathyroid hormone and moderately raised levels of secretin. She underwent an urgent parathyroidectomy and an MRI confirmed large pancreatic lesions

and islet cell tumours. Polymerase chain reaction (PCR) and Southern blot analysis indicated a positive test for MEN1 mutation with a deletion in menin gene at exon 2, codon 131fs25 aaX. A similar mutation was found when her father and grandfather were tested, while her brother tested negative. **Conclusions:** MEN1 has an estimated prevalence of 0.02-0.2 cases per 1000 population. The gene responsible for MEN 1 is located on chromosome 11q13. There are more than 400 mutations of this gene with no apparent genotype-phenotype correlations.

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## Can immunology workload monitoring aid management of Vitamin B12 assay performance?

**Max Reed, Aotea Pathology Ltd, Wellington**

**Purpose:** To evaluate the potential usefulness of intrinsic factor antibody requests in Immunology as an external QC of Vitamin B12 results from Biochemistry. **Methods:** Total B12 request numbers were compared over a 15 month period, against B12 results <150 pmol/L, B12 monthly patient means, monthly mean patient mean cell volumes (MCV), request numbers for intrinsic factor antibodies and positivity rates for intrinsic factor antibodies over the same timeframe. **Results:** Over the 15 month period studied, consistently 6% of B12 results per month were < 150pmol/L, and the average number of IF requests < 35 per month. When the incidence of B12 < 150 rises above 6% the number of intrinsic factor antibodies also rise. **Conclusions:** Although we do not have controls specifically targeting the low level of the Vitamin B12 reference interval, the perceived increase in intrinsic factor antibodies workload is mirrored by both the increase in Vitamin B12's <150 pmol/L and the increase in positive intrinsic factor antibodies. Therefore, workload monitoring of intrinsic factor antibodies does not aid management of Vitamin B12 assay performance.

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## Culture and identification of *Clostridium difficile* from EIA positive samples

**Mary Stevens, Canterbury Health Laboratories, Christchurch**

**Purpose:** To culture and identify *C. difficile* from EIA positive and equivocal faecal samples and perform breakpoint susceptibility testing on these isolates. **Methods:** After alcohol-shock treatment samples were cultured onto *C. difficile* agar and incubated anaerobically at 36°C for 48 hours. Colonies visually resembling *C. difficile* were identified using Bruker MALDI-TOF and/or 16S rRNA sequencing. Antimicrobial susceptibility breakpoints for ciprofloxacin (8 µg/mL and 2 µg/mL), vancomycin (32 µg/mL and 8 µg/mL), metronidazole (32 µg/mL and 8 µg/mL), amoxicillin/clavulanic acid (16/8 µg/mL and 4/2 µg/mL) and meropenem (16 µg/mL and 4 µg/mL) were determined by agar dilution. **Results:** Eighty five isolates were identified as *C. difficile* using MALDI-TOF. Isolates not identified by MALDI-TOF were subsequently identified using 16S rRNA sequencing. Antimicrobial susceptibility breakpoints were determined for 91 *C. difficile* isolates. All were inhibited by the lowest concentration of vancomycin, metronidazole, amoxicillin/clavulanic acid and meropenem. Eighty nine isolates were resistant to ciprofloxacin. **Conclusions:** Alcohol-shock treatment, combined with a selective agar, was an effective method of culture for *C. difficile*. MALDI-TOF was a reliable, rapid and inexpensive tool in the identification of this organism. All of the Canterbury isolates showed susceptibility to vancomycin, metronidazole, amoxicillin/clavulanic acid and meropenem, while most were resistant to ciprofloxacin.



## A comparison of chromogenic media used in the detection of *Streptococcus agalactiae*

*Clare Tibbs, Canterbury Health Laboratories, Christchurch*

**Purpose:** *S. agalactiae* (Group B Strep (GBS)) remains a leading cause of invasive disease in neonates. Screening of pregnant women for GBS carriage is recommended to prevent perinatal transmission. The aim of this study was to evaluate the performance of four chromogenic media for the detection of GBS in high vaginal swabs from pregnant women. The media was compared with blood agar, and was evaluated in terms of sensitivity, specificity, ease of use and cost. **Methods:** One hundred vaginal swabs from pregnant women were analysed. The swabs were pre-enriched in LIM broth, incubated overnight and subcultured onto each of the following media: blood agar, FRL CHROMagar™ StrepB, bioMérieux ChromID, Oxoid Granada, and Bio-Rad StrepB Select. Agar plates were then incubated and read, following conditions specified by each manufacturer. Suspicious colonies were confirmed with a Remel Lancefield streptococcus latex grouping kit. **Results:** Twenty five patients were found to have GBS colonisation. Blood agar had a sensitivity of 92%, specificity of 95%, a positive predictive value (PPV) of 85% and a negative predictive value (NPV) of 96%; CHROMagar™ (88%/83%/59%/95%); bioMérieux (96%/92%/80%/99%); Oxoid (72%/96%/86%/91%); and Bio-Rad (100%/91%/78%/100%). **Conclusions:** The bioMérieux ChromID agar had the best overall performance for the detection of GBS in this study. In addition it was easy to interpret and cost effective.

## Direct identification of uropathogens from urine using MALDI-TOF

*Julie Creighton, Canterbury Health Laboratories, Christchurch*

**Purpose:** The matrix-assisted laser desorption/ionisation time-of-flight mass spectrometry (MALDI-TOF MS) has dramatically changed the identification of micro-organisms in the clinical microbiology laboratory. The potential of this technology to rapidly identify uropathogens, direct from urine samples, using minimum urine and a straightforward method, was explored. **Methods:** One hundred fresh urine samples were selected, based on raised white cell count and/or the presence of significant quantities of bacteria. 1.3ml of urine was mixed with 200µl of saponin, spun at 13,000rpm for 5 minutes; the pellet was washed and spun twice, with 1µl of pellet spotted onto the target plate, in parallel. A simple 70% formic acid extraction was performed before the overlay of matrix solution and analysis using the Bruker Maldi-TOF. **Results:** Maldi-TOF analysis was compared to conventional growth and identification methods (BD-Phoenix). Most of the samples tested grew significant organism counts of a uropathogen(s). The Maldi-TOF direct method agreed with conventional testing in approximately 50% of positive cultures, however there were many samples that gave no identification. There were no false positive results by Maldi-TOF. **Conclusions:** Mass spectrometry show potential for rapid and accurate identification of uropathogens direct from urine samples. Results were less successful than anticipated but this could be due to the small initial volume if urine processed. Further method refinement is warranted.

## RCPA haematology QAP: recent initiatives in virtual microscopy

*Susan Neville, RCPA Quality Assurance Programs Pty Limited, Australia*

**Purpose:** The introduction of virtual microscopy, as a tool to produce digital images of blood smears, has allowed us to expand into areas of blood film morphology previously not possible, such

as paediatric morphology. **Methods:** In 2011 a pilot survey, which included two paediatric case studies, was sent to approximately 550 laboratories enrolled in the haematology QAP morphology program. The responses were graded using the current scoring system used to assess performance in the blood film morphology program. **Results:** The two blood films were from patients with transient abnormal myelopoiesis and haemolytic disease of the newborn. The scores obtained by participants, for the diagnostic interpretation, varied in both cases, which may have been due to the difficulty of the case study and to some participants' limited experience in paediatric morphology. The overall scores for the descriptive component were pleasing with the majority of participants noting the major features present on the blood film. **Conclusions:** Virtual microscopy has allowed the RCPA haematology QAP to use digital images instead of glass slides, for assessment of paediatric morphology, which has not been possible in the past. After an overall review of the responses received in this pilot study and the positive feedback received from the participants involved, the RCPA Haematology QAP plan to offer a paediatric morphology program in 2013.

## Improving access to health for high risk patients

*Dr Emma Parry, Auckland City Hospital*

Maternal fetal medicine is a subspecialty branch of obstetrics and gynaecology. It is a subspecialty which is moving from infancy into adulthood. Great leaps have been made in diagnosis of fetal anomalies and there are now new fetal therapies available. As with many areas of medicine it is hard for everyone to keep up to date. It was recognised that as a small country New Zealand has only a handful of obstetricians and gynaecologists who are comfortable to manage some of these most complex cases. The individuals are widely spread and often relatively isolated. This has led to problems of retention and recruitment within the subspecialty. The New Zealand Maternal Fetal Medicine Network (NZMFMN) was established to attempt to solve some of these problems. The primary aim of the NZMFMN is to provide excellent up to date care to women and their fetuses wherever they live in New Zealand.

## Differentiation of disease - yesterday: today and tomorrow

*Assoc Prof Surender Juneja, Diagnostic Haematology*

Our ability to distinguish various diseases has evolved from relying entirely on clinical features in the old days to the expectation and availability of molecular features today. Diseases have been diagnosed and differentiated on the basis of clinical features since times immemorial. In the 1800s microscopy became available allowing visualisation of various pathological features including pathologic diseased tissue or microorganisms. Examination of cellular details along with special staining with cytochemistry became available in the mid 1900s. Immunohistology was playing an increasing role in diagnostic biopsies in the 1950s. Cytogenetics became available from the 1960s onwards since the description of Philadelphia chromosome in CML, which was the first description of a chromosomal abnormality in any malignancy. In 1980s flow cytometry became incorporated into the modalities which could improve the diagnostic accuracy. From the late 1990s onwards molecular genetics have become an important and integral part of how diseases are diagnosed and characterised including providing prognostic information. In addition to better characterisation of diseases at diagnosis, these modalities also allow more accurate assessment of response to treatment including assessment of minimal residual disease post-treatment. This allows intervention at an early stage in case of persistent disease or early relapse. These newer modalities provide valuable information with regard to the diagnosis, biologic heterogeneity and prognostic features of a disease. It is predicted that in the foreseeable future newer

diagnostic technologies like multicolour flow cytometry and molecular diagnostics will play an increasingly important role in characterisation of diseases and provide important prognostic information, so that patients can be managed more effectively. This should allow individualised risk-adapted treatment at diagnosis, on follow up and when the disease relapses.

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## **Obesity. Hormonal and biochemical aspects of obesity**

*Dr Jeremy Krebs, Wellington Hospital*

Overweight and obesity are rapidly becoming the most prevalent and most important preventable cause of disease in the world. Obesity is associated with a wide range of co-morbidities including most importantly type 2 diabetes, dyslipidaemia and cardiovascular disease but also osteoarthritis, gallbladder disease, obstructive sleep apnoea, certain cancers and even infertility. In fundamental terms, obesity is the consequence of a long-term imbalance between energy intake and energy expenditure, with excess energy being stored primarily as fat. The cause of obesity is a complex inter-relationship between genetic factors, behavioural and other lifestyle factors, and the environment. With the exception of a handful of extremely rare single gene defect causes of obesity, the genetic influences are polygenic and currently ill defined. The current epidemic of obesity must be largely attributed to behavioural and environmental factors, specifically reduced physical activity and inappropriately high energy intake.

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## **Surgical management of obesity: what do we know and what can we learn?**

*Dr Richard Stubbs, University of Otago, Wellington*

Surgery is emerging as an important player in the management of severely obese individuals not just because of what it can do for them personally, and not simply because of the economic benefits that can follow obesity or bariatric surgery, but also because of what we can learn about obesity and metabolic problems that we never knew. Currently bariatric surgery is the only reliable tool for achieving major sustainable weight loss in the severely obese. A number of different operations are being regularly performed around NZ and the world and in increasing numbers. They work in different ways, they bring different problems, they achieve different things, and it is important that these differences are appreciated by those who may either consider surgery, or be in a position to advise on the place of surgery in management. Gastric bypass surgery or Roux-en-Y gastric bypass, as it is often called, has long been regarded as the gold standard of the procedures in terms of weight loss that can be achieved and the permanence of that weight loss. This has not changed. The more recent contenders of laparoscopic adjustable banding (Lap Band) and laparoscopic sleeve gastrectomy have emerged and gained favour because they are more easily performed for both the patient and the surgeon. Yet, neither is as reliable. As gastric banding is losing ground nationally and internationally, sleeve gastrectomy is gaining ground, but in time will probably also decline in popularity. Through all this, the reliability of gastric bypass becomes more apparent, at least to the surgeons who have been involved for longest. Severe obesity is not simply an acquired behavioural state, it is a disease. If it is to be controlled, the control must be life-long. Therein lays the problem and the challenge. Over the last 10 years we and others have come to recognize and document the innumerable metabolic benefits that follow bariatric surgery, weight loss and gastric bypass in particular. Type 2 diabetes is resolved in 75-85% of severely obese individuals undergoing gastric bypass. The same is commonly seen for hypertension and dyslipidaemia. But most interestingly the benefit is seen within a week of surgery, and has little to do with weight loss or eating less. The figures are not quite so high

for banding and sleeve gastrectomy, for after these operations the benefit is more linked to weight loss and eating less than to the procedure itself. This knowledge carries important messages. There is real prospect that what we are learning from the field of bariatric surgery will change the management and course of metabolic disease in the future.

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## **Obesity : personal or societal responsibility**

*Dr Robyn Toomath, Auckland City Hospital*

Epidemiology has provided ample evidence for the genetic basis of obesity and in recent years specific genotypes have been identified in cases of monogenic obesity. In addition genotypes that are associated with a predictable risk of obesity are being defined in individuals with mild to moderate obesity. In most examples to date the link between the genotype and the phenotype is appetite which explains much of the variability in response to the obesogenic environment. By contrast, there is very little evidence for control of body size by personal endeavour and to explain the continued framing of obesity as a matter of free will we must look to commercial and political influences. The importance of correctly identifying drivers of obesity is key to predicting successful therapies. The pharmaceutical industry has failed to deliver despite early optimism and surgery is expensive, risky and inappropriate for a condition that now affects most New Zealand adults.

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## **Anatomical pathology - the human face of autopsy**

*Prof Robin Fraser, University of Otago, Christchurch*

Birth and death are two major events in life. Both involve pain, the first transient and forgotten, so they say, by the hormone memory-buffer, Pitocin, and alleviated by the joy of a new family member. Death also involves pain, palliated in the dying by opiates, analgesics, hypnosis and religion. Superimposed pathology such as pneumonia, with disturbed physiology and biochemistry, may compound or decrease this distress. But family loss and grief is alleviated by sharing it with others. If death has come in the correct family sequence - grandparents before parents before children - then the mortal's life celebrations will lessen the grief with remembrance, pride, laughter and love. What is the right age to die? When has the life been a 'good innings', do we have a choice? This is debatable. But if anyone could bring palliation at a funeral, in my opinion the pathologist should try. Coronial post-mortems in the majority of cases are performed when sudden deaths are from accidents or 'natural causes', when there is no diagnosis from the patients' own doctors. Certainly the full details of death may take time, with important input from road engineers, police, toxicologists and forensic scientists, and correlated by the coroner. But for the majority of 'mortals' a funeral occurs within several days of autopsy. In these cases the pathologist has a good idea as to the mode of death and I believe the family and friends want to know. The funeral is the time for celebration, story-telling, grieving, sharing and compassion. I believe the most important thing I have been party to in the last decade or so is seeing the pathologists and inquest staff giving comfort and explanation, usually over the phone and within an hour or so of the autopsy, to encourage the next of kin to understand the cause of death, the amount the patient suffered and the encouragement to celebrate. This with our coroners' encouragement. As an ex-country general practitioner I suggest we view the dead and their family as our patients. Dr Pullar I believe would approve. My autopsies would have so much less meaning if I did not have the backing of our mortuary technologists, laboratory, histopathology scientists/technologists, inquest staff, coroners and the ESR laboratories. I let the next of kin know that 'all we can tell' will eventually be revealed. But this is what 'I believe right now', immediately after the autopsy. I have never been refused when I ask the immediate family, 'Let me explain to you, as I would to medical students, what

caused your Dad or Mum's death'. It is much harder if the word is 'child' and the cause is 'probably suicide'. But I am convinced our patients have the right to know before the funeral of their loved one.

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## ISH technology

**Liangtao Zhang, LabPlus, Auckland DHB**

In situ hybridisation (ISH) is a molecular diagnostic technique, which utilises the labelled complementary DNA or RNA probe to localise and detect specific nucleic acid sequences. These sequences are located within the cells of the morphologically preserved tissue sections, cytological preparations and whole mounts, or on chromosomes. In recent years, development of the different nonradioactive labelling and detection systems has made ISH available to a wide variety of diagnostic applications in cytology, histology and genetics. As a simple and powerful tool, ISH is being used increasingly in histology and cytology laboratories. It aids pathologists and cytologists to characterise genotype-phenotype correlations, confirm or exclude a histological/cytological diagnosis when the cell or tissue morphology is uncharacteristic, or the conventional staining profile is uninformative. It can also offer predictive and prognostic indications for some cancer patients—recently it has been used in assessment of breast cancers to identify patients who would benefit from trastuzumab (Herceptin) therapy.

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## Electronic ordering of lab tests using eLab

**Dan Mulholland, Dave Currie and Vicki McKnight, Aotea Pathology, Wellington**

In late 2010 Aotea Pathology launched 'eLab' - an electronic ordering system for lab tests. eLab enables medical practitioners to order pathology tests electronically, either from the requester's patient management system (PMS), or directly from the web. eLab is a HealthLink adaptation of a cloud-based ordering system originally developed for labs in Denmark. eLab transfers the test order (i.e. patient details, requester, tests etc.) from the requester's PMS into the laboratory LIS. The patient is given a printed lab form with a barcode on it. When the patient presents for testing the barcode is scanned, and the order is imported/processed. eLab was initially launched as a pilot at a few GP surgeries in the Wellington Region. From late 2011 to mid-2012 eLab was rolled out to all Medtech users in the region. Today 50% of Aotea Pathology's lab test requests are received via eLab. The main benefits to the lab are quicker processing of tests, and more accurate electronic data entry i.e. no transcription errors off the lab form. The eLab project required a lot of time and effort to implement, however the project has been successful and we are pleased with the outcome. Aotea Pathology and HealthLink are now working on the next round of enhancements to the eLab system.

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## A brief history of HbA1c: from medical curiosity to preferred diagnostic test

**Dr Michael Crooke, Aotea Pathology, Wellington**

HbA1c was discovered in 1958 but the structure involving linkage of a hexose was not described until 1968. Rabbar had already found an 'abnormal' haemoglobin in 2 of 1200 patients during 1967 and, after noting that both had diabetes, he published his seminal paper in 1968, showing the abnormal haemoglobin in every one of a further 47 cases of diabetes. By 1969 he had confirmed that the abnormal haemoglobin was HbA1c. Trivelli used an improved method to show, in 1971, that HbA1c was elevated about two fold in diabetic subjects but made no connection with severity of hyperglycaemia or complications of diabetes. Variation of HbA1c

with changing levels of glucose was first observed in 1976, in a study of just 5 patients. The authors noted that this would allow the relationship of glycaemic control to the development of sequelae to be assessed and the design of the DCCT trial came from this observation. Glycated haemoglobin was used in clinical laboratories from 1977 but early methods were tedious and unreliable and measured mainly total HbA1, with no clear clinical targets. These did not come until the DCCT trial results in 1993 showed a striking relationship of improved glycaemic control and lower levels of HbA1c to reductions in complications of diabetes. The meticulously controlled methods used in the DCCT led to the formation of the National Glycohemoglobin Standardisation Program in 1996, with the intent of harmonising various methods with the 'reference' method used in the DCCT, thus validating the clinical targets from that trial for global use. The NGSP has been hugely successful in harmonising results and certifying methods, with greatly reduced between method variability, but the method at the core of the NGSP is not a true reference method. The IFCC has developed a complete reference measurement system based on the concepts of metrological traceability but although this is universally accepted as valid there has been considerable discord on how results based on this traceability should be reported in terms of the targets established through DCCT and linked to the NGSP. Historically, glucose has been used to diagnose diabetes but prior to 1979 there was little consistency or clinical validity in the cut points used. In 1979 the cut points were unified but the levels chosen were to some extent arbitrary. The basis for diagnosing diabetes was re-examined in 1997, with a focus on establishing measures of glycaemia that correlated with complications specific to diabetes, especially retinopathy. HbA1c was considered but what emerged was that fasting glucose should be the preferred test, with the 2hr glucose in the OGTT being far from a gold standard. Although the correlation of HbA1c with retinopathy was strong in research studies, the Expert Committee recommended against using it in diagnosis, mainly because of lack of assay standardisation and this view was reiterated in 2003. An updated report from the Expert Committee in 2009 completely reversed these views, comparing the standardisation of HbA1c assays favourably with those for glucose, as well as noting better biological variability for HbA1c and the difficulties with pre-analytical variability for glucose. In 2010 the American Diabetes Association recommended HbA1c as the preferred diagnostic test for most people and the use of HbA1c for diagnosis was endorsed by the WHO in 2011, although with caveats. NZSSD has also taken this view, although with adoption of molar units, a slightly higher cut point and guidance on follow up of borderline results.

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## Johne's disease and Crohn's disease - is there a link?

**John Aitken, Otakaro Pathways Ltd, Christchurch**

Johne's disease is a chronic wasting disease of ruminants. The causative organism is *Mycobacterium avium* ssp paratuberculosis (MAP). MAP has been implicated in Crohn's disease in humans. MAP is widespread in the environment. Different MAP strains exist, and some are species specific. Patients with Crohn's disease are treated with anti-MAP antibiotics, and we are currently providing technical support for an Australian clinic for Crohn's disease diagnosis. Recent work by our group has provided insights into pathogenicity of MAP in human patients. The proposed role of MAP in Crohn's disease has important implications for agriculture in New Zealand.

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## Gene markers in histology

**Dr Richard Massey, Pathology Associates**

It has been known for decades that genes are central to cancer. While our collective knowledge of genetics has steadily increased, the impact of genetic information on cancer diagnosis has been limited. There has been slow steady adoption of genetic

information in diagnosis and therapy. This has been piecemeal and represents an interesting but small component of our workload. Unfortunately, genetic information has largely remained as interesting but irrelevant information in cancer diagnosis and treatment. Recent developments are about to change everything. We are now entering an age of genetic information driven personalised therapy. This is driven by the identification of the tyrosine kinase proliferation pathways, their cancer promoting mutations and, most importantly, the development of specific inhibitors for the mutant proteins. Anatomic pathology is now faced with the challenge of rapidly adapting to the demands now being placed upon us. Anatomic pathologists and scientists are about to become cancer geneticists, whether we like it or not.

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## The emerging roles of medical scientists in humanitarian assistance operations

*Lidia Hristov, Sullivan Nicolaides Pathology*

There is a growing demand for medical scientists (MSs) to provide pathology services on short notice to high risk operating environments. Recent major humanitarian aid (HA) operations including the Rwanda genocide, the Indian Ocean tsunami and the Haiti earthquake have identified that the delivery of pathology services remains to be challenging. High risk areas such as Afghanistan, Colombia, Somalia and the Darfur region of Sudan that pay little attention to humanitarian law and principles pose extra stress to HA providers. Additionally, the operational uncertainty makes planning and forecast difficult and it is likely that each affected population will have a different demographic profile for treatment. The MSs required to support task-specific land-based operations in complex terrain must learn new skills to meet these emerging challenges. The further development of standards, accountability and training requirements should enhance their overall delivery efficiency. The provision of specialised pathology support on HA operations is dependent upon many new factors. Firstly, they must possess communication skills enabling them to work more effectively together, both interculturally and interprofessionally, so that critical decisions can be made more quickly. Secondly, performance of mission-specific tasks must include operational flexibility and multitasking considerations in support of wider interests. Thirdly, survivability and mobility must be improved, so that the MSs can operate with better preparation to sustain prolonged operations.

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## Laboratory medicine and pathology practice at Mayo - how to balance a large internal with a large referral practice

*Prof Stefan Grebe, Mayo Clinic, USA*

The Mayo Clinic is the oldest and largest integrated group practice in the world. During the last 147 years it has grown from the Mayo brothers' two-man Rochester practice to a non-profit, physician-led, practice with three main locations (Rochester, MN, Jacksonville, FL, and Scottsdale, AZ) and ~20 smaller facilities in Minnesota, Iowa and Wisconsin, employing >58,000 people and serving >1.1 million unique patients per year. The Clinic has had a dedicated pathology practice since 1905. By 1914 this had evolved into separate pathology- and laboratory medicine departments. The growth of the two departments paralleled that of the rest of the clinic until the early 1970ies, when the research laboratories were split off, and the two clinical departments merged. This resulted in spare testing capacity and led to the founding of a for-profit arm, Mayo Medical Laboratories (MML), to market esoteric tests and consultation services to outside clients. Since then, MML has grown from ~80 external customers and <2000 per year to >5000 customers and >10 million tests per year, with most testing being performed in Rochester. The challenges of integrating large

volumes of esoteric outside testing with equally large intra-clinic volumes of a more mixed nature centre on:

1. Maintaining first rate, customized and timely service for all internal testing, while coping with substantial growth of the external practice
2. Standardizing and integrating testing and consultations across performing labs
3. Improving productivity, quality and service, while decreasing cost, to stay competitive in the US referral testing market
4. Prioritizing new test development across internal and external demands
5. Pushing education and practice recommendation across multiple Mayo sites and to thousands of external clients

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## Role of the HPV laboratory in public health

*Dr Elizabeth Unger, Centres for Disease Control and Prevention, USA*

Currently available prophylactic HPV vaccines target the two high risk HPV types that account for approximately 70% of cervical cancers world-wide. These vaccines have the potential to substantially reduce the burden of cervical cancer, and many countries have begun implementation. In addition to monitoring the implementation, coverage and safety of HPV vaccination, monitoring the impact of these vaccines is an important public health priority. An impact on cervical cancer cannot be anticipated for at least a decade after full introduction, due to the natural history of HPV oncogenesis. Monitoring early and intermediate endpoints of infection and cervical pre-cancers presents unique challenges, and requires close collaboration with laboratorians.

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## Inherited bleeding disorders in women

*Dr Julia Phillips, Wellington Hospital*

Girls and women inherit autosomal bleeding disorders such as von Willebrand disorder, inherited platelet function defects, FXI deficiency and the rare coagulation defects with the same frequency and severity as their male relatives. However, they have more opportunities to bleed because of menstruation and childbirth. Some female carriers of the genetic mutations responsible for haemophilia A and B, have haemophilia as a consequence of Lyonisation of the X chromosome. Although haemophilia in females is usually mild, women and girls can suffer from moderate or even severe haemophilia. In addition, menstruation and childbirth cause women with inherited bleeding disorders to have more bleeding symptoms than men with the same factor levels. The severe inherited bleeding disorders are rare and the mild inherited bleeding disorders are common. Approximately 0.5% population are affected by a bleeding disorder, most often von Willebrand disorder (vWd) or a platelet function defect. The predominant symptom in women with bleeding disorders is usually menorrhagia (heavy menstrual bleeding). This may interfere with a woman's ability to work or socialise, or cause iron deficiency and can significantly reduce her quality of life. Bleeding into and from ovarian cysts may also occur. Pregnancy and obstetric delivery in women with inherited bleeding disorders can be complicated by antepartum haemorrhage, miscarriage and post-partum haemorrhage, especially late post-partum haemorrhage and death from bleeding. Epidural anaesthesia may be contraindicated due to the risk of permanent paralysis as a result of spinal haemorrhage. The baby may also be affected by the bleeding disorder. Diagnosis of the inherited coagulation disorders requires correlation of bleeding symptoms and family history with the results of laboratory investigations. Most coagulation factor deficiencies and the severe platelet function defects will be detected using APTT, PT, fibrinogen and PFA-100 screening. The full diagnosis of vWd requires functional as well as antigenic

assays. FXIII deficiency and fibrinolytic defects will not be detected by routine screening assays and will require further specific assays for selection. The PFA-100 assay is not sensitive to mild platelet function defects. Platelet aggregation, platelet granule release assays and electron microscopy may be required to detect these conditions. Many options are available for the management of menorrhagia in women with bleeding disorders. These include the use of hormonal therapies such as oestrogen containing combined oral contraceptive pills, COCP, depot progesterone preparations, progesterone-releasing intra-uterine devices, fibrinolytic inhibition with tranexamic acid, DDAVP for some forms of vWd, symptomatic carriers of haemophilia A and some platelet function defects, specific factor replacement, endometrial ablation and hysterectomy. The management of pregnancy and obstetric delivery in women with bleeding disorders requires close collaboration and good communication between the haematologist, the obstetric team and anaesthetist. Prophylactic factor replacement may be required during pregnancy for some conditions. Epidural anaesthesia may need to be avoided. For delivery, DDAVP may be helpful for some forms of vWd and some symptomatic carriers of haemophilia A. Active management 3rd stage will reduce the risk of early post-partum haemorrhage and tranexamic acid can be used to reduce the risk of late post-partum haemorrhage. Where the baby may have a bleeding disorder, difficult forceps and ventouse extraction delivery should be avoided and a cord blood sent for diagnosis of the bleeding disorder.

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## **Pitfalls in the diagnosis of various haematological malignancies**

*Assoc Prof Surender Juneja, Diagnostic Haematology*

Optimal assessment of diagnostic and prognostic information in haematologic malignancies can be difficult if there is a failure to obtain and integrate appropriate clinical, laboratory and imaging investigations with morphology. Morphological diagnosis should start with adequate and technically good quality material. Fresh samples should be taken for investigations like flow cytometry, cytogenetics, molecular tests and for tissue banking. Results of full blood examination including blood film findings and bone marrow examination can be invaluable in diagnosis, sub-classification and staging of haematologic malignancies. Biochemical investigations like lactate dehydrogenase (LDH) can provide clues to the grade of lymphoma. Immunohistochemistry, carried out with proper controls is almost essential in every case at diagnosis and at relapse for diagnostic and prognostic information. Correlation with flow cytometry is critical to the diagnosis and assessment of disease post-treatment. Cytogenetics and molecular diagnostics also play a vital role in select cases. Correct diagnosis requires a thorough knowledge of the current classification (WHO 2008). Close liaison with the clinicians looking after the patient and interaction with a multidisciplinary team are also very important in optimising diagnostic/prognostic investigations. Pitfalls in the diagnosis of haematologic malignancies in adequately resourced setting include inadequate tissue/specimen, suboptimal specimen handling and preparation, lack of appropriate knowledge particularly in complex cases, failure to follow expert reporting guidelines and inadequate clinical interaction before and after the specimens are taken.

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## **The burden of proof for new diagnostic tests**

*Prof Rita Horvath, Prince of Wales Hospital*

Due to societal, economic and demand pressures on healthcare, there is an increasing realization that the costs associated with the introduction of new technologies can only be justified if they deliver proportional benefits to patients. Consequently, the ability of novel medical tests to improve patient outcomes is becoming more central in decisions about their market entry, clinical use, reimbursement and coverage. These considerations

and new regulatory requirements affect the way novel medical tests are developed and evaluated. In the absence of international agreement and the paucity of methodological standards and tools for the assessment of tests used for a variety of purposes and roles, manufacturers, laboratory professionals, researchers and regulators are equally confused on what studies to do or accept as evidence for the clinical performance and effectiveness of medical tests. The evaluation of medical tests is more difficult and differs in many ways from the evaluation of therapeutics. One of the most important differences is that medical testing rarely improves health outcomes directly; biomarkers used for several different purposes (diagnosis, monitoring, prognosis, etc.) are often part of a more complex intervention; and most clinical outcomes follow from subsequent clinical management decisions guided by the test results. The five essential components of medical test evaluation are: analytical performance, clinical performance, clinical effectiveness, cost-effectiveness and impact of testing. We have defined and tightly integrated these components into a unifying evidence-based framework. This dynamic framework clarifies the link and sequence between the various stages of test evaluation and describes the journey of a new biomarker in becoming a medically useful test in the research translation continuum. No new test should be subjected to tedious trials and released to the market if it is unlikely that the test will result in improved clinical actions and measurable outcomes. Therefore in our framework the clinical purpose and role of testing and the intended application of the biomarker in a well-defined clinical pathway drive all stages of the test evaluation cycle and define the most appropriate study designs that have the potential to provide the highest level of evidence as proofs. The key concepts and principles are illustrated by using HbA1c and high sensitivity Troponin tests as examples. The framework presented aims to support and improve the understanding of key stakeholders of the necessary steps to be taken when evaluating a test and promotes that larger and more costly studies are only initiated if there is prior evidence of sufficiently high quality of the test's value; a principle that also provides the ethical justification for inviting patients to participate in large clinical trials, without adding further unnecessary burden to health care costs and society.

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## **The burden of proof for genetic tests**

*Dr John Whitfield, Queensland Institute of Medical Research*

Genetic tests are becoming applicable to a wide range of clinical and public health questions: can we predict whether or when a person will develop disease, can we predict how they will respond to treatment, can we detect and classify disease? Most importantly, even if we can make accurate predictions will they change the course of the disease for the patient and/or make healthcare more efficient? Evaluation of genetic testing should follow the established processes of defining the question, assembling and evaluating existing evidence, deciding what further studies may be needed, and coming to evidence-based conclusions. It should lead to the production of evidence-based guidelines, monitoring of their application, and refinement as new facts become apparent. The effectiveness of testing is disease-, test- and context-specific. Out of the many genetic tests which might be considered, prediction of the common and biologically overlapping conditions of cardiovascular disease (CVD) and type 2 diabetes (T2D) will be taken as examples. Like other predictive tests, there are two questions; can valid predictions be made and can those predictions be used to influence outcomes? If the answer to the first is no, then we can avoid the difficult and expensive trials which would be needed to answer the second. Both CVD and T2D are influenced by genetic differences between people and recent studies have shown significant associations between single-nucleotide polymorphisms (SNPs) and either the diseases or biomarkers of disease risk. Many of the publications reporting results of genome-wide association studies have considered the predictive value of

genotypic risk scores. These have quasi-continuous distributions and can be assessed in the same way as existing predictive tests or test combinations. There are substantial differences in risk between people at the top and bottom ends of the distributions and some high-risk people can be identified, but at present genetic risk assessment does not add value to conventional risk-factor measurements. Risk assessment may improve with more detailed genotyping, and we should ensure that accurate, current and evidence-based information is available to medical professionals, to the public and to policy-makers.

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## The importance of strep throats in communities at high risk of rheumatic fever

**Dr Margot McLean, Regional Public Health**

Too many New Zealand children live in cold, damp and overcrowded homes. This sets them on a pathway which can lead from repeated skin and throat infections caused by Group A Streptococcus, to acute and recurrent episodes of rheumatic fever, to heart valve disease and premature death. New Zealand's rates of rheumatic fever have been described by Professor Norman Sharpe, chair of the Heart Foundation as a 'shameful situation, embarrassing and intolerable in the sense of our designation as a developed country'. Māori and Pacific children have rates many times higher than other groups. The problem has finally gained wide public and political attention and the Prime Minister has recently set a goal that rheumatic fever rates will decrease by two-thirds by 2017.

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## The global burden of childhood pneumonia and prospects for prevention

**Prof David Murdoch, University of Otago, Christchurch**

Pneumonia is the leading 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. Early case-finding and treatment and the introduction of vaccines, such as those against *Haemophilus influenzae* type b and *Streptococcus pneumoniae*, have the potential to markedly reduce pneumonia mortality and morbidity. The Pneumonia Etiology Research for Child Health (PERCH) project is a large case-control study that aims to determine the etiology of and risk factors for severe pneumonia in children from seven countries in Africa and Asia. This study is deploying state of the art diagnostics in each study site in order to provide a contemporary picture of the causes of childhood pneumonia in regions with the greatest burden of disease. The results will inform future research efforts for the prevention of pneumonia, including the development of new vaccines.

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## HrHPV testing: A follow-up study of HrHPV positive cases generated by the Roche Cobas 4800; the cytology and histology correlation

**Elizabeth Pringle, Diagnostic Medlab**

Diagnostic Medlab implemented HrHPV testing in October 2009 using the Roche AmpliCor test. In May 2011 this was replaced with the Roche Cobas 4800 system. The cobas 4800 HPV test is a qualitative in vitro test for the detection of 14 high risk HPV types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68) in a single analysis in patient specimens. The test specifically identifies HPV 16 and 18. These two genotypes put women at the highest risk for the development of cervical cancer. There is good evidence that appropriately applied HrHPV testing can be a useful and cost effective in the management of women with abnormal

cervical smears. HrHPV has a high negative predictive value of approximately 99% and therefore more sensitive for detecting the risk of high grade abnormalities than cytology. The workflow for HrHPV testing at DML involves cytology processing of the samples collected in the ThinPrep liquid-based cytology medium followed by HrHPV testing, therefore has a practical advantage of cytology and HrHPV testing on the one cervical sample. There are three categories for HrHPV testing:

1. The triage of women 30 years and over with ASC-US or LSIL cytology (without an abnormal smear in the last 5 years).
2. The follow-up of women who have been treated for a high grade lesion.
3. Post colposcopy management of women with discordant results.

The DML HrHPV study looked at >6,000 HrHPV results using the Roche Cobas 4800 methodology for a 12 month period and correlated the positive results with the cytology interpretation and follow up histology.

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## Laboratory schedule project

**Sarah Prentice, Northern DHB Support Agency**

In 2011 the 20 DHB General Managers Planning and Funding endorsed a project related to facilitating a clinical review of publicly-funded laboratory tests in order to recommend which laboratory tests should be publicly funded in primary and secondary care, and additions and/or deletions to current schedules used by DHBs. There is a reasonably consistent Schedule underpinning contracts with community laboratories but it has not been reviewed for a number of years and it is recognized that there is a need to review and update the schedule. The focus of work is a clinical review of all tests on the schedule with the objective of recommending to the 20 DHBs which laboratory tests should be publicly-funded in primary and secondary care. This includes making recommendations on additions and/or deletions to current schedules used by DHBs and any restrictions that might be placed on tests in terms of who may refer or circumstances under which they may be ordered. A Laboratory Schedule Review Project has been established and work is being progressed through six sub-groups comprising pathologists and other laboratory experts in the following areas; chemical pathology, haematology, microbiology, immunology, anatomic pathology and genetics.

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## Using HPV testing in clinical practice: current New Zealand guidelines

**Dr Margaret Sage, Medlab South**

Testing for high-risk HPV (HrHPV) viruses was introduced to the New Zealand management guidelines for women with abnormal cervical cytology in October 2009. The NCSP funds HrHPV tests for women in three clinical situations:

1. Women 30 years of age or older who have a low-grade cytology result i.e. ASC-US or LSIL, without a previous abnormal cytology result in the preceding 5 years.
  2. Women with a previously treated high-grade squamous lesion, as part of a 'test of cure' regimen.
  3. Women with discordant cytology and histology results, to assist specialists with clinical management.
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## Promoting safety in an organisation's culture

*Russell Buckley, Airways Corporation NZ*

Planes fly into each other, children drown, patients are wrongly medicated, ships hit reefs and hunters get shot. In the post-mortem analysis that follows such catastrophes, it is often the social, rather than the technical factors that are identified as the culprit. This in turn leads to blame and that to punishment and, sadly as so often happens, other planes flying into each other, more children drowning, more patients being wrongly medicated, different ships hitting different reefs and more people being shot. Professor James Reason argues convincingly, the causation of accidents is far from being singular. According to him, they are multi-factorial with contributions occurring at different levels; from slips and mistakes through to an organisation's culture. The decision made under urgency by a pilot to wrongly comply with the directive of an air traffic controller rather than follow the traffic collision avoidance advisory may be seen on one hand as 'pilot error' but on the other it can be seen as culturally motivated. A young man is mistaken for a deer and shot. At the individual level this can be attributed to a confirmation bias when identifying the target but at a higher level its seed was our communities social attitude towards spotlighting, which despite being illegal in public places still remains prevalent in some parts. Or perhaps more illustrative, is the case of Batman movie buffs being gunned down in a country that as a result feels it needs to sell even more guns. The aviation industry has long recognised the role of culture in human performance. While accidents may happen at the coal face their genesis occurs much further up the in the organisation, often beginning in its culture. Culture impacts virtually every type of interpersonal and inter-organisational interaction. It can profoundly bias technology and cultural considerations are often pivotal in the design of equipment and tools.

## Management of sleep in the 24hr Society

*Alex Bartle, Sleep Well Clinic*

Shift work implies working outside the regular hours of 7am - 6pm. This might include early morning starts, evening work, or working through the night. Whilst evening work is less likely to impact on sleep, early morning starts or working overnight clearly do. We are not designed to be awake at night and sleep in the daytime, and a number of people find it impossible to adapt. However, increasingly our society is demanding that services should be available for 24hrs, seven days per week. Through necessity therefore, we struggle with shift work. Understanding the process of sleep and circadian rhythms helps us to manage this unnatural sleep/wake pattern, in order to keep awake at night and sleep during the day. Shift work is here to stay, and at least 20% of contracts signed today contain a shift work clause, and is likely to become increasingly prevalent. Learning to manage shift work is therefore vitally important.

## PC3 labs; nothing to be scared of?

*Joanne Mitchell, Canterbury Health Laboratories, Christchurch*

The physical containment level 3 facility at Canterbury Health Laboratories (CHL) was opened earlier this year and is the first of its kind associated with a hospital laboratory in New Zealand. It is ten years since the outbreak of SARS coronavirus that prompted its build and outbreaks of highly infectious respiratory viruses continue to trouble the global community. Meanwhile, although the worldwide incidence of Mycobacterium tuberculosis infections is declining slowly, multi-drug resistant forms have been detected in virtually all countries surveyed. The CHL PC3 facility was built to provide a containment environment for the routine handling of samples likely to contain such pathogens. Considerable

engineering expertise has gone into building the containment system but the safe practices and procedures applied by those who work there are equally important in maintaining that containment. PC3 laboratories are still a novelty for hospital laboratories in New Zealand and there is a lack of knowledge about their role and function. Education about biohazard containment is relevant not just to the scientists and technicians who work within PC3 but also to laboratory administrators, managers, researchers, support workers and indeed the wider general public.

## Haemoglobinopathies/thalassaemias

*Dr Huib Buyck, Wellington Hospital*

Inherited disorders of haemoglobin production range from asymptomatic conditions such as thalassaemia trait, to more severe or even life threatening disorders requiring life-long therapy such as sickle cell anaemia and transfusion dependent beta thalassaemia major. Medical laboratory scientists are frequently the first to identify patients with disorders of haemoglobin production when abnormal red cell indices or characteristic morphologic changes are noted on the blood film, but they can sometimes present a diagnostic challenge. Whilst certain haemoglobin abnormalities such as haemoglobin E and single alpha thalassaemia trait are not uncommon in the NZ M ori and Pacific Island populations, other haemoglobinopathies including HbS and beta thalassaemia are becoming more common in NZ. It is important that these abnormalities are appropriately recognised and diagnosed. Knowledge of the presence of a hemoglobinopathy trait allows patients the opportunity of counselling about the risks to future offspring of a more serious disorders. Failure to identify couples at risk of serious red cell disorders, such as haemoglobin Barts, can result in devastating situations such as intrauterine death and present substantial risks to the health of the mother. A good working knowledge of disorders of haemoglobin is essential for all medical laboratory scientists working in haematology.

## Existing and new BNP peptides

*Dr Chris Pemberton, University of Otago Christchurch*

B-type natriuretic peptide (BNP) has been at the forefront of worldwide heart failure diagnosis for over a decade, it is the only peptide biomarker in the last 10 years to receive the European and American Heart Association guidelines 'A' category for evidence of utility and it was a New Zealand idea. BNP is secreted from the heart in normal health and circulates to lower blood pressure and induce natriuresis/diuresis. In acute decompensated heart failure (ADHF), blood levels of BNP rise markedly (up to a 100-fold), primarily from the increase in wall stretch/stress that the ventricle incurs. The specificity and sensitivity of BNP to diagnose ADHF is good (~90% and 75% respectively) and its positive predictive value is high at ~90%. Currently, two forms of BNP are measured: these are 'mature' BNP and the amino terminal form of the propeptide termed proBNP. Both have excellent utility in diagnosing heart failure. We have recently shown that a third form of BNP is present in the circulation, called BNP signal peptide. The peptide does not appear to have the same utility in the diagnosis of ADHF but instead, may have a diagnostic role to play in the diagnosis of acute coronary syndromes (ACS).

## High resolution analysis of the human genome: running fast only to stand still

*Don Love, LabPlus, Auckland DHB*

The human genome comprises 6Gb of DNA and 30,000-odd genes (give or take). Given this as a starting point, the task of a

molecular lab in a hospital setting is to confirm a clinical diagnosis in as short a time as possible and at minimal cost by identifying the (mutant) needle in the human genome haystack. Much of this testing is largely confined to either targeted mutation analysis or conventional Sanger-type DNA sequencing; however, the current trend is to do much more at the same price, or (given the current financial climate) at a significantly reduced price. There comes a time, therefore, when a lab has to adopt new technology that must be evaluated at next-to-no cost, with no impact on current service delivery and no extra personnel.

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## How do you like your gonorrhoea - dead or alive?

**Dr Collette Bromhead, Aotea Pathology, Wellington**

Nucleic acid amplification tests (NAATs) have been recommended for the routine diagnosis of *Chlamydia trachomatis* (CT) in New Zealand since 2008<sup>1</sup>. However, problems with the specificity of particular NAATs for *Neisseria gonorrhoeae* (NG) has seen culture persist as the method of choice in NZ's low prevalence population (67 per 100 000)<sup>2</sup>. Recently there has been a trend to move to NAAT based testing for NG using new generation automated PCR systems which include dual-target detection to reduce the potential for false results caused by sequence variation. There is no specific guideline on NG testing in New Zealand, therefore laboratories are working in isolation with regard to test choice, validation, confirmatory assays and concurrent use of culture. At the same time there is increasing concern over resistance to empiric antibiotic therapy. However NAAT's cannot provide antibiotic susceptibility information as organisms are lysed during testing. The changes we make in testing will improve rates of disease reporting but may affect our ability to monitor changes in antibiotic susceptibilities.

<sup>1</sup> Recommendations for Chlamydia testing in New Zealand. NZ Ministry of Health, 2008.

<sup>2</sup> The Environmental Institute of Science and Research Ltd. 2011. Sexually Transmitted Infections in New Zealand: Annual Surveillance Report 2011. Porirua, New Zealand.

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## The past history and future directions of the PPTC

**Dr Ron Mackenzie, Pacific Paramedical Training Centre, Wellington**

Established in 1980, the Pacific Paramedical Training Centre (PPTC) is a not-for-profit organization located at Wellington Hospital, New Zealand. Its legal status is that of a Registered Incorporated Society and is registered with the Charities Commission. In 1990 the PPTC attained the status of Collaborating Centre of the World Health Organization, Western Pacific Region and since then this status has been maintained and further developed. The services offered by the Centre include teaching in the medical laboratory sciences, an external quality assurance programme, and training in, and implementation of laboratory quality management systems and consultancy. A number of both government and non-government agencies including the New Zealand Ministry of Foreign Affairs and Trade, New Zealand Institute of Medical Laboratory Science, Norman Kirk Trust and the New Zealand Red Cross financially support these programmes.

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## The PPTC external quality assurance programme

**Christine Story, Pacific Paramedical Training Centre, Wellington**

A major activity of the Pacific Paramedical Training Centre [PPTC] is the provision of a Regional External Quality Assessment [REQA] Programme to medical laboratories in the Pacific region and South East Asia. This programme, which was originally commenced in

1985 as an evaluation process of students attending residential courses, was updated in 1990 when the Centre was conferred Collaborating Centre status by WHO. There are currently 41 laboratories participating in all or part of the programme and of these 26 are national laboratories in Pacific Island countries. The PPTC is able to provide this programme free of charge through financial support provided by NZ Aid Programme, WHO and the NZ Institute of Medical Laboratory Science.

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## The PPTC training programme

**Philip Wakem and Navin Karan, Pacific Paramedical Training Centre, Wellington**

One of the basic objectives of the PPTC is to provide training in appropriate medical laboratory technology and blood transfusion technology for the technicians working in Pacific islands hospitals. The teaching programmes offered are governed by one principle: they must be appropriate, affordable and sustainable for the health care setting in which they will be used. The emphasis is on appropriate and practical short-term training that will ensure immediate benefit for the trainees in their work setting. Training is provided in one of four ways:

1. By means of short term courses of up to one month at the Centre in Wellington.
2. By in-country courses with PPTC tutors travelling to provide on-site training.
3. By short term training attachments in appropriate New Zealand medical laboratories where training in a specific medical laboratory skill is required
4. Through distance learning programmes.

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## The PPTC LQMS programme

**Russell Cole, Pacific Paramedical Training Centre, Wellington**

The World Health Organisation (WHO) has recently developed an Asia-Pacific strategy for strengthening health laboratory services (2010-2015) which was endorsed by Ministers of Health for the WHO Western Pacific region in October 2009. The strategy takes a health systems strengthening approach to its objective of assisting countries to provide comprehensive laboratory services, aimed at improving health outcomes. This has created some momentum for an increased focus on laboratory services in the Pacific. The PPTC's work on laboratory quality management is increasingly guided by the WHO Asia-Pacific strategy for strengthening health laboratory services 2010-2015, and many countries in the Pacific are preparing for or have begun significant health sector reform. The PPTC is to play a progressive role in the development and implementation of LQMS in selected Pacific island countries and its laboratory quality management coordinator is responsible for the supervision of this programme.

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## Science of the century: the amazing story of immunisation

**Dr Nikki Turner, University of Auckland**

Only clean water and antibiotics have had an impact of childhood death and disease that is equal to that of vaccines (World Health Organization). The impact of vaccination on diseases both internationally and in NZ is highly significant with excellent control for many diseases, and elimination for some. Despite this, many are still missing out on the health benefits of immunisation programmes. There are a range of logistic and communication challenges for immunisation programmes. NZ continues to face



problems with vaccine preventable diseases, particularly currently with measles and pertussis. The science behind vaccinology is strong and there are new highly effective vaccines on the world market, used in other national programmes and available on the private market in NZ e.g. rotavirus, varicella, meningococcal vaccines, adult pertussis and HPV for men. These vaccines are often underutilised both due to cost barriers and provider and consumer lack of awareness. Other underutilised areas are in better vaccine application for occupational health issues. Immunisation programmes have made a dramatic impact on the health of the world, the science is compelling and many more gains are possible.

## Editor's note

Only abstracts that contain useful information and/or data are included. Abstracts that contained sentences such as "data will be presented" or "results will be discussed" have been excluded; and such like sentences in published abstracts have been deleted.

## Complementary medicine

*Dr Shaun Holt, Victoria University, Wellington*

The majority of New Zealanders use natural and complementary therapies. Some of these therapies have been proven to work in good clinical trials, but the majority have not been tested, do not work or can be harmful. How do we know what works and what does not? Without scientific training and the time to assess the research it is impossible for most people, who have to rely on often inaccurate information on the internet, in the media, from friends and family and from health professionals who are not trained in the area. There are some pearls of knowledge but they are hidden in a sea of nonsense.

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# Journal questionnaire

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Below are 10 questions based on articles from the November 2012 Journal issue. Read the articles fully and carefully, most questions require more than one answer.

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

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

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

The site will remain open until Friday 15th March 2013. You must get a minimum of 8 questions right to obtain 5 CPD points.

The CPD Co-ordinator Jillian Broadbent marks the journal questionnaire, not the Editor. Please direct any queries to her at [cpd@nzimls.org.nz](mailto:cpd@nzimls.org.nz).

## November 2012 journal questions

1. What do the mean cell volume (MCV) and mean cell haemoglobin (MCH) represent?
2. What reflects the body's iron status and over what time span?
3. The area under the curve (AUC) for both % LScRBC and % Micro R were both close to 1.0. What did that indicate?
4. Peripheral primitive neuroectodermal tumours (PNET) affect mainly whom and what anatomical sites does it commonly involve?
5. What are PNETs normally composed of?
6. Why does the cytologic diagnosis of PNET pose a diagnostic challenge?
7. What rules out the diagnosis of lymphoma in the case of PNET?
8. What could possibly be the explanation for the observed differences in the detection rate of bacteria between the Gram stain/culture method and the PCR assay?
9. What may these reasons be attributable to and why?
10. Which organisation registers medical laboratory scientists/technicians and issues the Annual Practising Certificate; and who enrolls for and administers the CPD Programme.

## Questions and answers for the August 2012 journal questionnaire

1. How are reticulocytes classified in standard microscopic examination of blood films?  
**As a red cell containing at least two blue dots or strands of filamentous reticulum.**
2. What are the main causes of RBC destruction during active training?  
**Mechanical damage and oxidative stress on circulating red cells**
3. What are the effects of a high dose of recombinant human erythropoietin?  
**A marked increase of blood viscosity and polycythaemia including thrombocytosis.**
4. What may alter blood gas composition in the interval between

drawing arterial blood and its analysis?

**Continued anaerobic and aerobic metabolism in the blood after collection.**

5. What were the most significant changes when storing blood samples on ice or in the fridge?  
**A rise in lactate levels and PaO<sub>2</sub> and a decrease in Ca<sup>2+</sup> over 2 hr.**
  6. Apart from bacterial endocarditis, what other conditions can *Kingella kingae* cause?  
**Lower-respiratory tract infections, meningitis, ocular infections and stomatitis.**
  7. Which predisposing conditions do adults acquiring *Kingella kingae* infections frequently have?  
**Rheumatoid arthritis, Felty's syndrome, liver cirrhosis, systemic lupus erythematosus, renal disease, sickle cell anaemia, malignancies and HIV.**
  8. Before the Christchurch donor centre could re-open after the earthquake, what procedures had to be followed?  
**All equipment had to be tested and calibrated. The building itself had to be assessed for safety and repairs made to ensure the building was suitable to work in for staff and donors. The staff themselves had to be assessed for suitability to work and emotional support provided.**
  9. Which laboratory parameters increased significantly after administration of chloroquine?  
**Bilirubin, AST, ALT, ALP, urea and creatinine**
  10. What were the two most commonly omitted data on laboratory request forms and what can this lead to?  
**Patient's age and location of patient. Can lead to misdiagnosis and mismanagement of patient.**
-

# LABORATORY INFORMATION MANAGEMENT SYSTEM



DIAGNOSTICS  
Laboratory

Laboratory services play a critical role in healthcare. To meet new demands labs must have a LIMS that allows them to adapt to change, support sophisticated automation and manage complex integration. The pay-off? Pathologists and laboratory staff unburdened by menial tasks - freeing them to support clinicians with expert insights and better service.

Used by more than 300 labs, our LIMS is a comprehensive, user configurable solution adapted to suit New Zealand and Australian requirements.

Formerly iSOFT, we are now a part of CSC's Healthcare group.

To learn more, visit [CSC.COM/LABORATORY](http://CSC.COM/LABORATORY) or email [healthsolutions@csc.com](mailto:healthsolutions@csc.com)



CSC Laboratory graphical results display



# Minutes of the 68th Annual General Meeting held at the Wellington Town Hall on Wednesday 29 August 2012 commencing at 7.30am

## PRESENT:

The President presided over approximately 35 members.

## APOLOGIES:

Apologies were received from Mike Legge, Phil Wakem, John Elliot, Christine Story and Tony Mace  
Accepted

## PROXIES

Laura Macdonald received 17 proxies.  
Carried

## MINUTES OF THE PREVIOUS MEETING

Motion:  
Moved C Pickett, seconded T Taylor  
*That the minutes of the previous Annual General Meeting held on 5 August 2011 be received.*  
Carried

Motion:  
Moved J Bird, seconded J Broadbent  
*That the minutes of the previous Annual General Meeting held on 5 August 2011 be accepted as a true and correct record.*  
Carried

## BUSINESS ARISING FROM PREVIOUS MEETING

NIL

## REMITTS

Motion:  
Moved R Hewett, seconded R Siebers  
*That the following remits be accepted:*

1. "That Policy Decision Number 4 be reaffirmed"

Policy Decision No 4 (1991): That the Code of Ethics as circulated to all members be adopted by the New Zealand Institute of Medical Laboratory Science (Inc.)

2. "That Policy Decision Number 6 be reaffirmed"

Policy Decision No 6 (1979): That the Council must be informed in advance of national workshops, seminars or similar gatherings which are being conducted under the aegis of the NZIMLS.

Carried

## PRESIDENT'S REPORT

Motion:  
Moved K Beechey, seconded K Taylor  
*That the President's Report be received.*  
Carried

## ANNUAL REPORT

Motion:  
Moved K Beechey, seconded K Taylor  
*That the President's Report be received.*  
Carried

## FINANCIAL REPORT

Motion:  
Moved R Hewett, seconded J Bird  
*That the Annual Report be received.*

## ELECTION OF OFFICERS

The following members of Council were elected unopposed:

President:	K Beechey
Vice President:	C Pickett
Secretary/Treasurer:	R Hewett
Region 1 Representative:	L Macdonald
Region 2 Representative:	J Bird
Region 3 Representative:	K Allan
Region 4 Representative:	T Barnett
Region 5 Representative:	T Taylor

The results of the elections for:

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

Motion:  
Moved R Hewett, seconded T Barnett  
*That the election of M Matson to the position of Region 1 Representative be accepted.*  
Carried

Motion:  
Moved R Hewett, seconded A Calcert  
*That the election of officers be approved.*  
Carried

## PRESENTATION OF AWARDS

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

### Qualified Medical Laboratory Technician Awards

Biochemistry:	Sarah Scoullar, Aotea Pathology
Cytogenetics:	Lynne McKenzie, Canterbury Health Laboratories
Histology:	Chrisyl D'Silva, Diagnostic Medlab
Microbiology:	Danielle Hayne, Medlab South Christchurch
Virology:	Sophie Westlake, Canterbury Health Laboratories
Phlebotomy:	Kelly Craig, Pathlab Bay of Plenty

### Qualified Specimen Services Technician Award

Specimen Services: Lisa Bloore, Waikato DHB

## Honoraria

Motion  
Moved R Siebers, seconded T Barnett  
*That no honoraria be paid.*  
Carried

## AUDITOR

Motion:  
Moved R Hewett, seconded T Day  
*That the Auditors Hilson, Fagerlund Keyes be appointed as auditors.*  
Carried

## GENERAL BUSINESS

### PPTC

On behalf of the PPTC, Rob Siebers thanked the NZIMLS for their generous donation for the last year and previous years.

### 2013 Conference

To be held at the Claudelands Event Centre, Hamilton

### 2014 Conference

To be held in Dunedin.

The meeting closed at 7.50am

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# Fellowship of the New Zealand Institute of Medical Laboratory Science

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**Are you a medical laboratory scientist?**

**Do you have a post graduate qualification?**

**If yes to the two above you may be exempt from sitting Part 1 (examination) of Fellowship of the NZIMLS and go straight to Part 2 consisting of a dissertation of 3000 - 5000 words.**

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

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

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

For full Fellowship regulations and the application process visit the NZIMLS web site: [www.nzimls.org.nz](http://www.nzimls.org.nz) or contact the Fellowship Committee Chair: Associate Professor Rob Siebers at [rob.siebers@otago.ac.nz](mailto:rob.siebers@otago.ac.nz)

### Fellowship Committee

Rob Siebers, FNZIMLS  
Ann Thornton, FNZIMLS  
Jillian Broadbent, FNZIMLS

# Pre Analytical Special Interest Group [PAS SIG] seminar 2012



The PAS SIG seminar was held at the Waipuna Hotel & Conference Centre, Auckland on Saturday 6 October 2012. There were 239 registrations from members coming from as far away as Wellington, Bay of Plenty, Gisborne to far north as Whangarei.

The Waipuna Hotel & Conference venue accommodated the participants very well. The conference room was well lit, had good air conditioning and all the appropriate equipment supplied. An IT person was made available to help load the presentations onto the screen with a small screen for the speakers. Morning tea was provided before the seminar began and there was an excellent lunch and afternoon tea. The quality of the food was splendid and provided ample amount for everyone.

There were 12 speakers presenting 11 wide-ranging topics. The morning session topics were "Baby friendly Phlebotomy, Breast is Best, Helping Sick Children Through Play, Calculations – Making the Scary Easy, Pre Analytical Technology and A12DET – Patient Identification initiative". After lunch, "Automation, Changing Laboratory Workflow, Writing SOP's, Work Place Injuries, A case with low plasma alkaline phosphatase, & Oral glucose tolerance test and HbA1c for diabetes and Professionalism". There were two calculation questions for the members to have a go at with the answer provided later in the day. Some of the speakers gave excellent points of view to their chosen topics, others allowed for interaction which proved to be enjoyable for the members at the conference.

The NZIMLS sponsored prize was presented to the best first time speaker – Susan Taylor on her talk "Calculations – Making the Scary Easy". Her talk made an unsure subject a little bit more pleasant for the candidates who are due to sit their exams in November. Theresa Sheehan, Bettina Heaton, Jane Kendall, Avrill Williams, and Ailsa Bunker chaired at various times throughout the day and everyone did a fine job. David Kendall took a photo of the first time presenter winner. Most of the speakers have made their presentations available for the NZIMLS website and we invite the members to download them as they should be up fairly soon. The seminar ended on an interesting note with a few of the 'Burning Questions' which the members wrote out for some of the SIG technical experts to answer.

The PAS SIG Convenor Theresa Sheehan wishes to thank Fran van Til for assisting in the registrations. Sponsors: BD, Auckland and Diagnostic Medlab Ltd, Auckland. We hope the members enjoyed their interesting day and hope to see them at the next seminar which has yet to be decided early next year.

**Theresa Sheehan**  
Convenor

Our Pre Analytical Special Interest Group has taken the position that it is both unnecessary and unsafe to use petroleum jelly (Vaseline) in preparing the site of a micro capillary collect.

There are several reasons:

- The use of petroleum jelly may contaminate the sample and affect the blood test results
- The use of petroleum jelly may cause infection as frequently

the same pot in some organisations has been used for multiple patients

- The use of petroleum jelly may contaminate the patient and may cause the wound not to heal properly or have other unknown issues from having this foreign substance on the skin and in the wound.
- Modern collection equipment and correct techniques do not require any extra 'help' in order to take a quality sample, testified by many organisations never using petroleum jelly as part of their technique ever.
- No text books, CLSI documents or other reputable, current literature support the use of petroleum jelly for micro capillary collects.

Just how the technique of petroleum jelly (Vaseline) being smeared over the micro-collection site (supposedly to improve drop formation) began is not known. The use of petroleum jelly for micro capillary collects is not considered to be best practice in the opinion of the NZIMLS Pre Analytical Special Interest Group.

## South Island Seminar 2012

The 2012 South Island Seminar was held on Saturday 17<sup>th</sup> March at the Chateau on the Park in Christchurch. It was nice to have the SIS again; last year's event had to be cancelled at the last moment due to the earthquakes. We hosted 228 delegates to the conference, and 82 stayed on to a lovely dinner at night.

The two invited speakers gave interesting talks. Dr Debbie Walkden gave an overview of malaria and Dr Cheryl Brunton from the Public Health Office spoke to us about issues resulting from the earthquakes. In her address Dr Brunton described how the public health office monitored gastro and respiratory infections after the earthquakes. We were also shown maps of Christchurch that showed where chlorination of water took place, and where *E.coli* counts were higher. 90,000 people were displaced in various ways as a result of the earthquakes.

The talks that generated the most feedback were passionate presentations by four Canterbury Health Laboratories students who gave us an overview of their research projects. Such enthusiasm from the next generation of scientists, we wish you well in your studies.

There were 16 presentations. Abbott awarded the best overall presentation to Amy Christie from the New Zealand Blood Service who gave a case study on Rh 'D' typing. Bio-Rad gave the prize for best first time presenter to Kym Winter from the CHL. Her talk was about Castleman's Disease. She co-presented with Diane Whitehead. Kym's presentation gave us a different laboratory's perspective on the case study. The NZIMLS gave a runner-up award to Rupy Kaur, CHL, who discussed the effects of smoking on biochemical analytes in the screening for Down Syndrome.

Thanks to all the presenters for giving us an interesting range of topics. Our evening dinner had a St Patricks day theme with some colourful costumes, and a display of Irish dancing from some young performers. Also thanks to our sponsors, the NZ Blood Service, Abbott, Abacus ALS, Bio-Rad, Roche, and the NZIMLS.

**Helen Norton**



# TWENTY FOURTH ANNUAL NICE WEEKEND

17th – 19th May 2012

Bayview Wairakei Resort

## A Transfusion Science Educational Opportunity Organised by the NZIMLS TSSIG

The NICE Weekend (National Immunohaematology Continuing Education) is an educational meeting for all people working in Immunohaematology and/or blood services. As usual it will be held at the Bayview Wairakei Resort Hotel. Registration starts 5pm Friday evening. NICE Weekend finishes approx. 2.00pm Sunday.

As always, all Scientific Delegates are required to participate. They must present either a poster, or an oral presentation lasting 2 to 5 minutes, on **any topic related to Immunohaematology or blood transfusion**. It can be a case study, a discussion, a question, a problem for others' to solve, etc. This will be followed by questions and discussion of the topics raised. This compulsory participation makes everyone nervous (yes, even the "old hands") but it really is one of the reasons why the NICE Weekend is so successful.

There are awards, supplied by trades companies, for the best presentation and poster. We also like to distribute CDs with all the weekends' power point presentations and posters to delegates who attend. If you would like to contribute an award, or sponsor CDs please contact Raewyn Cameron or Grace Agustin

Coming along and join us. Showing your support for NICE Weekend is very much appreciated and it's a great opportunity to meet all sorts of people from all over NZ and some from Australia, in the Transfusion Medicine Industry.

### The registration fee entitles you to:

- two nights (Friday 17th May and Saturday 18th May) accommodation on a twin share basis (single room extra cost)
- breakfast, morning and afternoon teas, and lunches on Saturday and Sunday
- Dinner & disco on Saturday night. (Dress theme is "STORYBOOK" (generally everyone dresses up).
- Friday night NICE games – a fun night with a few silly (not too strenuous games). All for fun and a great way to get to know other attendees in a laugh-a-lot, non-professional environment! AND IT'S FREE!
- FEES TO BE CONFIRMED.

### Accommodation

Accommodation is on a twin-share basis. You will be sharing a room with another attending delegate (same sex of course!). You may specify who you would like to share with if you wish to catch up with old friends. If you do not specify anyone, the organising team will endeavour to room you with another delegate from a similar sized site or within your own region. The idea is to meet other blood bankers and maybe make a new blood bank friend.

If you are not comfortable with sharing you may choose to pay the **extra single room surcharge**.

*(PLEASE NOTE: If this is your choice it will also be your cost. Employers do not usually pay this unless you have come to some*

*arrangement.)*

Accommodation on other nights can be arranged by Raewyn or Grace to get the discounted NICE weekend rate at Bayview Wairakei Resort.

### User Groups

User Groups are usually held on the Friday prior to NICE weekend. You may wish to organise your travel and leave days around these. They will all be held on site at Bayview Wairakei. These are organised through the individual companies and not by NICE team. Please contact them directly for further information. We, the co-conveners do usually know what's going on though and may be able to help you.

Transport costs will be your own responsibility.

Please plan to arrive at the venue on Friday evening, as we have a full programme planned.

### Trade representatives

Company representatives do attend our NICE weekend (they have to pay just like you!) as they have a vested interest in keeping up with the world of transfusion. They are not required to present but are around for the weekend – so make yourself known to them. They are a vital part of NICE weekend's sponsorship (keeping your prices down) and are also a lot of fun!

### NICE first timers

If this is your first NICE Weekend, we will introduce you to everyone, explain anything you don't understand and make you feel at home. We will try to room you with someone who has been before to help you along.

**Please send registrations in by 31st March 2013.**

Registration forms will be available on line at [www.nzimls.org.nz](http://www.nzimls.org.nz) soon.

### Registration Notification

You will be notified and sent any further information when your registration has been received. If you don't hear from us we have not heard from you.

**If you have any questions please contact the co conveners:**

Raewyn Cameron (Rotorua)  
07 349 7908  
027 418 0592  
Raewyn.cameron@lslr.net.nz

Grace Agustin (Riccarton)  
03 3439056  
022 156 0590  
grace.agustin@nzblood.co.nz

# Haematology SIG 2013



Come wine and dine in Art Deco City – the first to see the sun!

**Saturday 2<sup>nd</sup> March**  
**Napier War Memorial**  
**Napier, Hawke's Bay**



Calling for presenters (15-30mins)  
covering anything Haematology!  
Contact [Sarah.Hardingham@hbdhb.govt.nz](mailto:Sarah.Hardingham@hbdhb.govt.nz)

Please register at [www.nzimls.org.nz](http://www.nzimls.org.nz)





# Science on the Wildside



NZIMLS South Island Seminar

30 March 2013

Hokitika



### Greetings from the PPTC

The PPTC wishes to extend to you the very best wishes for the remainder of this year 2012.

### Courses held at the Centre

#### Microbiology update

A microbiology update course was provided by the PPTC in August of this year at its centre in Wellington, and the following students attended: Daisy Phal from Yap [Federated States of Micronesia], Joseph Ghidu, Solomon Islands, Maango Tara and Teiora Koraubara from Kiribati, and Sitanilei Hoko from Tonga.

The microbiology course provided students with an update on developments in microbiological procedures. The theoretical and practical aspects of current methods used in the isolation, identification and antimicrobial susceptibility testing of microorganisms were covered along with discussions on emerging and re-emerging bacterial organisms likely to cause infectious diseases.

Serological and other rapid methods for the identification of bacterial and viral diseases including Hepatitis A, B, and C, HIV and other STIs, were discussed as well as the role of the Microbiology laboratory in the surveillance of nosocomial infections and identification of infections of public health importance.

The PPTC Board of Management would like to thank both Navin Karan and Russell Cole for the excellent contribution made in developing and teaching this course.

It was the greatest pleasure to have, Dr Api Talemaitoga, present to the students their certificates at the final farewell ceremony. Dr Api Talemaitoga, Clinical Director Pacific Health, joined the Ministry of Health in July 2008 and has a wealth of experience both in New Zealand and across the Pacific. His role is to help make health services and the system more responsive to the health needs of Pacific populations living in New Zealand.

#### Dr Api Talemaitoga, presenting to the students



#### Microbiology students and PPTC Staff 2012



#### Cytology attachment [Wellington Hospital and Aotea Pathology]

When there is demand for training courses in specialised topics, the Centre can arrange attachment to a pathology laboratory for up to 3 months within the New Zealand hospital or private laboratory system. In past years, the Centre has arranged successful attachments in medical cytology, histology, microbiology and laboratory management.

The New Zealand laboratory that is selected by the PPTC must be able to provide:

- Skills that are required by the visiting student.
- Continuous teaching and training to visiting students without a disruption to its own workflow.
- A workload that is similar in size to the Pacific Island home laboratory.
- A repertoire of tests that the student would perform in the home laboratory

*Rosemary Tekoaau [Kiribati] receiving her certificate award from Associate Professor Rob Siebers on completion of her attachment to the Cytology Departments of both Wellington Hospital and Aotea Pathology laboratories*



**Rosemary Tekoaau and cytology staff from both Wellington Hospital and Aotea Pathology**



Samoa with the aim of continuing LQMS implementation. And that will conclude 2012.

### **Centre based courses for the remainder of 2012**

#### **Blood bank [5th November – 30th November]**

The course will include units of study covering the theoretical and practical aspects of the following topics; routine blood grouping, blood group antigens, crossmatch techniques, antibody detection, transfusion reactions, haemolytic disease of the newborn, screening blood for infectious agents, blood donor selection, organisation of a blood bank and the appropriate use of blood components in transfusion medicine. Practical sessions will also be provided, focusing on correct technique and fundamental basic procedure. One week of the course will be set aside for an overview of current techniques in the detection of transfusion transmissible infections including, HIV, Syphilis, Hepatitis B and C.

We are sincerely grateful to Susan Evans and the blood bank staff, New Zealand Blood Service, Wellington Hospital, for the excellent tuition and practical training that is provided throughout the duration of this course.

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*The PPTC was saddened to hear of the death of Dr Raj Gupta earlier in October of this year. Dr Gupta, a world acclaimed cytopathologist contributed greatly towards the education and training of our students over many years. We express our deepest sympathy to his family.*

### **Country visits**

In September, Navin our Teaching and Training Co-ordinator and Russell our Laboratory Quality Co-ordinator travelled to Fiji to visit the hospital laboratories in Lautoka, Labasa and Suva. They were also able to visit Suva Private Hospital, Auztech and Nasese private laboratories. This provided an opportunity to assess Laboratory Quality Management as well as the training needs of each of the laboratory's visited.

Navin then travelled to Rarotonga, to assess and evaluate the Hospital laboratory's quality management system and Russell travelled to Rarotonga a week later to provide training in STI diagnostic procedures.

Phil travelled in October to conduct a haematology laboratory quality management evaluation of the newly established Marine Training Centre laboratory in Kiribati and towards the end of October, Navin is scheduled to re-visit Fiji to carry out a STI diagnostic workshop which is to be based at the Suva Private Hospital laboratory.

The Hospital laboratory in Nukualofa, Tonga will be visited early in November by Russell who will continue the implementation of the laboratory's quality management system. Also in November, both Navin and Christine will attend the Fiji Institute of Medical Laboratory Science conference in Nadi, and Filipo Faiga will travel to Vanuatu to carry out training in Biochemistry.

In early December, Russell will visit Kiribati and Navin will visit



# New Zealand Institute of Medical Laboratory Science

## The Barrie Edwards & Rod Kennedy Scholarships

- 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.



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 for each.

Applications 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

## 2013 NZIMLS CALENDAR

*Dates maybe subject to change*

Date	Area	Contact
January 2013	Membership due for renewal by 28 February	<a href="mailto:sharon@nzimls.org.nz">sharon@nzimls.org.nz</a>
January 2013	CPD points to be entered before 31 January	<a href="mailto:cpd@nzimls.org.nz">cpd@nzimls.org.nz</a>
Mid February 2013	Material for the April issue of the Journal must be with the Editor	<a href="mailto:rob.siebers@otago.ac.nz">rob.siebers@otago.ac.nz</a>
February 2013	Council Meeting	<a href="mailto:fran@nzimls.org.nz">fran@nzimls.org.nz</a>
2 March 2013	Haematology SIG Seminar, Napier	Sarah Hardingham <a href="mailto:Sarah.Hardingham@hawkesbaydhb.govt.nz">Sarah.Hardingham@hawkesbaydhb.govt.nz</a>
30 March 2013	South Island Seminar, Hokitika	Eileen Chappell <a href="mailto:eileen.chappell@westcoastdhb.health.nz">eileen.chappell@westcoastdhb.health.nz</a>
30 April 2013	Applications close for Fellowship Examinations	<a href="mailto:fran@nzimls.org.nz">fran@nzimls.org.nz</a>
17-19 May 2013	NICE Weekend, Wairakei Resort	Raewyn Cameron <a href="mailto:Raewyn.Cameron@lsr.net.nz">Raewyn.Cameron@lsr.net.nz</a>
20 May 2013	Applications close for QMLT/QSST Examinations	<a href="mailto:fran@nzimls.org.nz">fran@nzimls.org.nz</a>
May 2013	Microbiology SIG Seminar	
May 2013	Council Meeting	<a href="mailto:fran@nzimls.org.nz">fran@nzimls.org.nz</a>
May 2013	North Island Seminar	
25 June 2013	Nomination forms for election of Officers and Remits to be with the Membership (60 days prior to AGM)	<a href="mailto:fran@nzimls.org.nz">fran@nzimls.org.nz</a>
Mid July 2013	Material for the August issue of the Journal must be with the Editor	<a href="mailto:rob.siebers@otago.ac.nz">rob.siebers@otago.ac.nz</a>
16 July 2013	Nominations close for election of officers (40 days prior to AGM)	<a href="mailto:fran@nzimls.org.nz">fran@nzimls.org.nz</a>
3 August 2013	Ballot papers to be with the membership (21 days prior to AGM)	<a href="mailto:fran@nzimls.org.nz">fran@nzimls.org.nz</a>
11 August 2013	Annual Reports and Balance Sheet to be with the membership (14 days prior to AGM)	<a href="mailto:fran@nzimls.org.nz">fran@nzimls.org.nz</a>
18 August 2013	Ballot papers and proxies to be with the Executive Officer (7 days prior to AGM)	<a href="mailto:fran@nzimls.org.nz">fran@nzimls.org.nz</a>
18&19 August 2013	Council Meeting, Hamilton	<a href="mailto:fran@nzimls.org.nz">fran@nzimls.org.nz</a>
20 - 23 August 2013	Annual Conference, Hamilton	<a href="mailto:fran@nzimls.org.nz">fran@nzimls.org.nz</a>
22 August 2013	Annual General Meeting, Wellington	<a href="mailto:fran@nzimls.org.nz">fran@nzimls.org.nz</a>
Mid September 2013	Material for the November issue of the Journal must be with the Editor	<a href="mailto:rob.siebers@otago.ac.nz">rob.siebers@otago.ac.nz</a>
October 2013	PreAnalytical Seminar	
October 2013	Histology SIG Seminar, Nelson	<a href="mailto:alannah_z@hotmail.com">alannah_z@hotmail.com</a>
6 November 2013	QMLT and QSST Examinations	<a href="mailto:fran@nzimls.org.nz">fran@nzimls.org.nz</a>
12-13 November 2013	Fellowship Examinations	<a href="mailto:fran@nzimls.org.nz">fran@nzimls.org.nz</a>
November 2013	Immunology SIG Seminar	
November 2013	Mortuary SIG Seminar	
November 2013	Council Meeting	<a href="mailto:fran@nzimls.org.nz">fran@nzimls.org.nz</a>

# BRIDGING SCIENCE AND

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# HAMILTON

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## NZIMLS ASM 2013

Claudlands Event Centre, Hamilton

19 - 23 August 2013

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Whether you see your future within a leading medical laboratory team or managing a state-of-the-art laboratory, you'll find AUT offers the best way forward. To find out more, get in touch today.



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The university for the changing world