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### New Zealand Institute of Medical Laboratory Science



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

### In this issue

Von Willebrand disease is a congenital bleeding disorder and the laboratory plays a significant role in the diagnosis. Rikki Penn and colleagues compared the Instrumentation Laboratory HaemosIL von Willebrand Factor activity assay with the Siemens von Willebrand factor ristocetin cofactor assay as a potential replacement for the Siemens assay. They analysed 59 patient samples and showed that the two assays showed good correlation of results below the 80% level while the HaemosIL assay showed better intra-batch precision but inter-batch precision revealed little difference between the two assays. They state that the HaemosIL assay could be useful in the laboratory investigation of von Willebrand disease but whether it is a suitable replacement for the von Willebrand factor ristocetin cofactor assay needs further investigation.

Compared to vitamin D deficiency, vitamin D toxicity is rare. Vichet Khieng and Catherine Stevens report a case where the patient was initially thought to be hypervitaminosis D. The patient had a vitamin D level of >250 nmol/L on more than one occasion whilst appearing to be clinically vitamin D deficient. They found that an interfering factor caused falsely high results in competitive assays and falsely low results in a sandwich assay. Roche Diagnostics in Germany were sent the patient's sample and they were able to show that the interfering factor was to the solid phase, but did not identify the interfering factor. The nature of the interference could affect any of the Elecsys assays such as troponin T, beta HCG or tumour markers where the consequences of erroneous results could be serious. The take home message is that for diagnostic purposes, laboratory results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

In New Zealand there is a decreasing pathology workforce (pathologists and medical laboratory scientists) due primarily to recruitment at one end and an aging workforce at the other. In 2006 the Medical Laboratory Think Tank was established to investigate role extension for medical laboratory scientists in the New Zealand health workforce planning. In this issue Mike Legge discusses the think tank's proposal of a two-stage qualification process for the training of a new occupational group in diagnostic pathology – the clinical scientist. This proposal is currently under consideration by the Royal College of Pathologists of Australasia.

# The clinical scientist in diagnostic pathology

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#### Introduction

Under the auspices of the District Health Boards Executive, New Zealand (DHBNZ) a working party has been considering the concept and practicalities of creating a new occupational group in diagnostic pathology – the clinical scientist. Although this occupational group has existed in the UK for some time it is a new occupational group for New Zealand and Australia. In the UK, Ireland and USA there has been an increasing need to review and redefine professional roles throughout health care, which occurred especially in the UK when there were major reviews of occupational groups in the National Health Service (NHS) in 2000 and 2001.

A significant development of the reviews were the establishment of non-medical practitioners in particular nurse practitioners who carry out many procedures formally undertaken by medical practitioners and the creation of a single group of healthcare scientists to cover the 35 occupational groups employing approximately 40,000 people in the NHS. In addition to the NHS review, the Royal Colleges of Anaesthetics, Medicine, Pathology, Radiology and Surgery conducted their own reviews to investigate the role of non-medical practitioners in extended care areas, which would normally be the domain of a medical practitioner.

The outcome of the various reviews was the development of the National Practitioners Programme which would provide guidance to the NHS on: implementation of a flexible career and skills escalator concept and enable individuals with transferable, competence based skills to progress in a direction which meets workforce, service and individual needs. This has led to the development of practitioner programmes for surgical care, peri-operative specialist, anaesthesia, medical care, emergency care, critical care, endoscopy and assistant practitioners in mental health, maternity services and operating theatres. Associated with these developments has been very close liaison with healthcare professional bodies such as pharmacy, physiotherapy, nursing and medical laboratory scientists (biomedical scientists in the UK). In addition the reports by Lord Carter of Coles (2006, 2008) clearly identified that there should be a clear career structure for all healthcare scientists.

#### The UK clinical scientist

In the UK there are two branches of pathology laboratory orientated sciences in the health service, clinical science and biomedical science. Both titles are protected under law and are required to be registered with the Health Professional Council (HPC). Clinical scientists come under the auspices of the Association of Clinical Scientists and the biomedical scientists under the Institute of Biomedical Scientists, both of which have undergraduate degree entry requirements and post-graduate training. The biomedical scientist is the equivalent of the New Zealand medical laboratory scientist. For the UK clinical scientist minimum entry in to the occupational group is a good first or second-class honours degree in an appropriate subject followed by an extensive four year training scheme in a specific discipline, which leads to certification and state registration. Currently the recognised disciplines of clinical science are: audiology, clinical biochemistry, clinical embryology, clinical genetics, clinical immunology, clinical microbiology, haematology, histocompatobility and immunogenetics, medical physics and clinical engineering. In addition, although there are no formal training courses in clinical physiology, cellular science and developing sciences (used when experience crosses more than a single discipline), they can be considered for training and registration.

Entry in to clinical scientist training is a formal four year process with entry in to specific training programmes commencing in October of each year at recognised clinical training centres. During the four year training period the trainees are paid a salary and funded to complete a MSc. After successful completion of the four years an application is made to the Association of Clinical Scientists for a Certificate of Attainment which automatically provides for an application for registration with the HPC, which is renewed every two years. This then qualifies the individual to become a practitioner scientist and is eligible to proceed to the Royal College of Pathologists (UK) examinations if desired. There is a requirement for Continuous Professional Development (CPD) and for maintaining a portfolio.

#### The clinical scientist in pathology

The Royal College of Pathologists (UK) has for some time allowed non-medical graduates to undertake study and sit their examinations for the Diploma, Membership and Fellowship. Typically training as a clinical scientist in pathology would normally take eight years, four years as pre-registration training (as described above) then a further four years in higher specialist training to a minimum of an MSc, all of which is under supervision. The end point of the training is sitting the Royal College of Pathologists Membership examinations (MRCPath), which are identical to or very closely related to the specialist medical pathology registrars' examination. It is generally anticipated that many Clinical Scientists will have completed a PhD (or Professional Doctorate) during this training period; although it is not a requirement (approximately 70% will hold a PhD). The gualified clinical scientist is required to be registered with the HPC and can practise independently either at a consultant level or under the guidance of a consultant clinical scientist or medical practitioner in the specific discipline.

Currently the scientific disciplines within pathology are: cellular science, clinical biochemistry, clinical cytogenetics, clinical embryology, clinical immunology, clinical microbiology, haematology, histocompatobility and immunogenetics, molecular genetics, toxicology, transfusion medicine and virology. Currently approximately 25% of the Royal College membership is non-medical clinical scientists working across a wide range of pathology specialities. The Royal College of Pathologists recognises that attainment of consultant status will be medical consultant equivalents and this status is similarly recognized by the Clinical Pathology Accreditation (UK) Ltd in its standards for laboratory accreditation which states: "Each discipline shall be professionally directed by a consultant pathologist or a clinical scientist of equivalent status".

### The role of the Institute of Biomedical Science (IBMS)

This is the UK equivalent of the NZIMLS and has over a period of many years established its own post-graduate examination systems. Typically, entry level as a biomedical scientist is with a degree in biomedical science, which has been taken at an IBMS accredited university. Fellowship is a requirement for advancement to senior positions and is by examination with a Specialist Diploma, which is equated with an MSc by many UK universities. Scientists can advance further by gaining specialist qualifications as Extended or Expert Practice, which allows them to proceed to Advanced Specialist Diploma in a specific area of diagnostic pathology. The specialist gualifications identify specific levels of expertise; Expert Practice is the consolidation of high levels of skill and scientific or technical expertise, Extended Practice reflects a move from core disciplines in to new areas or areas traditionally associated with another profession and Advanced Practice is taking roles and responsibilities at the highest level of clinical practice or consultation. This structure has been recognised by the Royal College of Pathologists as a suitable entry route for training as consultant clinical scientists in pathology. Funding is available for the training programmes.

#### What is happening in New Zealand?

In 2006 the District Health Board New Zealand (DHBNZ) established a Medical Laboratory Think Tank to investigate role extension for medical laboratory scientists in the New Zealand health workforce planning. The membership comprised of representatives from DHBNZ, NZIMLS, Medical Laboratory Science Board, pathology laboratories, Royal College of Pathologists of Australasia (RPCA), (NZ Branch), and AUT, Massey and Otago Universities (BMLSc programmes). The group was working on identifiable workforce shortfalls for both pathologists and medical laboratory scientists and to consider the development of extended roles for medical laboratory scientists as clinical scientists. It was considered that this change would improve health delivery, improve career progression and recognition what was already happening in some New Zealand laboratories, especially those with no pathologist or a visiting pathologist. I

Information provided both by the NZIMLS and the RPCA indicated that there is a decreasing pathology workforce due primarily to recruitment at one end and an aging workforce at the other. In addition specific shortages for pathologists were recognised both in specific disciplines and potentially new or developing areas of diagnostic pathology. In considering possible options the concept of the clinical scientist emerged as the most suitable model to investigate based on the experiences of the UK. The RCPA was approached and indicated in 2009 that it was "willing to explore how best to implement a system of training in conjunction with the Think Tank". Subsequently the RPCA informed the DHBNZ Working Party that it was forming a Faculty of Science within the RPCA and a working group was being established. In response, the Think Tank group nominated Chris Kendrick (Massey University and MLSB member) and Mike Legge (University of Otago) to represent the group in any direct negotiations with the RPCA. We undertook to prepare a proposal for a Clinical Scientist qualification system for New Zealand, which was approved by the Think Tank members and submitted to the RPCA, a response is awaited.

## Summary of clinical scientist training in New Zealand

The proposal was to develop a two-stage qualification process based on the BMLSc, which was considered to provide a good background to diagnostic pathology and already had a registration requirement. Part A (first part of the training) would be an approved MSc programme of advanced study in one of the clinical sciences in a diagnostic pathology laboratory under supervision which would include academic papers and a clinically orientated research project based on the speciality. Completion of Part A of the training would be expected to take three to four years. Nonvocationally trained postgraduates who are registered with the MLSB may also be eligible for training but may require additional clinical science papers for eligibility. The second part of training (Part B) would be advanced study (following completion of Part A) in one of the clinical science disciplines under supervision similar to that by the RPCA specialist pathologist training. In the final year the clinical scientist trainees would prepare to sit the RPCA examinations for clinical scientists.

### Considerations in establishing the clinical scientist in New Zealand

Currently the proposal is with the RPCA and awaits further discussion on structure, their thoughts on a qualification proposal and time frame for implementation. However, the Think Tank has also considered implementation issues. First, that the post-graduate courses must be university based to provide a recognisable qualification route, second that it is most likely that training could only be undertaken in the larger diagnostic pathology laboratories to provide the necessary clinical material, infrastructure and supervisory expertise, third that there would have to be specifically targeted funding to ensure that training time was appropriate (the Clinical Training Agency was considered a possible funding agency), who would the most appropriate registration agency be (in the UK clinical scientists are a separate registration group under the HPC) and recognition of stepping off points along the way for those acquiring higher level skills but not wishing to complete the final RPCA examination stage as these individuals will be trained to a high skill level. In this scenario the IBMS (UK) model of qualifications of Extended and Expert Practice might be appropriate. Another consideration was whether using the Royal College of Pathologists (UK) qualification route should be adopted as it is possible to qualify overseas using their system but it was thought more appropriate to work with the RPCA.

## The role of the pathologist and the clinical scientist

Evidence from the UK now clearly identifies that there are clear niches for both the medically qualified pathologist and the clinical scientist. The Royal College of Pathologists (UK) have shown that pathologists have more time for direct clinical consultation and greater involvement with their clinical colleagues as well as time for research for those who are research orientated and a general reduction in workload. Clinical scientists are less involved with direct patient care and treatment, and have a higher involvement with scientific matters, research and management. Both professional groups have approximately equal time for reporting, teaching, clinical liaison and CPD.

#### New and emerging areas in pathology

Although the traditional areas of pathology will still remain the mainstay of diagnosis and treatment, developments in both new technologies and medical biology will change approaches to identification of disease and disease management. Scientists are qualified in many of the rapidly emerging areas such as molecular genetics and molecular diagnostics, molecular microbiology, gene array technologies, medical bioinformatics, stem cell biology, systems biology, biochemical and immunogenetics, pharmacogenomics, etc. These and other areas of biology are making significant impacts on modern medicine and may ultimately replace some of the more traditional approaches in diagnostic medicine such as digital pathology and in-vitro imaging technologies. Many of the new and emerging technologies represent the pathology of the future with, for example, the opportunities to identify and classify a tumour based on its molecular signature and identify its response to treatment based on an individual's genetic profile to the drugs to treat the tumour. These and related areas are where the medically qualified pathologist, the consultant clinical scientist and the clinician can work together for improved patient outcome.

#### Conclusion

Given the widespread international acknowledgement that there is a pending crisis in the training and supply of pathologists it is appropriate to consider alternative routes to bridge this problem. The increasing use of diagnostic pathology services and the new diagnostic technologies will place extra demands on an already aging workforce in a profession, which is experiencing a significant crisis in recruitment. In the Northern Hemisphere measures are being taken to overcome the pathologist shortage with the training of non-medical graduates in specialist pathology disciplines, which has to be a serious consideration in both New Zealand and Australia. The changing nature and delivery of health care services will need a high quality workforce which can respond in a flexible manner to new ways of working and new roles, supported by appropriate training and education strengthened by appropriate continuing professional development. The concept of the consultant clinical scientist is now well established in the UK and has not created significant issues in either the skill base or the interface between medicine and patient care. For this to be successful in both New Zealand and Australia it will require acceptance and development of a recognizable career pathway, which would involve the RCPA, NZIMLS, AIMS, AACB, HGSA and other organizations representative for health care scientists. Suitably qualified medical laboratory scientists have the potential to fill many of the roles undertaken by pathologists with the clear exception of patient management and treatment. Nevertheless, the acceptance by the Royal College of Pathologists (UK) and the National Health Service (UK) that appropriately qualified nonmedical scientists can achieve consultant status is the strongest indication yet that the system will work.

#### Acknowledgements

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# Diagnosing a heart attack – are biomarkers the be-all and end-all?

Stewart Mann, MA, DM, FRCP, FRACP, Associate Professor of Cardiovascular Medicine, University of Otago, Wellington

Forty years ago, at the peak of the coronary epidemic in western societies, diagnosis of myocardial infarction (MI) was often a qualitative and imprecise exercise. Then, as now, evidence was largely assembled from clinical symptoms, ECG changes and serum biomarkers. However, there were no biomarkers specific to myocardium and interpretation of changes to lactic dehydrogenase and serum glutamic oxaloacetic transaminase (later rechristened aspartate transaminase) was necessary despite known alternative sources of excess from liver. There was a high incidence of major and unequivocal myocardial infarctions with ST elevation on the ECG - "STEMIs" but also occasional more borderline syndromes. Treatment often involved prolonged bedrest (followed by similarly prolonged rehabilitation) and a focus on the management of arrhythmia with some controversy around the benefit of anticoagulation. Sudden death, cardiogenic shock and pulmonary oedema were common so both the clinical and social implications of a diagnosed heart attack were profound.

Symptoms continue to be the key in diagnosis and ECG technology has not changed. While imaging technology has improved radically, it is rarely easily available in the acute phase of an evolving coronary syndrome so the focus of improving diagnosis has been the development of rapid assays of much more sensitive and specific biomarkers. Creatine kinase was of course specific to muscle and its MB fraction more so to myocardium but even this has now been swept away by the troponin revolution. Cardiac troponins T and I (cTnT and cTnI) are highly specific to the myocardium and ever more sensitive assays pick up lower and lower levels, including now levels found in healthy subjects.

The presentation, management and outcomes of acute coronary syndromes have changed over these 40 years. Age-standardised death rates from coronary disease are now some 40% of their levels in 1968, due both to changing risk factors and to medical interventions; case incidence and case fatality have both fallen. The falls in smoking rates, blood pressure levels and lipids which have been responsible for the largest part of the reduction are however in danger of being offset by increasing obesity and consequent diabetes (1). We have also seen a decline specifically in sudden death and larger infarcts (eg STEMIs) and admissions now consist much more frequently of smaller, more borderline syndromes (non-STEMIs and unstable angina). Coronary disease has become less focused on single major events and more typically follows a chronic disease pattern with occasional recurrent crises.

The availability of new treatments has dictated a need to have internationally standard classifications of acute coronary syndromes to facilitate scientific evaluation of treatments. Committees convened under the auspices of the American College of Cardiology, American Heart Association, European Society of Cardiology and World Heart Federation deliberated in 2000 and again in 2007 (2) to produce definitions of myocardial infarction. These have focused on biomarkers (and in the latest version specifically on troponins) as being a fundamental component of the diagnosis and exhorted diagnostic companies to come out with assays that would meet a requirement of measuring the 99<sup>th</sup> percentile of a healthy population with a coefficient of variation of 10% or less. In 2010 this has now been achieved although the increased sensitivity has come at a cost of decreased clinical specificity. To guard against over-diagnosis of MI, the definition requires a rise or fall in biomarker level to be documented although did not specify the degree of change needed to satisfy the diagnosis.

Despite a changing level being a requirement for diagnosis even in the 2000 definition, in recent years many clinicians had come to regard a single raised level in combination with a suggestive clinical history as a positive diagnosis. Over this period conventional management of a non-STEMI has included admission and a trip to the cardiac catheter laboratory for angiography, stenting of a "culprit" stenotic coronary lesion if identifiable and treatable, or other indicated intervention such as coronary bypass surgery. For this commonly diagnosed condition, this has necessitated transfer of many patients to an interventional centre during their index admission. A positive diagnosis has therefore had major clinical (not to mention financial) implications.

Those in New Zealand who utilise Troponin T assays are currently in the process of changing to a new 5<sup>th</sup> generation assay. Whereas the 4<sup>th</sup> generation one was reliable down to levels of 0.03ng/mL, the new one is accurate to 0.014 ng/mL (3) which is the 99th percentile (as specified by the international definition). An overseeing clinical reference group has decided to take advantage of the change in assay to use more sensible units so that 0.14 ng/mL becomes 14 ng/L. Detectable levels (below this threshold) can be found in some 50% of normal healthy individuals and levels above the 99% threshold can be found associated with a growing list of alternative conditions. A number of different approaches have been made to assess the impact of the new test but it is clear that a single level in the new high sensitivity range is not nearly specific enough to use as a triage tool in an acute coronary syndrome. Early work in Wellington does suggest that around 30% of those with possible acute coronary syndromes and negative 4<sup>th</sup> generation troponin T tests will have a level above the 99th percentile but only around 3% will show changes in sequential samples that would qualify for a diagnosis of myocardial infarction (4). From a combination of method comparison studies and stability studies in healthy individuals and those with consistently raised levels (e.g. cardiomyopathy), a minimum change of 20% in level if above 50 ng/L and 50% change if below that threshold seems to accord best with clinical diagnosis. This accords closely with a published proposed triage algorithm (5).

Another advantage of a more sensitive test is that patients with a myocardial infarction will show diagnostic changes earlier. It is still a little unclear how soon an infarct can be ruled out but a negative test (<14 ng/L) 6 hours after the onset of chest pain appears to confer about 90% rule-out confidence. The algorithm we have advised in the Wellington region is shown in Figure 1.

One consequence of moving to the new test is the need for medical staff to think more carefully about the significance of a positive test in the context of the clinical presentation of the patient. In recent years, a 'positive' troponin test has been used as the key decision breaker for admission and for triage to angiography. In truth, the patients who benefit most from acute intervention are those at highest risk as calculated from a range of factors, of which a raised biomarker is just one. To get the maximum benefit from our resources in this area, we need to introduce routine risk scoring systems such as proposed by the TIMI group (6), GRACE researchers (7) or a simple one derived from a recent meta-analysis (8) that interestingly, does not include biomarker results at all!

In some ways the new tests have made life more complicated for clinicians, both in assessing patients with possible acute coronary syndromes and when troponin tests are requested in a myriad of other circumstances where relevance is questionable. Commentaries on the new high sensitivity tests have rued the transition from "a lousy assay but a great test" to a "great assay but a lousy test' (9) and challenged the results to fit into a neat Bayesian model (10). However, the reintroduction of a need for additional thought and clinical reasoning into the assessment and triage of patients must surely be welcome along with the increased precision and speedier processing of patients that the sensitive assays can provide.

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Table 1. Elevations of cTn above the 99th percentile in the absence of an acute coronary syndrome.

#### "Healthy population"

- 1/100 (by definition)
- Endurance exercise Cardiac Causes
- Chronic stable angina
- Congestive heart failure
- Arrhythmias, heart block
- Cardiac contusion, ablation, pacing, cardioversion, biopsy Cardiomyopathy: HCM, Takotsubo
- Inflammation e.g. myocarditis, endocarditis, rejection
- Rhabdomyolysis with cardiac injury
- Infiltrative diseases, e.g., amyloidosis, haemochromatosis, sarcoidosis,

scleroderma

- Drug toxicity, e.g., adriamycin, herceptin, clozapine
- Aortic dissection, aortic valve disease

#### Non-cardiac clinical causes

- Acute and chronic renal failure
- Acute neurological disease, including stroke, or subarachnoid haemorrhage

#### Use of high sensitivity troponin to diagnose myocardial infarction



- Pulmonary embolism, severe pulmonary hypertension
- Exacerbation of CORD
- Hypothyroidism
- Phaeochromocytoma
- Burns affecting >30% of body surface area
- Critically ill patients with respiratory failure, or sepsis
- Snake bites

Figure 1. Algorithm introduced in the Wellington region for triage of acute coronary syndrome diagnosis using high-sensitivity troponin T.

## Comparison of the Siemens vWF:RCo and the Instrumentation Laboratory HaemosIL von Willebrand factor activity assays for the diagnosis of von Willebrand disease

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#### Abstract

von Willebrand disease is a bleeding disorder caused either by a quantitative or a qualitative abnormality in the plasma protein, von Willebrand factor. The diagnosis and classification of von Willebrand disease relies upon a panel of screening and confirmatory laboratory tests. In this study the Siemens von Willebrand factor ristocetin cofactor assay was used to test 59 patient samples submitted to Waikato Hospital Laboratory. The samples were also tested using the Instrumentation Laboratory HaemosIL von Willebrand Factor activity assay which is a potential replacement for the Siemens assay. The two assays showed good correlation of results below the 80% level. The HaemosIL assay showed better intra-batch precision, however, inter-batch precision revealed little difference between the two assays. The Siemens assay was more time consuming to perform, however, reagent costs were lower than the HaemosIL assay. This study demonstrated that the HaemosIL assay could be useful in the laboratory investigation of von Willebrand disease. Whether it is a suitable replacement for the von Willebrand factor ristocetin cofactor assay remains unanswered. The lack of sufficient samples with low von Willebrand factor and the unavailability of samples from von Willebrand types and subtypes did not allow for a complete evaluation of the performance of the HaemosIL assay in this study.

Keywords: von Willebrand disease, von Willebrand factor, activity assay

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#### Introduction

von Willebrand disease (vWD) is a congenital bleeding disorder with an incidence of approximately 1.3% of the human population (1). The disorder varies in its clinical presentation from asymptomatic to severe bleeding. vWD is caused by a mutation in the vWF gene or gene promoter located on chromosome 12. This can result in either a quantitative or qualitative defect in the plasma protein von Willebrand factor (vWF). vWD is subdivided into 3 types and 4 subtypes based on the type of vWF abnormality (2). Type 1 vWD is a partial quantitative deficiency in vWF, Type 2 (subtypes A, B, N and M) is a qualitative defect and Type 3 an extreme quantitative defect where vWF is absent (1).

vWF has an important role in primary haemostasis promoting platelet adhesion to sub endothelial structures such as collagen and platelet to platelet interaction following vessel injury. Both phases are important in the proper formation of the primary platelet plug. vWF also plays a role in the secondary phase of haemostasis preventing the degradation of Factor VIII in the circulation and its rapid inactivation during the clotting process (3).

Patients are diagnosed with vWD following both clinical and laboratory evaluation. The patient may present with a history of excessive bleeding or easy bruising and there may be some related family history. Laboratory tests used most commonly to evaluate fibrin formation, do not directly evaluate plasma vWF. Laboratory investigation is usually comprised of the prothrombin time (PT), activated partial thromboplastin time (APTT) test, the platelet count, the bleeding time test (now mostly historical) and the platelet function assay (PFA) developed for the PFA-100 analyser (4).

A normal PT, normal/abnormal APTT and a prolonged closure time for both the collagen/ADP and the collagen/epinephrine cartridges in the PFA-100 assay, will lead to further laboratory investigations. Confirmatory tests for vWF disorders are the vWF:Ristocetin cofactor assay (vWF:RCo) assay, the vWF antigen assay, the factor VIII coagulation activity assay, and the collagen binding assay (5). The vWF:RCo assay measures plasma vWF by testing the ability of vWF to induce platelet agglutination in the presence of the antibiotic ristocetin (3). The HaemosIL vWF activity assay was manufactured to provide an alternative method to assess in vivo platelet/vWF factor interaction and is a potential alternative to the vWF:RCo (6). The HaemosIL assay directly measures plasma vWF through its ability to bind a latex bound monoclonal antibody (7).

At the Waikato Hospital laboratory the Siemens vWF:RCo activity assay is currently used for the investigation of VWD. In this study the HaemosIL vWF activity assay and the Siemens vWF:RCo assay were used to quantify vWF in plasma. Samples used in the study were those that had been submitted to the Waikato Hospital laboratory for vWD investigation. The two assays were compared in terms of cost, ease of use, precision and correlation, to determine whether the HaemosIL assay could replace the vWF:RCo assay for vWD investigations.

#### Materials and methods Siemens vWF:RCo assay

The vWF:RCo is the classic functional assay used for the investigation of disorders associated with vWF. At Waikato Hospital laboratory the Siemens vWF:RCo assay is run on the Behring Coagulation

Timer (BCT) analyser. In the assay plasma vWF binds to the platelet gp1b receptor on lyophilised reagent platelets and agglutinates the platelets in the presence of ristocetin. Agglutinated platelets decrease reagent turbidity which is measured at OD<sup>405</sup> nm with reduced light transmittance proportional to plasma VWF (5). vWF levels are obtained using a pre-programmed standard curve and presented as vWF %. Samples with a vWF result below 50% were retested against a calibration curve established for low values.

#### HaemosIL vWF activity assay

The HaemosIL (Instrumentation Laboratories) assay was performed on a Sysmex CA7000 coagulation analyser. In the HaemosIL assay plasma vWF is determined by turbidometric assay after it reacts with a reagent monoclonal anti-vWF (gp1b $\alpha$  platelet binding site) bound to latex particles (7). Decreased turbidity of the reagent is measured at OD<sup>405</sup> with vWF levels determined from a preprogrammed standard curve.

#### Samples

Blood samples from 59 patients sent to the laboratory for vWD testing over a 10 week period were included in the study. Whole blood collected into 3.2% tri-sodium citrate was centrifuged at 2000g for 10 minutes as soon as possible after arrival in the laboratory. Plasma separated into capped plastic tubes was stored frozen at -20°C. Samples were batch tested weekly following thawing of the plasma for 5 minutes at 37°C. Blood samples were collected into 3.2% tri-sodium citrate from twenty random blood donors to establish a normal range. Plasma samples were separated and stored as for patient samples. Both patient and donor samples were later batch tested.

#### Instrument calibration and quality control

Performance of the Siemens and IL assays were controlled using Siemens Control plasma N and P and IL ST1 and ST2 controls. Control samples were run for each assay on the two analysers prior to patient testing: control plasma N had a vWF:RCo level of 100% (8) and control plasma P a level of 30% (9). The IL ST1 control plasma had a value for the VWF Activity Assay of 55% and the ST2 20%. Valid results for control plasmas required values within ± 2 standard deviations from the target mean before sample testing could proceed. Calibration curves were derived for the vWF:RCo assay using the Siemens standard normal plasma and for the HaemosIL assay the IL calibrator plasma. Each curve was prepared as part of the calibration cycle for each assay on both analysers.

#### **Statistical analysis**

The results of the vWF testing were evaluated by Deming regression analysis and Spearman's ranking. In addition, results data was compared by Bland Altman plot. These provided correlation and mean difference values for both assays. Both procedures utilised Microsoft Excel and Analyse-it software (10). Intra-batch precision of the two assays was assessed from the coefficient of variation (CV) calculated from 10 replicate tests on a single plasma sample. Inter-batch precision was assessed using CV values obtained from the testing of the control plasmas N and P with batches of test plasmas. The same method was used to establish the precision of the HaemosIL assay using IL ST1 and ST2 plasmas.

#### Results

Testing of the 59 patient samples using the Siemens and the IL assays provided a range of results from 30.4 - 259.30%. Deming regression was used to compare the correlation of the two methods. With the ratio of variances set at 1 this provided a slope of 0.925 (0.705 to 1.145 - 95% confidence interval). Results showed good correlation between the two methods with r = 0.901 (Figure 1).

Figure 1. Deming regression analysis of the Siemens and IL assays.



The results were also compared using a Bland–Altman plot to demonstrate the overall difference between the two methods. A mean difference of -6.68% (Figure 2) showed a close relationship between the results. At lower levels near the cut-of points the results were more accurate. The Spearman non-parametric test of correlation provided an *rs* value of 0.92 and a *p*-value of <0.0001. his confirmed the close similarity of results demonstrated by the Bland Altman plot.

Figure 2. Bland Altman plot of the results of the Siemens and IL assays



#### **Precision studies**

Intra batch precision for the two assays was established by retesting a patient sample with low vWF and a healthy donor plasma with a normal level of vWF. Sample testing was repeated 10 times for each sample in the same run. Mean values were used to establish the coefficient of variation. Precision for the IL assay was 5.3% and 1.3% for low and normal levels of VWF respectively (Table 1). The CVs for the Siemens assay for the same samples were 8.2% and 8.6% (Table 1) respectively. Inter batch precision was determined from the results of the control plasmas P and N (Siemens assay) and the ST1 and ST2 controls (IL assay) run with each batch of patient samples. The CVs for the Siemens assay were higher than those for the HaemosIL assay, a finding reported by others (7, 11). The CVs for the HaemosIL assay were a little higher than expected, however, numbers were low (n=8) which may have overly skewed the results (Table 2).

#### Table 1. Intra-batch precision

		Siemens assay Low vWF Normal vWF		IL assay	
				Low vWF	Normal vWF
Mean 47.7		47.7	118.0	44.0	86.4
	SD	3.9	10.1	2.3	1.1
	CV	8.2%	8.6%	5.3%	1.3%

Table 2. Inter-batch precision

	Siemens assay Control P Control N		IL assay	
			ST1 Control	ST2 Control
Test number	8 8		8	8
Mean	n 26.4 (30%) 97	97.7 (100%)	63.2 (55%)	21.6 (20%)
CV	10.3%	9.4%	7.1%	9.5%

#### **Reference range**

The reference range (Cl 95%  $\pm$  2SD) for the IL assay was calculated from the testing of the plasma from 20 random (not selected for ABO group) healthy blood donors (Table 3). The results provided a reference range of 44.9 - 145.8%. This was comparable to the reference range of 50-150% for the Siemens assay currently in use at Waikato Hospital.

Table 3 HaemosIL vWF activity assay reference range

Mean	95.3
± 2 Standard Deviations	50.4
Reference Range	44.9 - 145.8%

#### Discussion

The results of the 59 patient samples tested using the HaemoslL and Siemens assays showed good correlation r = 0.901 (Figure 1) and a small mean difference of -6.68% between the two methods. The similarity of the results was closest in the lower range of normal, with results above 80% demonstrating a greater difference (Figure 2). While not ideal, the performance of the HaemoslL assay was still considered acceptable as differences in the upper range present less of an interpretative issue compared to those close to the 50% cutoff. The five outliers (Figure 2) were each above 80% with 3 of the 5 above 180%. The reasons for this level of disparity cannot be satisfactorily explained, however, the two assays measure plasma vWF differently and this may have been a contributing factor. Removal of these from the Bland Altman calculation did not alter the mean difference of values overly and so were retained for completeness.

Studies to demonstrate intra-batch precision showed the HaemosIL assay to be more precise than the Siemens assay. This has been reported by others. Poorer performance of the Siemens assay in inter-batch precision compared to the HaemosIL assay has also been reported (7,11). This was the finding in this study although difference between the two was not marked. Of note was the higher than expected CV values for inter-batch precision testing. A possible explanation for this was the relative inexperience of the operator and the fact that only a low number of results were available for the calculation.

The Siemens vWF:RCo assay took longer to perform as the BCT analyser, which is used solely for this test, required start-up and machine checks prior to each batch of testing. The HaemosIL assay was run on a Sysmex CA7000, the main coagulation laboratory analyser, which meant that delays were minimal with less machine preparation required. Costs and time involved in maintaining the BCT analyser together with the loss of laboratory bench space to store the machine, makes retaining the Siemens assay increasingly more difficult to justify. At Waikato Hospital the Sysmex CA7000 is used for the Factor VIII, vWF:AG and vWF activity assays for the investigation of vWD. The use of this machine and the HaemosIL assay, as a replacement for the vWF:RCo assay, has obvious attraction. In addition, the elimination of extra sample handling and storage and the risk of transcription error in results reporting required for the Siemens assay, further favour the centralising of vWF testing on to a single platform.

Reagent costs for the Siemens assay are less per test than those of the HaemosIL assay. The Siemens vWF:RCo reagent kit contains five vials each with 4mL of reagent. Reagent costs per test were estimated to be approximately NZ\$3.16. Once reconstituted the Siemens reagent had a 48hr shelf-life at 4°C. The HaemosIL assay reagent kit contained 2 vials of 4.5mL of reagent with the cost per test estimated to be NZ\$9.10. Once reconstituted the HaemosIL reagent was stable for 1 month at 4°C. Reagent stability is an advantage with the HaemosIL assay enabling vWF activity to be assayed in urgent cases. This is currently not offered because of excessive reagent wastage with the Siemens assay. Preparation of reagents for both assays was simple, however, unlike the Siemens reagents which were ready for use immediately after reconstitution (Siemens package insert), the HaemosIL reagents had to be left for 30 minutes following reconstitution before use. This delay could result in a significant disruption if the analyser unexpectedly ran out of reagent while testing a batch of samples. .

#### Conclusion

The findings of this study showed that the HaemosIL assay has the potential to become an alternative to the Siemens vWF:RCo assay or another laboratory test useful in the diagnosis of vWD. While both methods measure plasma vWF, each does so employing a different approach. Whether the two assays measure the same thing and whether both are able to similarly predict in vivo platelet adhesion in response to vessel injury remains the question. This probably mitigates against the replacement of the HaemosIL assay in place of the classic vWF:RCo assay.

The reference range calculated for the HaemosIL assay was very similar to that in use for the Siemens vWF:RCO assay at Waikato Hospital. While this was derived from a fairly small number of samples, this supports the other results of this study indicating similar performance characteristics of the two assays. Correlation studies showed good overall correlation of the results especially around the important 50% cutoff figure. Results were less well correlated with values greater than 80%. Precision studies also showed the HaemosIL assay to have improved intra and inter batch precision over the Siemens assay.

This study was limited by the finding of only three samples with a vWF:RCo level of less than 50%. Overall seven samples produced results that were ±10% of the 50% cutoff, the range in which the potential exists for patient diagnosis to be affected. A change to the HaemosIL assay in place of the Siemens vWF:RCo assay may be possible sometime in the future. Before this can happen more work to evaluate the performance of the HaemosIL assay against samples close to the 50% cutoff is required. In addition, evaluation of assay performance against samples from known vWD types and subtypes would also be required. Because of this it is not likely that many laboratories will replace the traditional Siemens vWF:RCo with the HaemosIL vWF activity assay. Instead it may find a place as another useful assay in the often technically challenging evaluation of vWD.

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#### **Author contributions**

RP conducted the study and substantially drafted the main article, HS supervised the laboratory work and critically reviewed the main article, and CK substantively drafted the final article for critical content. The authors declare no conflicts of interest.

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### Vitamin D toxicity? A case study

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#### Abstract

One of vitamin D's important roles is body calcium regulation. Vitamin D deficiency can lead to hypocalcaemia, and consequently cause bone related disorders. On the other hand, prolonged excessive vitamin D can lead to hypercalcaemia, and consequently cause renal stones. Compared to vitamin D deficiency, vitamin D toxicity is very rare. We report a case where the patient was initially thought to be hypervitaminosis D. In our laboratory, we use the ECLIA method from Roche Diagnostic to measure serum vitamin D. The patient had vitamin D levels of >250 nmol/L on more than one occasion whilst appearing to be clinically vitamin D deficient. Furthermore, results for vitamin D levels on the same samples by another laboratory with a different assay method came back as low normal. We carried out investigations for possible immunoassay interference. We found that an interfering factor caused falsely high results in competitive assays and falsely low results in a sandwich assay. The sample was sent to Roche Diagnostics in Germany for further investigation. Roche Diagnostics was able to show that the interfering factor was to the solid phase, but did not identify the interfering factor.

Key words: vitamin D, 25-hydroxyvitamin D, Elecsys Vitamin D3, interfering factor

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#### Introduction

Clinicians have used the media on numerous occasions to express their concerns regarding vitamin D deficiency in the general population, particularly among the elderly. Never has there been concern about vitamin D toxicity, also known as hypervitaminosis D. This is because an important role of vitamin D is in body calcium regulation. Vitamin D deficiency is known to be associated with rickets among children and osteomalacia among adults (1). However, in rare cases, highly elevated vitamin D levels can cause hypercalcaemia and, in the long term, can lead renal stones (2-4).

Vitamin D is categorized into two main forms: vitamin  $D_3$  and vitamin  $D_2$ . Vitamin  $D_3$  is produced in the skin by exposure to sunlight, whilst vitamin  $D_2$  from dietary sources such as fish oil, egg yolk, liver and certain plants. Both forms of vitamin D are metabolically inert. They become active through hydroxylation processes first in the liver, and subsequently in the kidney. In the liver, vitamin  $D_3$  is hydroxylated to 25-hydroxyvitamin  $D_3$  and vitamin  $D_2$  to 25-hydroxyvitamin  $D_2$ . In the kidney, both 25-hydroxyvitamin D are hydroxylated to 1,25-dihydroxyvitamin D, the active form (4).

Only the measurements of 25-hydroxyvitamin D and 1,25-hydroxyvitamin D have been proven to provide clinical value (5-7). In our laboratory we use the Elecsys Vitamin D3 (25-OH) assay from Roche Diagnostics. The assay only measures 25-hydroxyvitamin D<sub>3</sub>. The 25-hydroxyvitamin D is the main form of vitamin D in circulation, and 25-hydroxyvitamin D<sub>3</sub> form accounts for more than 95% of the 25-hydroxyvitamin D. The 25-hydroxyvitamin D<sub>2</sub> only becomes detectable when taking vitamin D<sub>2</sub> supplements. Furthermore, the 25-hydroxyvitamin D has a longer half-life

compare to the more labile 1,25-hydroxyvitamin D, and it also shows better correlation with the nutritional status of vitamin D (4).

#### Case report

A 36-year-old female patient first presented to her clinician complaining of bouts of fatigue and weight loss. The clinician requested routine haematology and biochemistry tests including a vitamin D level, and queried iron or vitamin D deficiency. The haematology and biochemistry results were normal. The iron study results also indicated adequate iron stores. The vitamin D level, however, was unexpectedly high at >250 nmol/L (reference range: 50 - 150 nmol/L).

#### Laboratory investigations

The Elecsys Vitamin D3 (25-OH) assay has only recently been introduced to our laboratory. Since its introduction, we have been closely monitoring the assay performance including assay calibrations, quality controls and patient results. Vitamin D levels above the detectable limit (>250 nmol/L) are not common. In this case, to ensure the validity of our result, we sent the patient's sample from her first visit to two laboratories for vitamin D. Laboratory A uses the same Elecsys technology to measure vitamin D, plus an inhouse dilution method. The vitamin D result from laboratory A was 413 nmol/L, which agreed with our result. Laboratory B uses Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS). The vitamin D level from laboratory B was 101 nmol/L, which disagreed with our laboratory and laboratory A results (Table 1). The method uses by laboratory B is considered the gold standard method for measuring vitamin D (8). Furthermore, the result from laboratory B correlated well with the patient's clinical picture.

The vitamin D level was repeated on a subsequent sample requested by the clinician. In addition, calcium and parathyroid levels were also requested to assess the parathyroid status. The vitamin D level remained high at >250 nmol/L. The parathyroid level, on the other hand, was exceedingly low at 0.1 pmol/L (reference range: 1.6 - 7.0 pmol/L). These findings are consistent with secondary hypothyroidism along with elevated calcium levels (4). However, the patient's calcium was well within the normal range at 2.20 mmol/L (reference range: 2.05 - 2.60 mmol/L). The patient had no particular medical history that could explain the results obtained, nor was she on any supplement or medication that contained vitamin D.

For further investigation we sent the subsequent sample on the patient to laboratory B for vitamin D level and laboratory C for parathyroid hormone (PTH). Vitamin D result from laboratory B was 43 nmol/L. Laboratory C measures PTH on an Abbott Architect analyser using chemiluminescent microparticle immunoassay (CMIA). The parathyroid hormone was 1.7 pmol/L. Table 2 compares our laboratory results to laboratories B and C.

In addition, we ran the subsequent patient's sample for thyroid stimulating hormone and free T4 on the E170 and the Advia Centaur analyser in our laboratory. The Advia Centaur uses

chemiluminescent immunoassay technology. The results obtained were significantly different between the two analysers as shown in Table 3.

Interference in the Elecsys assays was suspected after thorough examinations of all the results and discussions with our pathologists. We noted that all falsely elevated results used competitive assay principle whilst all falsely low results used sandwich assay principle. Table 4 summarises all results performed on the E170 analyser.

Further tests were performed to exclude some common immunoassay interferences. Heterophilic antibody-blocking tube was used to adsorb heterophilic antibodies prior to vitamin D assay. The vitamin D result after heterophilic antibody blocking was still >250 nmol/L. The sample showed no visible haemolysis. Bilirubin level was within the normal reference range. This excluded the possibility of interference due to icterus. Lipid levels were also normal. Interference due to rheumatoid factors was also excluded. The patient was not noted to be on biotin therapy, which can potentially interfere with Elecsys assays.

In addition, we attempted serial dilutions on the patient sample to determine the actual concentration of vitamin D in the sample. The sample was manually diluted with a low vitamin D serum level available as recommended by the manufacturer. Linearity is normally observed in normal serial dilutions. In this case, however, the serial dilution was non-linear. This also supported the presence of interfering factor in the sample.

We referred the sample to Roche Diagnostics in Germany for further investigation. Roche Diagnostics screened the sample for possible interference against Ruthenium labelled antibody and streptavidin. The sample was adsorbed on uncoated microparticles and microparticles coated with streptavidin prior to vitamin D assay. The vitamin D level was significantly lower compared to the untreated sample.

Table 1. Comparisons of vitamin D results from differentlaboratories

Our Laboratory	Laboratory A	Laboratory B
E170 (nmol/L)	E170 (In-house Dilution) (nmol/L)	LC-MS/MS (nmol/L)
>250	431	101

 Table 2. Comparison of vitamin D and parathyroid hormone results

	Our Laboratory (E170)	Laboratory B (LC-MS/MS)	Laboratory C (Abbot Architect)
Vitamin D (nmol/L)	>250	43	
PTH (pmol/L)	0.1		1.7

 Table 3: Comparisons of thyroid stimulating hormone and free T4 results

	E170	Advia Centaur
TSH (mIU/L)	0.35	0.79
Free T4 (pmol/L)	27	14

#### Table 4: Elecsys assay results and assay principles

	Result	<b>Reference Range</b>	<b>Assay Principles</b>
Vitamin D (nmol/L)	>250	50 – 150	Competitive
Free T4 (pmol/L)	27	10 – 23	Competitive
PTH (pmol/L)	0.1	1.6 – 7.0	Sandwich
TSH (mIU/L)	0.35	0.3 – 4.0	Sandwich

#### Theory to the interference

Figure 1 illustrates the ECLIA competitive principle. This principle is applied to analytes with low molecular weight, such as vitamin D. The first reaction involves interaction between vitamin D in the sample to vitamin D-specific ruthenium labelled antibody to form an immunocomplex. Biotinylated vitamin D and streptavidincoated microparticles are added in the second reaction. Biotinylated vitamin D occupies the still free binding sites of the labelled antibody. The biotinylated immunocomplex subsequently binds to the microparticle via interaction of biotin and streptavidin. The microparticle is then magnetically captured onto the surface of an electrode. This follows by a washing step to removed unbound substances. A voltage is then applied to the electrode to induce chemiluminescent emission. The emission is measured by a photomultiplier. The amount of emission produced is inversely proportional to the concentration of vitamin D in the sample (9).

Figure 2 illustrates the ECLIA sandwich principle. This principle is applied to analytes with high molecular weight, such as PTH. The first reaction involves interaction between PTH in the sample, a biotinylated PTH-specific antibody, and PTH specific ruthenium labelled antibody to from a sandwich immunocomplex. The immunocomplex subsequently binds to streptavidin-coated microparticle in the second reaction via interaction of biotin and streptavidin. The microparticle is then magnetically captured onto the surface of an electrode. This follows by a washing step to remove unbound substances. A voltage is then applied to the electrode to induce chemiluminescent emission. The emission is measured by photomultiplier. The amount of emission produced is directly proportional to the concentration of PTH in the sample (9).

In the case of our patient, interference to streptavidin would cause falsely high results in competitive assays, as seen in with vitamin D and free T4 levels, and falsely low results in sandwich assays, as seen with PTH and TSH levels. The interfering factor competes with biotin for streptavidin binding. This reduces the interaction between biotin and streptavidin. Reduction in biotin and streptavidin interaction consequently leads to decreased chemiluminescent emission. In competitive assay, reduced chemiluminescent emission means high concentration of analyte in the sample because of the inverse relationship. Whereas in the sandwich assay, reduced chemiluminescent emission means low concentration of analyte in the sample because of a direct relationship (9). Figure 3 demonstrates the interference in the competitive assay while Figure 4 demonstrates the interference in the sandwich assay.



Figure 1. Competitive ECLIA principle (modified from Modular Analytics SWA: E Module - Immunology Principle; chapter 17, page 112).

**First Reaction** Second Reaction Light Reaction SOCKAL Concentration MAGNETIC FORCE & ELECTRICAL POTENTIAL BIOTINYLATED ANTIBODY PTH STREPTAVIDIN COATED MICROPARTICLE RUTHENIUM LABELLED ANTIBODY

Figure 2. Sandwich ECLIA principle (modified from Modular Analytics SWA: E Module - Immunology Principle; chapter 17, page 114).

Figure 3. Interference to streptavidin in competitive ECLIA



Figure 4. Interference to streptavidin in sandwich ECLIA



Roche Diagnostics in Germany concludes that an interfering factor to the solid phase, which most likely has caused the high Vitamin D3 value, was present in the sample. This finding is supported by all results obtained with different Elecsys assays and other immunoassay techniques.

#### Discussion

The introduction of automated immunoassay for vitamin D has provided a relatively easy and cost effective alternative to the standard method. Since the introduction of vitamin D assay into our laboratory, the number of request from clinicians has increased exponentially. This is the first confirmed case of vitamin D assay interference in our laboratory.

The Elecsys Vitamin D (25-OH) reagent package insert states that interference may cause by visible signs of haemolysis, grossly lipaemic, gross icteric and highly elevated rheumatoid factors sample, and high doses of biotin. These interfering factors were excluded during our preliminary investigation and the patient was not on biotin therapy.

Heterophilic antibodies are anti-animal antibodies present in human serum. Such antibodies are also a well known cause of interference in immunoassay (10,11). The Elecsys Vitamin D (25-OH) assay uses polyclonal sheep antibodies. Therefore, the presence of anti-sheep antibodies in the patient's serum may be a cause for interference. The assay has suitable additives included to minimize such interference. These additives, however, do not completely eliminate the risk of interference due to heterophilic antibodies. Unfortunately, the use of heterophilic antibody-blocking tube also had no effect on the vitamin D level compared to the untreated sample.

The Elecsys Vitamin D (25-OH) reagent package insert also states that, in rare cases, interference caused by extremely high titres of antibodies to streptavidin and ruthenium may occur. Roche Diagnostics in Germany uses an in-house method to successfully adsorb the interfering factor. They were able to successfully absorb the interfering factor and the vitamin D result obtained was comparable to the standard method. However, they did not include a detailed method in their report. Furthermore, the identity of the interfering factor remains unknown only that it is interfering in the solid phase of the assay. After further research we came to the conclusion that there are two possible interfering factors: antistreptavidin antibodies and endogenous biotin, both of which can cause the same interfering outcome. Anti-streptavidin antibodies are the most likely in this case because of repeated incidences of elevated vitamin D levels, indicating a constant present of the interfering factor in the body. However, we cannot exclude the other possibility as interference can occur in individuals with extremely high levels of endogenous biotin (12).

Roche Diagnostics in Germany did not provide the details on their in-house method. Therefore, we currently do not have a resolution to this problem should it occur again. So, our concern remains. In the case of erroneously high vitamin D results, consequences are less likely to be serious. The patient in this case was referred to an endocrinologist. Fortunately, no further interventions were undertaken because of good communication between the laboratory and the clinicians. However, because of the nature of the interference it could affect any of the Elecsys assays. It could be troponin T, beta HCG or tumour markers where the consequences of erroneous results could be more serious. Therefore, it is very important for laboratory personnel and clinicians to be aware of such interference. More importantly, as recommended by the manufacturer, for diagnostic purposes, results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

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#### Author contributions

Vichet Khieng was the primary author, conceived the study and carried out the laboratory testing. Catherine Stevens substantially rewrote parts of the manuscript for intellectual content. The authors have no conflicts of interest to declare.

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# Coherent 1989-2009: 20 YEARS

Microbiology

### Conference report Biomedical Science Congress, ICC, Birmingham, UK, 28-30th September 2009

The 2009 Biomedical Science Congress was organised by the Institute of Biomedical Science, UK. It was held at the Birmingham International Convention Centre from the 28<sup>th</sup> to the 30<sup>th</sup> of September 2009.

I arrived in Birmingham on Sunday the 27<sup>th</sup> of September and attended the welcome evening at the Brass House, adjacent to the Convention Centre. On speaking with other delegates it became clear that it was difficult to obtain funding for training and conferences in the UK at present due to the current financial constraints. I felt very privileged to be attending as a delegate from LabPlus, Auckland City Hospital.

The underlying theme of the congress revolved around advances in technology bringing about improvements in quality and lab efficiencies. On the first morning I registered and was immediately impressed by the variety and complexity of the presentations on offer. These included Histology, Clinical Chemistry, Cytology, Education and Management, Haematology, Immunology, Microbiology, Transfusion Science and Virology.

The conference venue, the Birmingham International Convention Centre, a suitably large venue that has been used by the Institute for many years, provided the perfect site for delivering such a programme.



The forecourt of the International Convention Centre.



The first floor of the exhibition



Roche staff demonstrating the new UltaVentana Immunostaining machine



#### Monday 28 September Automation: thin prep imager focal point Alan Wilson, Consultant Biomedical Scientist, Monkland's Hospital, Lanarkshire

Alan gave an account of the Scottish Cytology Imager feasibility study. He started by telling us that Cytology laboratories in Scotland have amalgamated from 19 to 9. Also the numbers of smears have dropped from 471,000 in 2002 to 271,000 in 2007. Cytology in Scotland is now 100% paperless. In England all Cytology Labs have to receive at least 35,000 smears per year to be accredited for Cytology provision. Currently in Scotland five labs receive fewer than 35,000 smears.

The Cytology review was commissioned in 2007 by the Scottish Government. The drivers were the aging workforce and the effect

of HPV vaccination. 80,000 samples were split between the Cytology automated screening systems (Imager) and manual screening. Labs send slides to one "hub" for imager screening. Specificity, sensitivity and reporting profiles were compared for the imager and manual process.

The results have shown that there was no significant difference on high grade pick up between manual and imager systems. In summary the imager provides improvement in productivity rather than quality. The use of the imager in Scotland has not been approved to date but it is thought that it will be approved in 2010.

#### Swine flu virus

#### Dr Chris Catchpole, Director of Infection Prevention and Control, Worcester Royal Hospital

This presentation gave us an up to date analysis of the swine flu situation in the UK. The presentation went through the clinical features, complications and lab diagnostic testing for this virus. Currently in England there have been 11,000 cases. It is thought that when winter comes to the UK up to one third of the population will be effected by swine flu.

#### Trained to train: a presentation in education, training and management

#### Nicola Cooper, Hull University

Nicola is a senior biomedical scientist and also an accredited trainer. Nicola pointed out that a recent advance in the UK biomedical science profession was the acknowledgement that training officers were vital to the profession. These are professionals who are trained to train. There is now a qualification for trainers called the Certificate of Extended Practice. This course is now in its third year and is run by the University of Ulster. It is a distance learning course and now trainers can have a qualification that proves to employers that they have been "trained to train".

### Preparing your CPD profiles Andrew Usher, Gloucester Royal Hospital

Andrew reminded the audience of the importance of Continuous Professional Development. He also said that from 2010 2.64% of lab staff in the UK would be audited. If a staff member was audited they would need to present a summary of practice history (500 words) regarding their role at work and also supply documentary evidence. He said in future the CPD would be on line. I was guietly pleased that we already have this on line in NZ.

#### Siemens scholarship: the role of biomedical science in healthcare

#### Presentation given by the winning student of the Siemens scholarship, Laura Irving

Laura went though two case studies as a way of demonstrating to non clinical students what we do as Scientists. This was Laura's first major presentation. Even with a few IT hitches she managed to pull off an informative and entertaining talk.

#### **Presidents welcome**

John Stevens, President of the Institute gave the welcome, opening address and introduced Professor Cumming.

#### Managing Change

#### Professor lan Cumming

Prof Cumming gave his opinion on managing change. The introduction of more medical laboratory aides, technology advances and financial constraints would feature highly over the next five years. The positives would be quality, innovation, productivity and prevention and the negatives would be sadness, anger, resentment and acceptance.

Prof Cumming acknowledged that morale in the UK as a biomedical scientist was at an all time low. However, he encouraged the audience to raise morale and prepare for the next challenge.

The Albert Norman Lecture: Advances in Organ Transplantation and the Associated Immunological Consequences Professor Andrew Bradley, Cambridge University

This presentation addressed the issues around organ transplantation in the UK. 33% of organ transplantations come from siblings, 29% from parents, 24% from the spouse and 6% are unrelated. There are currently 910 organ transplantations in the UK per year and 93% of them survive at least 5 years. I was surprised to hear that the mortality rate is only 1 in 2000.

Prof Bradley then went on to explain that if a parent or spouse wants to give an organ to a relative and there is not a successful match then the offer of an organ is put on an organ availability website. Then a complex series of transactions can take place to ensure more transplants can take place. This complex swopping of organs is seen as the way forward in the future of organ transplantation.

#### The Science Council "Future Careers Project" **Professor Peter Holgate**

Prof Holgate pointed out that many major professions have Royal Charters. The Institute of Bio Medical Science now has achieved this level. He encouraged UK Scientists to work towards becoming a Chartered Scientist. There are 5000 Chartered Scientists in the UK. The minimum level of acceptance to be a Chartered Scientist is a Master's degree. The Science Council, who oversee the role of Chartered Scientists, strive to influence science policy and advance professionalism.

#### **UKAS: clinical laboratory accreditation** Paul Stennat, Chief executive of UKAS

Paul explained that UKAS is a private company that works with the CPA board and operates on a memorandum of understanding with the UK Government. UKAS is now the accreditation body for the UK labs. It is a not for profit organisation. UKAS has members, not shareholders. It is also active in other areas of accreditation. For example diagnostic imaging. He summarised by quoting Lord Carter's report. This mentioned impartiality, accreditation should be mandatory and standards should start from when the sample arrives at the laboratory to how it is disposed of following reporting.

The first day of lectures closed at 5 o'clock. One hour later the exhibition of laboratory equipment opened. I have never seen so much lab equipment in one place and have attached some photos below to show the expanse of the venue.

That same evening I was fortunate to attend the President's Reception which took place in the magnificent Round Room of the Birmingham Museum and Art Gallery. After the reception we were all invited to view the recent finding of the largest collection of Saxon gold ever to be found. This certainly was a great opportunity as thousands of the general public were lining up every day to see the gold. The detail and workmanship of the pieces was tremendous.



**Tuesday 29 September** Planning & organising laboratory training Phil Cheetham, Nottingham Trent University

Phil delivered an interesting presentation on the planning and organising of laboratory training to a packed audience. He stated that in the UK there is no specific budget for training of lab staff. There was also no training for senior staff to carry out appraisals. He suggested this should change to structured training. This included the construction of a training plan. Existing resources should be used. HR should be asked to help with training. He went on to say that in every organisation there should be a training manager who would oversee training officers. This was greeted with enthusiasm from the audience.

### Accredited practice trainers: what are they? Samantha Jewell, College of Radiographers

Samantha informed the audience that radiographers in the UK already have accredited trainers and suggested the Institute should follow this lead. She said that traditionally it was only the staff who liked teaching others that got the job of training students and new staff. She advised us that accreditation not only assures quality in training but it also formalises good practice in workplace education.

In radiography there are two ways to get accredited as a trainer. The first is a programmed course and the second is an application form that requires detailed evidence of experience in training. Once trainers are accredited they are put on a register for five years. Revalidation is required after 5 years. The audience liked the idea of accreditation for trainers. However, they were sceptical that the Trusts would fund it.

### How to assess competence: a practical guide *Chris Murphy, University of Hull*

Chris defined competence as an incorporation of formal and informal knowledge and the ability to think. He said that portfolios of training and competence levels should be put together as a collection of evidence. The levels of competence should be competent, proficient and expert. He also felt that records of competency should be totally electronic and not in paper form. The advantages of electronic records of competency were to make assessment validation easier and increase the reliability of the assessment.

#### Professional doctorates or PhD: are they necessary? Dr Geoff Bosson, University of Northumbria

Dr Bosson opened by giving a history of Doctorates. In 1150AD Paris gave the first Doctorates for Law, Medicine and Theology. He then went on to show the route to a Doctorate, i.e. Bachelor degree, Master's degree and finally a Doctorate. In 1850 Paris introduced a PhD. In 1860 Harvard, USA introduced a Doctorate and in 1917 Oxford followed with their PhD.

He then went on to encourage delegates to pursue the path of a Doctorate. He said that a PhD proved the person had completed a structured investigation to advance knowledge. He went on to explain that a professional doctorate was a taught degree and a PhD was a research based degree. The advantage of having a PhD is a very personal process. It proves that the holder has the ability to complete an intensive course of research at the cutting edge. The disadvantages are that it takes on average three years full time or up to seven years part time to complete. The average cost in the UK is 5,000 pounds per year. Some support is available in the form of research grants. However family support and employer support are very important.

The afternoon session started with the presentation of short papers. The most interesting presentation for me was to be from Joanne Torez. Unfortunately she was not available to present it. One of her work colleagues gave the presentation.

# The development of a new histology paraffin block softening agent and the partnership with a company called Cell Path to market the product

Dense kerotic tissue is often difficult to section. A number of commercial tissue softeners were compared. Some contained acids and phenols which are environmentally unfriendly. A new softening agent made up of fabric softener and fairy liquid type products was compared to the existing available softeners and good results were obtained. St Thomas's NHS Foundation Trust then worked with the company Cell Path for the final commercial product. I look forward to trying this new environmentally friendly softener in our NZ lab.

#### Histodissection – the next step Gordon McNair, Antrim Hospital Ireland

This is one area in which I feel the UK is leading NZ. Gordon is also a lecturer at the University of Ulster on histodissection. He informed us that in 2002 in the UK a working group was formed to draft an examination for scientific staff who wanted a formal qualification in histodissection.

42 candidates have sat the examination over the past 5 years. The examination is called the Diploma of Extended Practice. The terms of reference are a training programme for dissection. This does not include reporting. Initially there are two categories: Breast and Gastro.

Eligibility to sit an advanced exam called the Advanced Specialist Diploma in breast pathology include: candidates must be a Fellow of the Institute, a registered biomedical scientist, two years dissection experience, have the basic diploma of extended practice and support of the Manager.

Following this presentation Gordon and Carole Turnbull from the Belfast City Hospital, who also trains Scientists in dissection, both said that if an opportunity arose they would both be delighted to come to NZ to mentor histodissection training or be involved in a qualification.

#### Lab of the future

#### Dr Stefan Dojcinov, University of Wales

Stefan saw the most advances in Technology to come through molecular genetics. He also saw the development of large "hub labs" that could cope with advanced technologies. All the other satellite labs would simply carry out the standard lab tests and the more complicated requests would go to the hub lab. In this way duplication of expensive testing would be eliminated.

This was the last presentation for the day. When I was leaving one of the organisers advised me that several of the delegates had noticed that I worked in NZ. Apparently they had expressed a keen interest in working in New Zealand. I managed to catch up with two of them later and encouraged them to investigate further. It came to me that it may be an opportunity for the New Zealand Institute of Medical Laboratory Sciences to have a stand at the next congress displaying the merits of working in NZ. The day finished at the Companies Members evening and time to relax after two days of stimulating presentations.

#### Fitness to practice: ensuring patient safety Neil Willis, University Hospital of Wales

Neil gave us an insight into the Health Professional council who oversee fitness to practice. This is a similar organisation to the NZ Board. He went through the process of the HPC receiving an allegation of malpractice. He also went through tribunal procedures. The majority of complaints come under misconduct, a lack of competence, a criminal conviction or health status. Sanctions include taking no further action, mediation, caution, conditions of practice, suspension and striking off.

#### A disciplined approach to disciplinary issues Gary Owen, Lead Officer for the Med Lab Scientists Union (Unite)

Gary began by explaining the difference between discipline and grievance. Discipline comes from the employer and grievance comes from the employee. The key stages of the disciplinary process are:

- 1. The alleged incident
- 2. Investigation.
- 3. Hearing
- 4. Decision
- 5. Appeal
- 6. Decision.

If the employee is not happy with the decision they have the right to ask for the case to be taken to a tribuneral. However in the UK the maximum compensation for winning the case is less than 5,000 pounds.

#### Standards of ICC and ISH: UK NEQAS Dr Merdol Ibrahim from the NEQAS Quality Assurance

#### Programme

Dr Ibrahim explained that NEQAS are now assessing 600 labs from 57 countries around the world. They are now sending out 5000 slides per run. There are four runs per year. NEQAS now have an on line system that can show labs what antibodies are working at the optimum level. He said that the main problem they came across was insufficient retrieval. Quite a high proportion of labs in the UK are still using pressure cookers for retrieval. He also said that he felt it was important for scientists and pathologists to discuss the assessments.

#### Current therapies in breast cancer

#### Marina Parton, Royal Marsden and Kingston Hospitals, London

Currently in the UK there are 13,000 deaths per annum and 42,000 positive diagnoses per year. Marina went on to explain that when a lumpectomy is carried out, radiotherapy is essential. If nodes are involved radiotherapy is also essential. She went on to say that if a positive diagnosis is found then surgery is essential within one week. If chemotherapy is needed then this must start before 31 days post surgery. Marina concluded by saying that in the future UK patients would be given personalised rather than standardised regimes to treat the disease.

#### UKNEQAS for CPT Assessment- the 3 Cs David Evans and Harry Elliot, Royal Victoria Infirmary, Newcastle

The audience were given electronic score cards and asked to score stained slides. Generally the audience scored very well.

#### EQA – a veterinary perspective Brian Kelly, University of Edinburgh

Brian gave a detailed account of the quality assurance scheme set up in the UK to assess stained slides in animal tissues. In the vet scheme there are 39 labs in the UK, 3 in Australia and one in Dublin. All of them handle tissue from animals. The animal tissues come from vet schools, government diagnostic labs, commercial labs and research institutes. The techniques assessed include H&E, MSB, Giemsa, Warthin-Starry and the Gram stain. Currently there is no accreditation scheme for vet labs. However, the vision is to equal the standard set by med lab science.

On that note the 2009 Biomedical Science Congress presentations concluded. I was pleased to be given this opportunity to attend an International Biomedical Science Congress. I came away with renewed enthusiasm and an update of knowledge. It is good to know that that LabPlus, Auckland City Hospital, NZ, is up there with the best practice and technology available anywhere in the world. I would like to thank LabPlus for the opportunity of attending this International Congress.

Dr Joe McDermott LabPlus, Auckland



# New products and services

### Radiometer ABL90 blood gas analyser wins Medical Design Excellence Awards 2010!

The ABL90 is a state of the art cassette-based blood gas analyser, built on the strong foundations of Radiometer's more than 50 years' research and development. The innovative design boasts smallest sample size, fastest time to result and minimum downtime and won the prestigious Medical Design Excellence Award for 2010.

The sample path of the ABL90 is short and straight, with only 65ul required for 17 tests: pH, Blood gas, 4 electrolytes, Glucose, lactate and full co-oximetry including Fetal Hb and Bilirubin. Results are available in record-breaking 35 seconds, including a check of the system and sample path before release of the patient result.

Downtime required for calibration and maintenance is dramatically reduced: the analyser uses only 2 consumables with 1 month maintenance free on-board lifetime. The consumables can be moved between analysers if required. Calibrations, quality control, system checks and corrective actions are automated and fast. As an example, the downtime for an average automatic calibration is only 2.5minutes every 4 hours. Traditional quality control principles are maintained, using 3 totally independent quality control solutions run automatically every 8 hours.

Connectivity to Radiometer's Radiance software allows remote monitoring, LIS/HIS connectivity and data management. For those Labs aiming towards paperless, the ABL90 via Radiometer's 1<sup>st</sup> automatic package downloads patient data from the bedside to the analyser in a totally paperless system.

This compact analyser (25x29x45cm) weighs in at only 11kg and offers a truly portable solution, able to perform up to 15 tests on battery back-up. The ABL90 is ideal for low to mid-volume POCT and laboratory sites and together with ABL80 and ABL800 series and Radiance middleware, Radiometer is able to offer a comprehensive solution for all blood gas requirements.

#### Radiometer announces the launch of whole blood Troponin T

The profile of Radiometers AQT90 STAT immuno-assay instrument has been further enhanced by the acquisition of the rights to the Roche Troponin T antibody.

The AQT 90 is a whole blood, random access analyser with typical turnaround times around 12 to 15 minutes. Ease of use, sampling through the cap and full connectivity make the analyser suitable for Point of Care, smaller Laboratories or as a back-up analyser. Sample volumes are flexible from 1 test per day up to 30 tests per hour.

The current test menu now includes Troponin T, Troponin I, Myoglobin, CK-MB, D-dimer, CRP, BHCG and NT-proBNP with INR and aPTT in progress for release in 2011.

Radiometer's goal is to provide stat options for the tests where clinical demands for fast turnaround times cause disruption to the main laboratory workflow. The AQT makes placement at POC a viable option by meeting the fast TAT needs of Clinicians while offering Laboratory quality results, connectivity and control to satisfy the requirements of Lab staff.

### For further information please phone Radiometer on 0800 723 722 or visit our stand at NZIMLS.

## Med-Bio Journal Award



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

Studies are judged under the NZIMLS Journal Prize)

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

### **NZIMLS Journal Prize**



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

Case studies bring together laboratory results with the patient's medical condition and are very educational. Many such studies are presented at the Annual Scientific Meeting, SIG meetings, and

the North and South Island Seminars, yet are rarely submitted to the Journal for wider dissemination to the profession. Consider submitting your case study presentation to the Journal. If accepted, you are in consideration for the NZIMLS Journal Prize and will also earn you CPD points. Please contact the Editor or any Editorial Board Member for advice and help. Contact details are on the NZIMLS web site (www.nzimls.org.nz) as are instructions to authors.

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

Winner of the NZIMLS Journal prize for 2009 was Sujata Hemmady, Department of Chemical Pathology, LabPlus, Auckland for her article "Adrenal carcinoma: a case study. N Z J Med Lab Sci 2009; 63 (2): 48-50

# Auckland University of Technology – NZIMLS Student Award

AUT held its annual awards ceremony on 28th May and celebrated students achieving excellence in medical laboratory science over the 4 years of their study. Elly Sekikawa the NZIMLS won prize for the most outstanding Bachelor of Medical Laboratory Science graduate. She is pictured receiving the cheque from Margaret Matson on behalf of NZIMLS. Elly also won 3 other prizes; for her top performance in Medical Microbiology, Clinical and Chemistry her research project work. **Congratulations Elly!** 



## News from the universities degree courses

### Medical Laboratory Science Programme, University of Otago

At the end of 2009 it was pleasing to see all our Fourth-year students graduate. In addition to graduation three of the students were awarded NZIMLS sponsored prizes for the best second, third and fourth year results. The second year prize went to Katrina Hong, third year prize to Merin Thomas and the fourth year to David Becker. Other prizes awarded were the Jim Le Grice prize to Samantha Watts for top Diagnostic Chemical Pathology student and the Colin Watts prize to David Becker, for the best overall student in the four year degree.

In 2010 the year started with the appointment of Professor Ian Morrison (a Clinical Haematologist) as the new Head of Pathology, Cat Ronayne (an ex-Otago BMLSc student) as a Professional Practice Fellow and Terry Taylor from Southern Community Laboratories as the new NZIMLS representative on our Board of Studies. Cat has taken responsibility for our second year paper "Introduction to Diagnostic Pathology".

So far this year we have been focusing on reviewing and consolidating our courses. As a result of this we are introducing a new Fourth-year Immunology paper to commence in 2011, which will relate specifically to Immunology as a clinical discipline.

Finally I would like to thank and acknowledge the help from all the diagnostic laboratories who take our students on Clinical Placements. The success of the degree programme is dependent on the goodwill and help from diagnostic laboratories in providing the Clinical Placements.



### **Roche Diagnostics NZ Ltd**

Diversity: the art of thinking independently together Malcolm Stevenson Forbes

At Roche Diagnostics NZ we are committed to creating an environment that encourages and supports diversity, sharing new ideas, new ways of working and developing the best solutions for our customers with the best outcomes for patients.

Make sure to drop into the Roche Diagnostics stand at the NZIMLS conference, grab a coffee and share your ideas with our team.

# Journal questionnaire

Below are 10 questions based on articles in the August 2010 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 recommend that you write your answers in a word document and then cut & paste your answers on the web site.

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

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

The site will remain open until Friday 15<sup>th</sup> October 2010. You must get a minimum of 8 questions right to obtain 5 CPD points.

#### August journal questions

- 1. Name the three types of von Willebrand disease.
- What is the important role of the von Willebrand factor in primary heamostasis.
   Name the usual laboratory investigations in surported cases of
- Name the usual laboratory investigations in suspected cases of von Willebrand disease.
- 4. What are the confirmatory tests for von Willebrand factor disorders.
- 5. How may a patient suspected of von Willebrand disease present clinically.
- 6. By what principles do the vWF:RCo and the HaemosIL assays measure plasma von Willebrand factor.
- 7. What is vitamin D deficiency known to be associated among children and adults.
- 8. What can highly elevated levels of vitamin D cause and what can it lead to.
- 9. What is the main form of vitamin D in circulation and which form of vitamin D becomes detectable when taking vitamin D supplements.
- 10. What factors may cause interference in the Elecsys vitamin D (25-OH) assay.

# Questions and answers for the April 2010 journal questionnaire

- What are the reasons for the significant differences in sensitivity amongst PCR methods for TB bacilli.
   Presence of amplification inhibitors, type of primer used, genomic sequence amplified and the number of mycobacteria.
- What is the gold standard for diagnosis of tuberculous pleural effusion, but what are potential problems.
   Pleural biopsy is the gold standard. Potential problems are that it is an invasive procedure and there are risks of complications.
- 3. In patients with tuberculous pleural effusion what is the positivity of pleural biopsy culture and what does histological examination reveal.

Positivity is 39% to 80% of cases. Histological examination reveals granulomatous inflammation in 50% -97% of cases.

 Apart from tuberculous pleural effusion, in what other conditions can elevated levels of adenosine deaminase be found.

Lymphoma, empyema, malignancy, pneumonia and rheumatoid-associated pleural effusions (rheumatoid arthritis or systemic lupus erythrematosus.

- 5. What do do the initials of HELLP syndrome stand for. Haemolysis, Elevated Liver enzymes, Low Platelet count.
- In HELLP syndrome, what is maternal morbidity mostly associated with.
   Disseminated intravascular coagulation (DIC), placental
- abruption, acute renal failure and ruptured liver haematoma. 7. What are the symptoms of HELLP syndrome. Epigestric pain, nausea and/or vomiting, non-specific viral illness-type symptoms, visual disturbances, headache,
  - bleeding from the gums, jaundice, and neck or shoulder pain.
- 8. What contributes to the significant maternal and fetal morbidity and mortality involved with HELLP syndrome. Disseminated intravascular coagulation (DIC), placental abruption and fetal death.
- What is the major concern of the use of point-of-care glucose meters and what has previously compromised their performance.
   The major concurn is analytical interference. Maltose and

heamatocrit previously compromised their performance.

 Which glucose meters showed the closest correlation with the plasma hexokinase reference method and what additionally did they demonstrate.
 The StatStrip and Advantage. They demonstrated the

The StatStrip and Advantage. They demonstrated the lowest absolute bias.

# Advertisers in this issue

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Greetings to you all from the three of us at the PPTC



John Elliot Director

The first half of 2010 has now passed and the PPTC continues with its busy schedule in the delivery of its teaching and training programmes both at home and throughout the Pacific.

#### Courses held at the PPTC in early 2010

A Haematology and Blood Film Examination course was held at the PPTC from the 1st - 26th March 2010 and five students from both the North and South Pacific regions attended. They were: Ricky Eddie from the Solomon Islands March Kloulubak from Palau

Yoichy Aut from Chuuk Telesia 'Apikotoa from Tonga Jiosese Mailulu from Nauru

The course as always was a great success and we are grateful to Phil our Programme co-ordinator for the excellent tuition and practical training given to the students throughout the duration of the course.

#### Students and staff of the Haematology Course





Christine Story Medical Laboratory Scientist

> This year, the PPTC has scheduled two further courses to be held at its centre in Wellington New Zealand. The course dates are as follows:

Phil Wakem

**Biochemistry** 26<sup>th</sup> July – 13<sup>th</sup> August Blood bank possibly 4th Oct - 29th Oct

#### **POLHN Distance Learning Programme**

A final opportunity for students to complete any remaining POLHN distance learning modules for the PPTC's Diploma in Medical Laboratory Technology is being offered during this year. Starting dates for each of the modules is scheduled as follows

POLHN 017 Blood Bank Technology 5 July 2010 POLHN 016 Microbiology: 6 September 2010 POLHN 018 Immunology: 1 November 2010

2011 will see a change in course requirements in terms of the practical element of the POLHN programme.

#### Visits to Pacific Island laboratories

Vanuatu: In April of this year, John travelled to Vanuatu as a UNFPA consultant to evaluate laboratory procedures used in the diagnosis of HIV and STI's and to carry out training in these areas. He spent time in the laboratories in Port Vila and Luganville.

#### Federated States of Micronesia (Chuuk, Pohnpei, Kosrae) and the Marshall Islands.

On the 8<sup>th</sup> of May, Phil began a three week journey to the North Pacific to visit hospital laboratories in Chuuk, Pohnpei, Kosrae and Majuro. During his stay in each of the countries, he was given the opportunity to meet with officials from each of the Health Ministries, address laboratory EQA and QC, perform quality assessments, discuss future directions of the PPTCs POLHN distance learning programme and teach blood cell morphology as time permitted. He was well looked after over the three weeks and sends a big thank you to all the staff for making his visit so successful.

### Programme Co-ordinator Upcoming courses to be held at the PPTC during 2010

WHO's strategy for strengthening health laboratories in the region

In 2009, WHO finalised a document entitled "Asia Pacific Strategy for Strengthening Health Laboratory Services (2010 – 2015)". To commence the implementation process of this document, WHO staff and consultants have visited six countries (Fiji, PNG, Kiribati, Tuvalu, Solomon Islands and Nauru) in the region to carry out laboratory assessments and discuss the introduction of a National Laboratory Policy and Plan with Ministries of Health. In each country this document was well received and a draft national plan was written and then discussed and left with senior laboratory and Ministry of Health officials for them to continue the drafting process for the plan. John was involved as the WHO Consultant in this process in Honiara and Nauru and he thanks the laboratory staff for their willingness to spend time discussing the various issues that currently hinder improvements in their service provision.

The next part of the implementation process is a WHO meeting to be held in Fiji in September at which there will be representatives from all Pacific Island Country health laboratories. This meeting, at which the PPTC will be taking a prominent role, will be used to help countries draw up national plans and policies for laboratories and in addition a draft document proposing a regional standard for health laboratories will be introduced, discussed and hopefully accepted.



### New Zealand Institute of Medical Laboratory Science

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

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

#### Examination

Consists of two parts:

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

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

#### Thesis

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

#### **Publications**

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

#### Exemption

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

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

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

For full Fellowship regulations and application process visit the NZIMLS web site: <u>www.nzimls.org.nz</u>

### **Special Interest Groups**



**NICE 2010** was a great success with 86 delegates attending the Wairakei Bayview over the first weekend in May. There was a wide variety of topical papers, case studies and posters, with much discussion generated from the floor as usual. Raewyn Cameron and Diane Whitehead did a wonderful job as co-conveners. We also thank all our industry sponsors for their support.

Martin Le Roux from NZBS Waikato won the Abbott award for the best presentation with a fascinating talk entitled "Possible detection of HIV elite controllers in blood donor populations". Martin is pictured receiving his award from Murray Craft of Abbott.

The Pharmaco poster award went to Fia Saumamao from MedLab Central Wairoa for his poster "A case of post diarrhea haemolytic uraemic syndrome with Anti-M".

The Bio-Rad first time speaker award went to Lee Neale from Waitemata DHB for her entertaining and informative case study "A recipe for disaster, or not?"

Congratulations to all prize winners.



The Organising Committee for the NZIMLS Annual Scientific Meeting in Paihia 24-27 August 2010 have invited Imelda Bromilow to be the Transfusion speaker.

Imelda is running an interactive workshop with case studies and antibody identifications and giving a paper on Laboratory errors. Consult the conference website <u>http://www.eenz.com/nzimls10</u> for more details.

Imelda was born and educated in the United Kingdom, and studied at Liverpool and Manchester Universities. She holds a Master of Science higher degree as well as professional qualifications in Transfusion Science and Haematology, and Management. She is a Chartered Biologist and worked as a Clinical Scientist at the Mersey and North Wales Blood Transfusion Service (NBS) until 1995, before moving to Switzerland where she served as the Scientific Affairs Manager for DiaMed AG, a company manufacturing clinical diagnostics, mainly for use in Immunohaematology laboratories and blood banks. Prior to moving to Switzerland, Imelda lectured at several Universities, teaching medical undergraduates as well as post-graduate students undertaking professional qualifications or higher degrees and medical officers who were studying for examinations at the Royal College of Pathologists in the UK. In April this year, she moved to Melbourne to take up the role of General Manager, Scientific Support for Lateral Grifols PTY. She is a Founder Member of the British Blood Transfusion Society (BBTS) and served on the Council for 3 years, including the original Steering Group for Education and Training in Transfusion. Her other professional affiliations include the International Society of Blood Transfusion (ISBT) and the American Association of Blood Banks (AABB).

Imelda has been involved in organising and lecturing on International Transfusion Science courses held in Switzerland, with speakers who are well known in our field of expertise. She also organised and lectured regularly on many courses held further afield, notably in Central America, India and South East Asia. The first Transfusion Science course that she organised here in Australia was open to Australians, New Zealanders and individuals from Asia. It will be held in Melbourne in September of this year and in 2011, the educational programme will continue. Promoting education in Transfusion Science in order to support safe blood transfusion remains one of her most passionate interests. She was presented a few years ago with an award from the International Society of Blood Transfusion (ISBT) for outstanding services to educational in Transfusion Science and Medicine.

Imelda is co-author of "Essential Guide to Blood Groups" with Dr Geoff Daniels, published in 2007 with a new and updated edition published in August this year. She has also authored/co-authored numerous papers published in peer-reviewed scientific and medical journals, presented scientific abstracts at international meetings, plus she was co-author with of a chapter on Immunohaematology in a textbook relating to Quality Assurance issues. Imelda has given many presentations at conferences all around the world but this is only her second time in New Zealand, having taken part in the NICE meeting earlier this year.

#### **BSIG-What a Gig!**

This year the Biochemistry Special Interest Group seminar was held at the Chateau on the Park, Christchurch on 12 June.

Unlike last year, with a last-minute venue change after the conference facility burned down, this year's meeting went without a hitch. The venue was outstanding, having secured the Camelot Room with its old world charm, and Christchurch turned on a beautiful day for delegates to enjoy lunch and coffee breaks in the surrounding gardens of the Chateau.

The scientific program was full and varied and of the 15 speakers, 8 were first time presenters. Although the majority of the people who spoke for the first time said they were very nervous, no nerves were evident and the presentations came across in a very polished way and all to a very high standard. The Biorad Best First Time Presenter prize was awarded to Eleanor Grant from Aotea Pathology with a presentation entitled *The Trick Sticky Antibody*. The Abbott Best Overall Presentation award went to Sue Grant from Canterbury Health Laboratories for her presentation entitled *Trace Metal Analysis using ICP-MS-To Infinity and Beyond*.

Three invited, local, speakers provided a diverse in-depth wealth

of knowledge each tailoring their individual fields of expertise to a biochemical spin. From Dr Alexa Kidd, Clinical Geneticist, Canterbury Health Laboratories who gave us a thought-provoking synopsis on the role of a Clinical Geneticist, to Associate Prof Chris Florkowski, Chemical Pathologist, Canterbury Health Laboratories who really tested our acquired knowledge over the years with an historical timeline of diabetes and a fun quiz.

The meeting was bought to a fitting conclusion with a presentation by Dr Martin Sage, Regional Forensic Pathologist, who shared with us that *It's Different Being Dead*.

The evening meal was a sumptuous three course dinner with a Mid-Winter theme at the Chateau brasserie.

Thank you to all the presenters, those who offered and those I bullied into submission, to the chair people, the judges, the helpful staff at the Chateau, the sponsors: Biorad, Abbott Diagnostics, Beckman Coulter, Roche and LabPLUS; and to all the delegates who gave up a precious weekend to attend the seminar.

Thank you all so, so much...you rock!

Sandy Woods BSIG Convenor

#### North Island seminar

Approximately 130 Medical Laboratory people from throughout the North Island attended the seminar held at the Plymouth International Hotel in New Plymouth on Saturday 15<sup>th</sup> May. An interesting program covering diverse topics was offered. Our four medical presenters in the morning session spoke on CRP in the ED situation, the female athletic triad, LFTs from a paediatric perspective and scene of death examination.

After lunch we continued with presentations on subjects ranging from vitamin B12, ethics, syphilis and endocarditis. Some very interesting case studies were heard.

Congratulations to Nick Heffernan from Aotea Pathology Wellington for winning the best first time presenter award (*A Holo promise – when B12 goes bad*!) sponsored by Biorad and to Judith Rowland from LabCare Pathology New Plymouth for winning best overall presentation (*An unusual case of endocarditis*) sponsored by Abbott.

Thanks also to Roche for continued sponsorship. A stimulating day program was followed by a very enjoyable dinner and dance at night.





The NZIMLS Journal is holding its very first photo competition, giving NZIMLS members the chance to win an Olympus digital camera and have their work published in the journal.

The competition theme is "Medical Laboratory Science", so whether it's related to haematology / histology, laboratory personnel, instruments, humour, or other, there's plenty of scope for keen photographers to showcase their talents.

Olympus, a leading manufacturer of professional opto-digital products, has generously donated a digital camera worth over AUD\$500 as the prize for the best photo. The camera is a Tough 8010 - 14MP (5x, 28mm wide, Shockproof 2m, Waterproof 10m, Snowproof, Crushproof 100kg, HD Movie 2G Internal Memory, USB & In-Camera Charging).

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

Entries close on **5pm on Friday 17 September 2010**, with the winning photo appearing in the November 2010 issue of the NZIMLS Journal.

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

For further information about the competition, go to: <u>www.nzimls.</u> <u>org.nz</u>



# NZIMLS Annual Scientific Meeting Bay of Islands, Northland 2010



NZIMLS / NZSC Annual Scientific Meeting Copthome Hotel & Resort Paihia, Bay of Islands, 23-27 August 2010

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- Workshops Tuesday 23<sup>rd</sup> August
- Plenary plus concurrent sessions Wednesday 24th Friday 27th
- Proffered papers wanted!
- For further information contact Ross Hewett at LabPLUS, Auckland City Hospital or on rossh@adhb.govt.nz







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