New Zealand Institute of
Medical
Laboratory
Science

ISSN 1171-0195 Volume 60 Number 3 November 2006

60 years in publication

New Zealand Journal of Medical Laboratory Science

Official Publication of the New Zealand Institute of Medical Laboratory Science Incorporated

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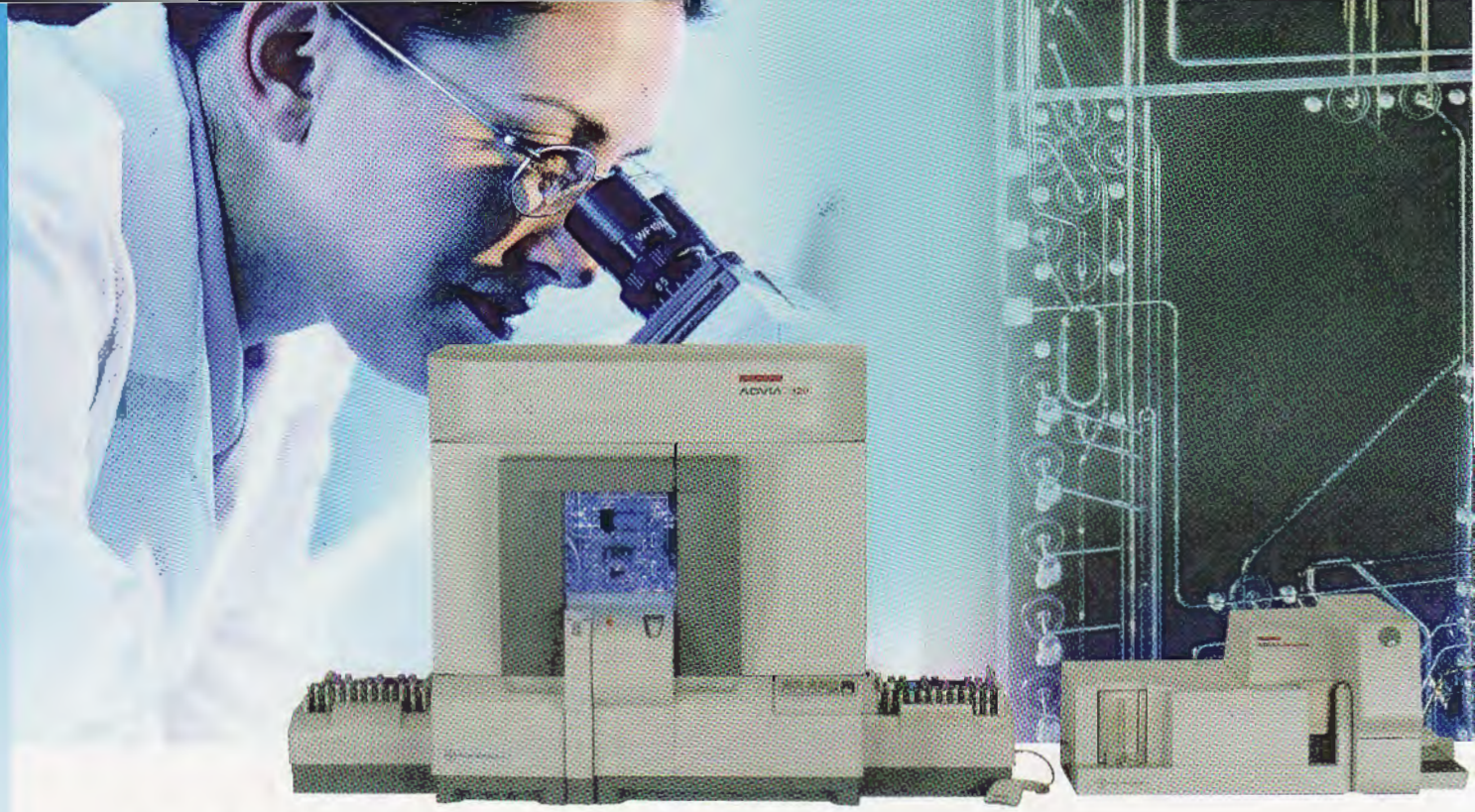

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 The Journal is published three times per year in April, August and November, printing by Centurion Print, PO Box 6344, Wellesley St., Auckland.

The Journal is abstracted by the Cumulative Index to Nursing and Allied Health Literature (CINAHL), Index Copernicus, Excerpta Medica/EMBASE, and the Australian Medical Index. The journal, through its Editor, is a member of the World Association of Medical Editors (WAME).

Advertisement bookings and enquiries should be addressed to the Advertising Manager: Trish Reilly, 48 Towai St., St Heliers, Auckland 5. Phone: (09) 575 5057, Fax: (09) 575 0698.

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E-mail: fran@eenz.com.

New Zealand Journal of
Medical Laboratory Science
Volume 60 Number 3
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TH Pullar Memorial Address
Echoes from the past, implications for the future
Robin Allen.....87-91

Original article
Comparison of real-time PCR with culture and EIA for the diagnosis of mucocutaneous infections with herpes simplex virus
Gloria E Evans, Kirsten A Beynon, Alvin Chua, Trevor P Anderson, Anja M Werno, Lance C Jennings, Sylvia K Y Mai, David R Murdoch.....92-96

Case studies
The hidden diagnosis - a case study
Barbara A Hoy.....97-98
Mycosis fungoides is not a fungal infection
Kirsten J Stack, Davis Roche.....99-101

Special article
Performance of the NZIMLS and the services it provides. Results from a questionnaire
Rob Siebers, Anne Buchanan, Ross Hewett.....102-105

Historical article
Massive exchange transfusion in a predicted case of haemolytic disease of the newborn
P H Curtiss.....106-108

Reports
President's report
Chris Kendrick.....110-111
Abstracts of presentations at the NZIMLS ASM, Napier, August 2006.....124-136

Regular features
Instructions to authors.....85
In this issue.....86
Med-Bio Journal prize.....86
Fellowship.....114
Journal-based questionnaire.....118
Pacific Way column.....112-113
Special Interest Groups.....114-117
Abstracts of articles in the *British Journal of Biomedical Science*.....120-122
Advertisers in this issue.....113

In this issue

In the article by Gloria Evans and colleagues, real-time PCR, enzyme immunoassay and centrifugation enhanced cell culture techniques for the diagnosis of herpes simplex virus were compared. The real-time PCR had increased sensitivity over the other two techniques, had genotype capability and was rapid, making it a suitable assay for the clinical laboratory.

In this issue there are three case studies. The first, by Barbara Hoy, presents a case of haemolytic uraemic syndrome. The case presentation was atypical and the final diagnosis was not initially suspected although vital clues were present in routine laboratory tests. This case led to the adoption of new protocols and more effective exchange of information in the author's laboratory.

The second case study by Kirsten Stack and David Roche is on a patient presenting with itchy skin lesions that was ultimately diagnosed as mycosis fungoides, which the authors state is not a fungal infection, but a T-lymphocytic lymphoma primarily involving the skin. Diagnosis of this case involved clinical and histological appearances, immunohistochemistry, and review by international experts in dermatopathology.

The third case study in this issue was the 1st case study ever published in the Journal in 1949. It involved a case of Rh incompatibility where massive exchange transfusion was successfully applied. It showed the importance of the laboratory in those times (and still does) of routine Rh typing in the ante-natal setting.

In a special article, Council members present the results from a recent questionnaire on the performance of the NZIMLS services. SIG seminars, continuing education and the CPD programme were seen by members to be very important. Members rated promotion of the profession by Council lowly. Although the response rate was disappointing, the results, together with the many comments made by members, should help Council in improving its services.

Also in this issue is the NZIMLS President's report, the TH Pullar Memorial Address by Robin Allen, and the abstracts of the recent Annual Scientific Meeting in Napier. Regarding the latter, as per editorial policy, any abstract stating that "results will be discussed" or "results will be presented" has been omitted. Thus, only abstracts that are informative will be found in this issue.

In this issue you will again find a new journal-based questionnaire. You will need to get at least 7 out of 10 questions right to earn 5 CPD points. Read the journal, questions are from most of the articles.

Med-Bio Journal Award

med·bio

Med-Bio offers an award for the best article in each issue of the New Zealand Journal of Medical Laboratory Science. All financial members of the NZIMLS are eligible. The article can be an Original, Review or Technical Article, a Case Study or a Scientific Letter. Excluded are Editorials, Reports, or Fellowship Treatises. No application is necessary. The Editor and Deputy Editor will decide which article in each issue is deemed worthy of the award. If in their opinion no article is worthy, then no award will be made. Their decision is final and no correspondence will be entered into.

The winner of the Med-Bio Journal Prize from the August 2006 issue was Lesley Newton from Canterbury Health Laboratories, Christchurch for her article "An unusual case of septicaemia". *N Z J Med Lab Sci* 2006; 60 (2): 59-60.

Echoes from the past, implications for the future

Robin Allen
Haematology Department, Waikato Hospital, Hamilton

Mr. President, distinguished guests, members of the Institute, colleagues and friends. I consider it a great honour to be asked by the Council to deliver the TH Pullar address at this year's annual scientific meeting.

Earlier this year I returned from three weeks leave to be greeted by the usual mountain of mail that seems to be the penance that one must suffer for having the temerity to absent oneself from the workplace for any significant period of time. In attacking the stack of correspondence, I came upon the letter of invitation from Council. Although taken aback that I should be deemed an appropriate member of the profession to deliver this address, I replied confirming my acceptance. It was only then that I cogitated on the implications. There was the profound realisation that the invitation is generally deemed to identify one as a member of the profession's senior citizenry. While you might be surprised to learn that I'm actually not as athletic as I appear, I shall at this stage beg to be excused from membership of said geriatric club.

Having recovered from what my grey hair had landed me in, my thoughts turned to addressing the question of a suitable topic. Should I take something from the conference theme? The proposal to get smashed in the Hawke's Bay certainly looked promising. The offering of an enology workshop, the fact that there are 55 wineries in the region and the promise of a conference dinner at one of the vineyards certainly indicated that this might be a fruitful subject upon which to opine.

There was also the suggestion that we had heard about the conference through the grapevine. Was this the intent, or was there an oblique meaning perhaps related to the current round of DHB driven rationalisations, and the way in which many members of the profession have learned of the various plans for restructuring and the possible ramifications.

"Heard it through the Grapevine" is of course also a well known song from the 1970s. In the lyrics one can perhaps elicit figurative comparisons to the participants in the current laboratory restructuring debacle. In the song, the narrator (perhaps this is a laboratory) has no clue that their relationship is in a bad state, and only learns after hearing gossip "through the grapevine" that the partner (the DHB) is cheating (or perhaps looking to get into bed with a new provider).

On a more serious note, this year the Institute celebrates 60 years since incorporation by the registrar of societies. Although formed in 1945, the original New Zealand Society of Bacteriologists was not registered with the registrar of societies until the following year, 1946. This is the same year that the Institute journal was first published.

Of significance, 2006 marks 40 years since the death of Thomas Henry Pullar, whose memory this address perpetuates. With this in mind, I thought it might be informative to revisit some of the key themes from previous addresses and consider the implications for the current state of the profession and future directions.

It is traditional to preface this address with some comments pertaining to the very significant contributions that Dr Pullar made in the field of pathology in New Zealand. This year it seems appropriate to quote from the 1976 Pullar address given by Sir John Staveley. Sir John, or Jock as he was known, was a pioneer in the field of New Zealand blood transfusion. He died three months ago at the age of 91. His distinguished career in laboratories started immediately following World War II at Auckland Hospital where he established the original blood transfusion service. During his long association with the transfusion service he earned the utmost respect of his laboratory colleagues including the many scientists who worked with him. Sir John was a visionary who, as early as the 1950s, advocated for a national blood service which was finally established in 1998. I quote from his thoughts on Thos Pullar.

"Dr Pullar was known universally by the nickname "Thos" and was greatly respected throughout the country both as a man of high principles and a sound clinical pathologist. He was born in Auckland in 1907, but was educated primarily in Scotland and England. He was appointed Pathologist to the Palmerston North Hospital in 1937 and he remained in that post until deteriorating health made it necessary for him to lighten the workload. In 1963 he moved to the milder climate of Tauranga and engaged in a part-time private laboratory practice. Unhappily, this lasted only three years. He died in 1966. The period during which his great contribution to the advancement of clinical pathology and medical education was made was during the Palmerston North segment of his career. Any aspect of medical laboratory work was of importance to him. He was intensely involved in the training and welfare of medical laboratory technologists".

As an addendum to Dr Staveley's comments, Thos Pullar was involved in the formation of the Medical Laboratory Technologists Board, and helped draft conditions of employment used in medical laboratories throughout New Zealand. He was actively involved with examinations, preparing syllabi for the intermediate examinations and was an examiner for many years. Given Dr Pullar's championing of medical laboratory science in New Zealand, it is highly appropriate that the Institute continues to honour his memory through this annual address

Having spent the greater part of my laboratory career in haematology, I was pleased to note that the honour of delivering the first Pullar address in 1967 went to Dr Frederick Gunz, a haematologist of international repute. Dr Gunz's topic was the then new subject of cytogenetics, a discipline which had developed as a separate field of human pathology only once it was possible to study human chromosomes in detail. Dr Gunz's address was an erudite scientific dissertation on the techniques involved in chromosome analysis, highlighting the newly identified chromosome abnormalities, particularly those associated with leukaemia. He highlighted the rapid expansion of knowledge in the field with an observation that until only eleven years previously the textbooks had all reported the number of human chromosomes as 48 - 23 pairs of autosomes and one of sex chromosomes. It was in 1956, only 50 years ago, that the necessary techniques were developed to

visualize and count chromosomes and identify the correct number in humans as 46.

What of cytogenetics in 2006? It is not my intention to review the considerable scientific advances made in this branch of human pathology over the past 40 years, but rather to draw attention to the current problems of recruitment to the discipline. Cytogeneticists are highly skilled, and are in short supply. In New Zealand not all BMLS programmes offer cytogenetics as an option. Cytogenetic laboratories are therefore often forced to look overseas for recruits, but applicants often fail to meet the requirements for registration with the MLSB, particularly with regard to the experiential prerequisites. I believe the plight of the cytogeneticists may well foreshadow problems likely to extend throughout the profession in the coming years. The introduction of new technologies, will lead to greater specialisation in laboratories. A number of influences, but significantly the current forces for change within the medical laboratory sector, in conjunction with population trends, will in all likelihood impact significantly on our ability to maintain a skilled workforce with the requisite skill levels.

In contrast to the wonderful scientific content of Dr Gunz's dissertation, Pullar addresses by notable pathologists over the subsequent four or five years generally took as their theme the management of laboratories. There was an assertion that this should be the prerogative of pathologists and that, with a trace of condescension, the technologist of the day was the "right-hand man of the pathologist." This somewhat paternalistic relationship between pathologist and scientist has in good measure been reconciled to history, although on occasion vestigial elements of the attitude are still evident. Medical laboratory scientists have assumed their rightful place in determining the affairs of the profession as well as in the management of laboratories. The health reforms of the 1990s, in particular, provided an opportunity for medical laboratory scientists to be influential and contribute to the development of the newly structured health system. It was these reforms that laid the groundwork for the current round of DHB driven laboratory rationalisations. For this reason, and because aspects of the reforms have featured in Pullar addresses, I'd like to revisit the reforms.

Although laboratory spending generally constitutes around 5 percent of a typical hospital budget, laboratory results are estimated to influence 70 percent of all clinical decision making. Clearly, any change in the delivery of clinical laboratory services has the potential for significant flow on effects. Yet, until the 1990s the medical laboratory system in New Zealand had remained largely unchanged since the 1940s.

During the 1970s there were clear signs that laboratory services were in need of reorganisation. The expenditure on hospital and private laboratories services were similar but increasing test volumes saw cost escalations of close to 20 percent per year.

In his 1978 TH Pullar address entitled "Plotting a proper course observations and thoughts on the unhealthy state of New Zealand pathology services" Rod Kennedy, then principal technologist at Auckland Hospital presaged what were to become recurring themes. His concerns were further developed in a report written for the Department of Health entitled "The rising laboratory workload: a critical appraisal of cause and effect". He asserted that large parts of the health service, including laboratories, were not well managed. He apportioned the blame for wasteful laboratory resource usage evenly between laboratory management and inappropriate use of laboratory services by medical staff.

In his Pullar address Rod advocated strongly for laboratory professionals to work cooperatively to cut out the deadwood, duplication and other wasteful practices, while in his report to the Ministry he made a number of recommendations aimed at achieving these outcomes, but they conflicted with the laboratory culture of the time which promoted increased test volumes without any moderating incentives for cost-effective practice.

Unfortunately the opportunity to address Rod's concerns was not taken at the time. It is therefore not all together surprising that the dual system of publicly and privately owned laboratory services, both state funded, duplicating expensive equipment, materials and staff structures were subsequently to become a prime target for the 1990s cost efficiency measures.

The fundamental structural change implicit in the health reforms of the 1990s was the introduction of the split between the funder, the newly formed Regional Health Authorities (RHAs) and the health providers. This was probably the most significant change to the structure of health services in New Zealand in 50 years and many of the changes implemented at the time remain in place. Equity of access and affordability of healthcare for all New Zealanders were the key goals, but of significance for laboratories was the stated drive for efficiency, flexibility and innovation.

Two Pullar addresses were given at the time of the reforms. Barrie Edwards in 1993, in an address entitled "Health reform Opportunities and appropriate responses", and the following year when Walter Wilson reviewed the reforms one year down the track. In looking back at these addresses it is instructive to be reminded of the concerns that many of us held at the time. The feeling prevalent in the profession that, while the ideals and objectives of the reforms were laudable and had the potential to deliver much improved health care, the implementation occurred largely without the involvement of those who were required to put the changes into practice.

What of the current round of DHB-driven rationalisation of laboratory services? Not unexpectedly, one outcome of the competitive health environment created by the 1990s reforms was the entry of a number of new players into the laboratory sector, with a further duplication of infrastructure and facilities. In a few instances the reforms did result in mergers of laboratories, but the health authorities subsequently became uncomfortable with the lack of competition and in some cases supported the establishment of new entrants, again further duplicating facilities. The impetus for the current changes started in 2001 when DHBs assumed responsibility for funding the community laboratory testing. This presented the DHBs with new challenges. Used to funding a hospital laboratory service on a capped budget, they now faced the costs of a market driven fee for service model as well as replication of facilities. Additionally, the DHBs were under government pressure to lower operating costs and saving money on laboratory services became a key component of the process. However, the current move to privatisation is an interesting concept for a government that in the past has been highly critical of the privatisation model.

During the current round of DHB tendering, questions have been raised over the tendering process, particularly in relation to the level of consultation. While it is unclear to what degree public submissions have been sought, significantly the Institute has not been consulted for a standpoint. The commercial and industrial perambulations of the tendering process certainly provide fertile ground for conjecture and speculation, and some contracts have been the subject of significant media comment. It is understandable that many of our members may hold strong personal feelings regarding the competitive model. However, as an Institute we should refrain from any temptation to become embroiled in the emotive issues that have accompanied some of the contractual outcomes. The proper role of the Institute is to represent and promote the profession and the interests of its members, and as such we must focus on the consequences for our members subsequent to laboratory reorganisation.

So what should be our greatest concerns for the profession resultant from rationalisation? The greatest fallout will be the loss of experienced medical laboratory scientists from the profession. Rationalisation inevitably equates with redundancy and loss of staff from the affected organisations. Significantly, in many instances this will mean staff with many years of experience. For some staff there may be the option of reemployment with a new provider. Others may be able to relocate to another laboratory within New Zealand, but for many, family commitments or the employment obligations of a partner will preclude this as an option. Given that rationalisation is pervasive throughout the country, in all likelihood employment prospects may not be any more favourable elsewhere. Except that large laboratories in the main centres, where demand for scientists is high, may for a short time enjoy the benefit of experienced New Zealand scientists applying for vacant positions rather than the non-registerable overseas applications that currently predominate.

Scientists are in strong demand internationally. New Zealand graduates are highly regarded and have little difficulty in securing employment in overseas laboratories, particularly Australia or Britain. It can therefore be expected that significant numbers of scientists will see the current situation as an opportunity to seek recognition for their skills offshore, a loss we can ill afford.

Of concern must be the maintenance of safe and adequately resourced laboratories during the rationalisation process. With laboratory contracts under negotiation or laboratories in a transition phase due to a change of contractor, staff could be expected to actively seek new positions. Disturbingly, laboratory management may see fit to manage the uncertainty by implementing embargoes on staff replacement. A consequence of this must inevitably be additional workloads for the remaining staff with an associated increased risk of errors as well as reduced time available for professional development. Similarly, non-replacement or delayed upgrading of laboratory premises and facilities is a significant issue at some sites risking suboptimal work environments and the potential for an adverse impact on the quality of the service provided.

While these issues of uncertainty during the contract renegotiation phase need to be monitored, it is my belief that we need to distance ourselves from the concerns expressed in the public arena which assert that a change in the provider of laboratory services will automatically result in degradation of the quality of the service provided. The quality of medical laboratory testing in New Zealand is world class, and despite recent changes in contracts the quality of that testing has not changed. It will still be predominantly the same highly experienced and quality focused New Zealand scientists who will staff the new or reconfigured enterprises. Critically however, the laboratories must be appropriately resourced to ensure that they operate within adequate safety margins. There are our own comparatively recent incidents to remind us of the potential for major lapses in quality when laboratories are inadequately resourced. However, a recent case involving a medical scientist in the UK is also a timely reminder. The scientist was accused of manslaughter due to a faulty crossmatch. During the trial it was revealed that the laboratory was operating at very low staffing levels and the judge acquitted the scientist on the grounds that the hospital was not providing the laboratory with sufficient resources and therefore the scientist could not be found criminally negligent.

The comments I have made are based on the assumption that laboratory testing remains within New Zealand laboratories. However, it is not beyond the realms of possibility that newly configured laboratories, particularly those which have an overseas owner or partner, may investigate the option to perform testing outside of New Zealand. Such a scenario could be precipitated by the inability of a new provider to secure adequate local resources and would potentially have a catastrophic effect on the New Zealand medical laboratory workforce.

An issue of considerable concern for the profession is the reduced number of laboratory training positions that will be available for BMLS students on 4th year placement, consequent to rationalisation. Laboratory commitment to BMLS training is not universal, with less than fifty percent of the medical laboratories in New Zealand currently offering placements. The universities already report difficulties in placing students and any reduction in the number of training laboratories will exacerbate this problem. A consequence is that students may be forced to seek placements overseas and, in doing so, secure positions outside New Zealand on graduating. Ominously, a decreased demand for scientists subsequent to laboratory consolidation, coupled with a scarcity of student placement positions, could threaten the viability of at least one of the BMLS programmes. Would a correction in the number of providers to match a reduced need for scientists be tenable to the profession? Would the remaining tertiary institutions have the capability to increase student intake in response to any subsequent changes in demand for scientists? One eventuality which comes to mind is the greying of the laboratory workforce and the impending exodus through retirement, over the next five to ten years, of significant numbers of highly experienced scientists. New Zealand laboratories would then be in the position of having to compete on the international job market for replacement staff. Remember that New Zealand is one of the four countries, along with Australia, Canada and the US, that had the biggest baby boom population. Our boomers start to hit 60 this year, meaning that in five years, it is likely that twice as many people will be leaving the workforce as entering it. There will be a war for talent.

Many of us will recall the huge efforts put in by past Councils to establish a tertiary level qualification and this great educational drive was reflected in a number of Pullar addresses of the 1970s and 80s. While the loss of the BMLS programme from one of the current providers may well be an inevitability, it behooves us to ensure that the excellence of medical laboratory scientist training in New Zealand is not compromised.

The implications for the profession from the current round of laboratory consolidations are dire. As an Institute we need to consider what the appropriate responses should be. Members will be aware that as a Council we have written to the Minister alerting him to some of our concerns and we have also issued a press release via the New Zealand Press Association. The Annual General Meeting on Thursday will provide an opportunity for members to debate the issues and provide Council with further direction.

We are not alone in bearing the consequences of restructuring. In the UK members of the IBMS are awaiting the findings of a far reaching review of national pathology services. It is widely expected that one of the recommendations will be for larger managed laboratory units to provide economies of scale and allow the introduction of greater automation and better use of staff. Interestingly, another anticipated recommendation is an extended role for the private sector in the future provision of pathology services.

I'd like to move on from laboratory rationalisation to another issue which I believe warrants the consideration of the profession. Twenty one years ago, Brian Main in his Pullar address, questioned the extensive use of laboratory assistants. He noted from Institute membership, that laboratory assistants outnumbered medical laboratory technologists, and that workload and cost meant that laboratories placed such considerable reliance on laboratory assistants for performing analytical work that some laboratories abrogated any commitment to the training of scientists. Thankfully this trend was arrested, and over subsequent years the relative number of scientists increased, in part due to increasingly stringent accreditation requirements which mandated a more professional workforce. However, while the number of laboratory assistants in the disciplines decreased, a move towards centralised pre-

analytical processing saw the introduction of core laboratories manned by a workforce consisting almost exclusively of laboratory assistants.

With the enactment of the HPCA act medical laboratory scientists and medical laboratory technicians deemed to be practicing medical laboratory science are obligated to seek registration with the Medical Laboratory Science Board and to maintain an APC.

For the purposes of defining the profession, the Board has defined medical laboratory science as the performance of laboratory investigations on the human body or specimens taken from the human body for the purpose of supporting the diagnosis, management, treatment and prevention of disease by other health practitioners. The practice of medical laboratory science includes, sample collection, the analysis of the samples, performing quality assurance procedures, evaluation and interpretation of results, and communicating the results. Some ancillary tasks are also included within the practice of medical laboratory science.

The Board has also declared a list of service categories that belong within the profession. These include the scientific disciplines plus phlebotomy. Notably absent is the category of specimen services. The fundamental aim of the HPCA act is the prevention of harm to the public, and it is for this reason that phlebotomy is deemed to belong within the profession and mandates the registration of phlebotomists. Conversely, the Board has ruled that work normally associated with the specimen services area, including specimen reception, numbering and sorting, does not fall within the definition of medical laboratory science and staff working in this area are exempt from registration. I believe that this concept of specimen services is too narrow and underplays the potential for public harm.

Approximately 90 percent of errors in a medical laboratory are extraneous to the analytical process. About two thirds of these will be pre-analytical, and will include errors in either sample collection or pre-analytical sample preparation. Even within the limited tasks of sample receipt, labeling and computer registration there is the potential for error, and by implication patient harm. However, in many specimen service departments the actual range of tasks performed by technicians will often extend beyond basic sample reception. Additional tasks typically include specimen centrifugation, aliquoting, analyser loading, blood film preparation, plating microbiology samples, perhaps even running the odd sample for blood gas analysis or assisting with the maintenance of point of care instruments. Some staff may be involved in the referral of specimens for specialist testing, requiring detailed knowledge of specimen preparation, sample stability and transport conditions. Communicating with users of the laboratory service also often falls within the duties required of these staff.

It is not possible to assert that all assistants employed in specimen services solely perform specimen reception duties and therefore do not fall within the scope of the profession of medical laboratory science. It may be that in the specimen reception area of community laboratories the assistant's role may well be restricted solely to specimen sorting and registration duties. However, this is not the situation in most hospital laboratories. Since the introduction of the core laboratories, specimen service technicians frequently perform tasks that clearly traverse the boundary with the purely analytical disciplines. Duties may even include direct patient contact when central registration staff are required to perform specimen collection tasks such as micro-capillary blood collects.

Our laboratory recently attempted to reduce the incidence of specimen labeling errors. The potential for harm to the public from inadequately labeled specimens was certainly considered newsworthy by the local press and even prompted the opposition health spokesman to call for an inquiry. Specimen errors originate at specimen collection, but we rely upon the skill and experience of our specimen services technicians to detect these errors and ultimately avoid adverse patient outcomes.

I believe that, for many assistants working in specimen services, particularly those whose duties cross boundaries with the analytical sections, their practice should be considered to fall within the ambit of medical laboratory science. To provide protection to the public, the Board should include these important workers within an appropriately designated service category.

The Institute recently developed and promoted a new examination for this group of employees. It was intended that this would be offered as a new QMLT qualification, however the QMLT is a prescribed qualification for registration with the Board as a medical laboratory technician and as such cannot be offered to a group of workers who the Board deems not to require registration. The Institute is committed to promoting education and professional qualifications for all medical laboratory professionals and to this end the examination has been renamed the Qualified Specimen Services Technician examination. While currently it is not recognised for the purpose of registration as a medical laboratory technician, it will importantly provide an opportunity for the development of our specimen services staff. This can only enhance the quality of the service offered by the laboratory, and by implication reduce the potential for error and harm to patients. Importantly, the qualification will be recognised for the purposes of technician salary progression as well as provide an achievable goal for technicians working in a area where staff turnover tends to be high due to the limited career opportunities.

There is another issue which has been alluded to in at least two previous Pullar addresses, the issue of gender imbalance within the profession. At the 1990 ASM Jan Parker delivered a Pullar address entitled "The under-utilised potential of women in medical laboratory science". Statistics Jan quoted revealed that while women constituted 76 % of the Medical Laboratory Scientist workforce only 12% of them held a graded position. In addition, in some large laboratories, females were not represented in charge or 2IC positions in the major disciplines. This gender disparity was also echoed in representation on the professional bodies leading our profession. At the time, neither the Institute Council, nor the Registration Board had been headed by a woman.

Times have changed. A contention in Jan's address that women were reticent to apply for senior laboratory posts is certainly no longer valid. An examination of the organisational structure of any of the larger laboratories would indicate a relative gender distribution across the senior positions that closely parallels the overall gender constitution of the laboratory workforce.

What about us blokes? While the female imbalance in senior roles has been largely ameliorated, what hasn't changed is the relative number of males in the profession. As early as 1972, Professor Peter Herdson in his Pullar address commented on the disproportionately large numbers of female trainees in laboratories. In a quip, reflective of the times, he lamented that it would be a sad day for New Zealand if the vast majority of young women commencing laboratory training gave away all thoughts of marriage for the betterment of pathology. His concerns presaged the enactment of EEO legislation and the general adoption of a more enlightened approach by employers to the needs of women and families. However, he also expressed concern at the low proportion of male trainees in laboratories and questioned what could be done to attract more young men.

It is now almost 35 years since Professor Herdson's observations and

the laboratory workforce statistics for men in the profession have not improved. Ministry of Health data shows that the workforce remains predominantly female, 71 percent as at 2004. In fact the workforce statistics indicate that the number of males in laboratories will decline further in the future. While men comprised 28 percent of the medical laboratory scientist workforce in 2004, for the cohort aged less than 35 years men comprised only 21 percent.

For the public, generally their only contact with a laboratory is with a phlebotomist, who is invariably female, and on the few occasions that our profession is deemed newsworthy, the images in the media are invariably of young women either examining cytology slides or plating microbiology plates. Even medical laboratory science careers material has a female perspective.

As a profession we suffer from being lumped in with other allied health groups, all with a female preponderance:- radiographers, physiotherapists, pharmacists, etc. There is no reason to believe that the gender bias will not be perpetuated and we are faced with the risk that young men may well be socialised not to consider medical laboratory science as a career option.

What can we do about attracting more men to the profession? Obviously the answer isn't to have more women in laboratories as this hasn't attracted the men. The solution is in fact complex, but simple first steps must include promoting the profession to young men at every opportunity. This could be through encouraging the men in our profession to be involved in careers seminars and presentations in schools. Some schools have schemes which seek workplace experience for students. We should encourage such opportunities even though they may be disruptive in a busy laboratory. Importantly, we should attempt to ensure that publicity material reflects an appropriate gender balance. In the long term, salary scales and career structures will need to be addressed.

Earlier this year it was reported that the Australian IT industry also suffers from a significant gender disparity. They have the opposite problem, with only one in five IT workers being female. In an attempt to shed the female computer geek image, and to attract more women to the profession, a spoof calendar was produced. The IT Screen Goddesses calendar featured female IT staff in poses from various movies, and initially had the support of the Australian Computer Society. However, this support evaporated after the society sighted the cover which showed a naked web designer lying on a bed of roses with strategically placed petals protecting her modesty. The photograph was a take on the scene from American Beauty. How about a calendar featuring suitably posed young, or not so young, male medical laboratory scientists? Would Council support such a publication? In anticipation of Council endorsement of a similar project I have taken the liberty of preparing Council's contribution to the publication.

Perhaps in the end there is little we can do to change the gender imbalance. Recent statistics suggest that we are witnessing an overall feminisation of the health professions, notably demonstrated in medicine where the Otago Medical School has reported that men made up 70% of medical graduates in 1978, but that this had nearly halved to 39% last year.

To conclude today's presentation I would like to exercise the speaker's prerogative of a glance to the future. While laboratory rationalisation is certainly our current preoccupation, what can we expect the issues of tomorrow to be?

The inexorable advance in technology will continue. This will influence the tests that are ordered, how they are analysed and probably the traditional discipline structure of laboratories. The -omics revolution will lead to direct clinical applications. We can expect to see a growth in the use of micro-array analysis, particularly for the molecular characterization of tumours. The promise of increased sensitivity and speed and reduced cost and labour makes nanodiagnostics an appealing alternative to current diagnostic techniques. The most promising applications being for tumour detection, immunohistochemistry, infectious agent detection, multiplexed diagnostics and fluoroimmunoassays. There will be significant ancillary issues associated with these new technologies, including appropriate standardisation and quality assurance.

There will be a need for new bio-markers for emerging infectious agents and for tumour detection. This will have particular applicability in the new concept of personalised medicine, encompassing genetic testing tailored to the treatment or preventative interventions of an individual's needs.

I have already commented on the aging of the workforce, but to date planning for this eventuality has at best been piecemeal. Ongoing laboratory consolidation will predicate further efficiencies, and will, I believe, require process re-engineering and the introduction of lean methodology. The further extension of POCT testing will have implications for laboratories. It is patently clear that we haven't seen the last of laboratory rationalisation, and if we wish to exert some influence on the outcomes then we must raise the profile of the profession. In the current round of publicity the pathologists have stolen a march on us. Our profession was not well served by the media nor was the public adequately informed of the role of the medical laboratory professionals who constitute 90 percent of the laboratory workforce. Council's recent press releases should serve to address some of the imbalance in the publicity, but without doubt we must become more politically astute.

It has been my pleasure to deliver this year's Pullar address and I thank you for your attention.

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Comparison of real-time PCR with culture and EIA for the diagnosis of mucocutaneous infections with herpes simplex virus

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Abstract

Aims: To compare real-time PCR, an enzyme immunoassay (EIA) and centrifugation enhanced cell culture (CECC) for the diagnosis of herpes simplex virus (HSV) infection.

Methods: A total of 156 mucocutaneous specimens were tested for the presence of HSV by all three methods.

Results: Overall, 55 specimens were positive by real-time PCR. In comparison, 46 specimens were positive by cell culture, and 27 by EIA. The detection rate was significantly higher for PCR compared with both other methods and was significantly higher for cell culture compared with EIA.

Conclusions: The real-time PCR assay had increased sensitivity over enhanced cell culture and EIA for the detection of HSV. The real-time detection of amplified PCR products, rapid processing time and genotyping capability, makes it a suitable system for the routine clinical laboratory.

Key words: HSV, culture, real-time PCR, EIA.

N Z J Med Lab Sci 2006; 60 (3): 92-96.

Introduction

The human herpes viruses, herpes simplex virus type 1 (HSV-1) and herpes simplex virus type 2 (HSV-2), commonly cause infections of the skin and mucous membranes, producing diseases, which cannot be clinically differentiated (1).

The laboratory diagnosis of HSV infection has traditionally relied on virus isolation in cell culture (2). This has the inherent disadvantage of requiring prompt specimen transportation to the laboratory to ensure viability of the virus, as well as the need for cell culture facilities, and has a minimum turn-around-time of 24-72 hours. Other methods routinely used, which do not rely on the detection of viable virus, include direct fluorescent antigen (DFA) (3) and enzyme immunoassays (EIA) (4). DFA can be performed within 4 hours and is cost-effective (5), but requires a good quality sample and the subjective interpretation of cellular staining. EIA can also be performed within 4 hours and is the least technically demanding diagnostic test.

PCR has been shown in recent studies to be a rapid and reliable method for detecting HSV infection (6-9). This method has also shown an increased sensitivity for the detection of HSV DNA in clinical specimens compared to antigen detection and culture methods (6, 7).

The aim of this study was to compare real-time PCR, HSV EIA and cell culture for the detection of HSV in mucocutaneous specimens submitted to a routine clinical laboratory.

Methods

Specimen collection and processing

One hundred and fifty six consecutive mucocutaneous specimens (76 skin, 70 genital and 10 site not stated) submitted to Canterbury Health Laboratories, Christchurch, New Zealand, for HSV diagnostic testing were included in the study. Dacron plastic shafted swabs (Medical Wire and Equipment Ltd.) were used to obtain each specimen. Each swab was broken off into 3 ml of virus transport medium (VTM), containing 2 mg/ml Penicillin G Sodium (Sandoz, Austria) and 2 µg/ml Amphotericin B (Bristol-Myers Squibb, Australia), transported at 4°C to the laboratory and processed within 48 hours.

Culture and DFA confirmation for HSV

A centrifugation enhanced cell culture plate technique (CECC) was used for virus isolation (5). A 250 µl volume of each specimen was inoculated onto A549 (Human Lung Carcinoma, EACC-87) and HEL 12469 (human epithelial lung, EACC-20) cell monolayers on a single 48 well plate (Nunclon™). Plates were centrifuged at 2500 g, for one hour at 37°C. The supernatant was removed and 500 µl of Gibco Minimal Essential Medium [MEM with 1% Foetal Calf Serum (10091-

148; Gibco) 200 mg/l Penicillin G Sodium, 2 mg/L Ciprofloxacin (Demo S.A., Greece), 1% GlutaMAX-1 (35050-061; Gibco)] was added to each well. Plates were incubated at 37°C with 5.0% CO2 and humidity and were examined for cytopathic effect (CPE) after 24, 48 and 72 hours of incubation. All cultures showing characteristic HSV CPE were confirmed as HSV using HSV (types 1 and 2) direct fluorescent monoclonal antibodies (Mabs) (Bartels Inc., Issaquah, USA) and sub-typed using HSV type specific Mabs (Bartels Inc., Issaquah, USA), when requested. All negative cultures were stained at 72 hours using bivalent Mabs to HSV (subtypes 1 and 2).

Nucleic acid amplification

DNA was extracted from 200 µl of patient's specimen inoculated in VTM using the QIAamp DNA mini kit spin column method (Qiagen, Hilden, Germany). Positive (confirmed pooled local isolates of HSV type 1 and HSV type 2) and negative (molecular grade water) extraction and amplification controls were included in each run.

The LightCycler real-time PCR assay used for HSV detection was a modification by Olfert Landt (TIB Molbiol, Berlin, Germany) as described by Burrows et al (6) from a method originally developed by Espy et al (18). LightCycler PCR assay developed by Olfert Landt (TIB Molbiol, Berlin, Germany) as described by Burrows et al (5). The assay targets the DNA polymerase gene, generating a 140 bp product. Modifications included the use of 4.0 mM of MgCl2, 0.5 µM of HSV-pol F (forward primer) and 0.1 µM HSV-pol A (reverse primer) and 0.2 µM of each labelled probe HSV-FLU and HSV-640 (TIB Molbiol, Berlin, Germany). The asymmetric primers were chosen to minimise the occurrence of the 'hook effect' (10). All PCR reactions were carried out using the LightCycler FastStart DNA master hybridisation probes kit (Roche Diagnostics, Germany). DNA was amplified using the following parameters: activation at 95°C for 10 min, followed by a 50 cycle profile consisting of heating at 20°C/s to 95°C with a 10 s hold (denaturation), cooling at 20°C/s to 60°C with a 10 s hold (annealing), and heating at 20°C/s to 72°C with a 12 s hold (extension).

After completion of the real-time PCR amplification, melting curve analysis was performed using the following parameters: 95°C for 0 sec, 45°C with a 10 sec hold to allow probe annealing, followed by heating to 95°C at 0.2°C/sec incremental steps with continual fluorescence detection to determine the probe melting temperature. PCR products were analysed by using the LightCycler melting curve analysis software and designated HSV genotype 1 or genotype 2 on the Tm (Figure 1). For samples which produced a melting curve that did not fit the interpretation criteria of the laboratory, i.e. within one degree of the two HSV control curves, conventional in-house PCR and restriction enzyme analysis (RE) was performed to confirm the result (12). These samples have found to have sequence variation in the HSV DNA polymerase gene, which may have complicated the melting curve analysis by producing Tm values that differed from expected values for HSV type 1 or HSV type 2 (17).

EIA

The Murex HSV EIA (Abbott Diagnostics, Murex Biotech Ltd, UK) was used which has HSV specific murine monoclonal antibodies and an enzyme amplification system for HSV type 1 and HSV type 2 antigen detection (11). Patient specimens inoculated in VTM were stored frozen at -80°C and thawed prior to batch testing. We varied from the recommended procedure as swab samples should have been processed in the buffer supplied to stabilise the antigen. This step was necessary as this was a retrospective study from frozen samples. All reactive results in the Murex HSV EIA results were confirmed using the Murex HSV verification kit following the manufacturer's instructions.

Confirmatory assays for HSV

All discordant results, such as those which failed to genotype by melting curve analysis (17) were confirmed by amplification of the extracted DNA by a conventional in-house PCR using primers targeting the glycoprotein D gene of HSV type 1 and HSV type 2 (12). The resulting 142 bp PCR product was electrophoresed and visualised on a 2% agarose gel. Positive amplified PCR products were then genotyped by restriction enzyme analysis (12).

Diagnostic tests were compared using McNemar's test

Results

A total of 156 specimens from cutaneous and genital sites were tested for the presence of HSV by CECC, EIA, and PCR. Fifty five specimens were found to be HSV positive and 101 specimens were negative. Of the 55 HSV positive specimens, 27 were found to be positive by all three methods, 19 were positive by culture and real-time PCR and negative by EIA, while 9 were positive by real-time PCR alone.

All EIA positive specimens were also positive by culture and real-time PCR, while all culture positive specimens were also positive by real-time PCR. Overall, real-time PCR had a significantly higher detection rate than both other methods (PCR vs. cell culture $p=0.003$, PCR vs. EIA $p<0.0001$), and cell culture had a significantly higher detection rate than EIA ($p<0.0001$). The 9 specimens positive by real-time PCR only were also positive using an alternative confirmatory conventional in-house PCR assay for HSV.

Discussion

The rapid diagnosis of HSV infections can be extremely clinically useful, especially when a clinical diagnosis is uncertain in the immunocompromised patient, the pregnant female, and the neonate, where atypical lesions may be present, or when antiviral therapy is contemplated. HSV is the most frequently detected virus in most clinical laboratories. Generally the introduction of rapid assays, such as immunofluorescence and EIA, have not improved the sensitivity of HSV detection over conventional cell culture (2, 9,10).

Traditionally, cell culture has been the gold standard in the diagnosis of infections due to herpes simplex virus and has the advantage of allowing typing by specific immunofluorescence stains. However, it is technically demanding, requires viable virus, and stringent adherence to prompt and adequate specimen transport to maintain virus viability (4°C). Turn around times range from 24 hours to several days.

EIA is a commercially available test, which is a standardised method and requires no specialist equipment or facility. Turn around times are rapid with the time of about 4 hours from specimen receipt to a result being available. Yet, EIA lacks sensitivity in comparison to cell culture and real-time PCR (6, 7).

Real-time PCR demonstrates high sensitivity and specificity with turn around times of less than 2 hours from specimen receipt to a result being available. In addition, HSV strain identification is available by melt-back curve analysis. However, result interpretation can be challenging as DNA can be detected in a sensitive assay without necessarily representing primary or recurrent infection but asymptomatic shedding (13,14).

In the present study, PCR had a significantly higher detection rate than both cell culture and EIA. It should be noted that the EIA was performed on a specimen that was inoculated into VTM (that was also used for all other testing), rather than the buffer supplied with the kit

The benefit of direct detection by real-time PCR has proven to be cost-effective on a per-run basis, when implemented with a high-throughput laboratory, particularly when replacing conventional, culture-based approaches to microbial detection (23).

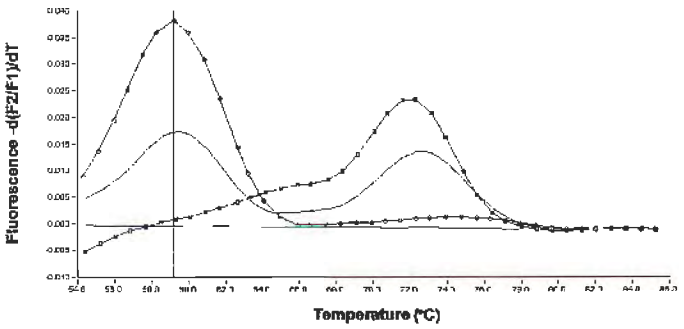

Figure 1. Melting curve analysis for typing of HSV PCR products. HSV genotype 1 has the lower melt curve peak of 59°C (mismatch). HSV genotype 2 has the higher melt curve peak of 72°C (complementary).

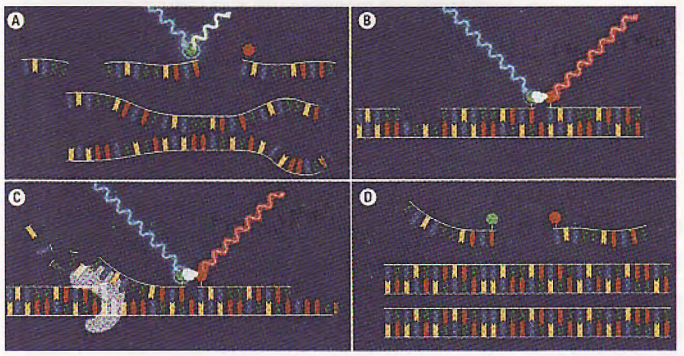

Figure 2. FRET labelled sequence-specific probes fluoresce when in close proximity to each other (when HSV is present).

A. Denaturation to form ssDNA. B. Annealing of labelled probes to adjacent regions. C. Extension Taq polymerase anneals at the primer site and extends the primers to form cDNA. D. Cycle completed producing a copy of the target sequence.

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The hidden diagnosis - a case study

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Abstract

A 27-year old female initially presented with thrombocytopenia and some abnormal liver enzymes. A repeat blood sample the following day showed microangiopathic haemolytic anaemia. Further investigation initiated by the laboratory suggested a diagnosis of haemolytic uraemic syndrome. Given this atypical presentation, the diagnosis was not initially suspected and, although diagnostic biochemistry tests were not requested, vital clues were present in the blood film and liver enzymes. This case led to the adoption of new protocols and a more effective exchange of information within the laboratory.

Key words: disseminated intravascular coagulation (DIC), thrombotic thrombocytopenic purpura (TTP), microangiopathic haemolytic anaemia (MAHA), haemolytic uraemic syndrome (HUS); von Willebrand's Factor (vWF); *Escherichia coli*, Shiga toxin producing *E. coli* O157:H7 (STEC O157).

N Z J Med Lab Sci 2006; 60 (3): 97-98.

Case history

A 27-year old female presented to her GP with slight diarrhoea, lower abdominal pain, headache and no appetite. Campylobacter was suspected and a faeces sample obtained for culture. The patient returned two days later with ongoing gastrointestinal upset, stomach cramping, nausea, and reported passing dark urine. She then presented at the laboratory with the clinical particulars stating "? mild liver disorder" (Table 1).

Table 1. Laboratory results

Haematology parameters	**Initial results**	**Reference intervals**
Haemoglobin	119	110-155 g/L
RBC	3.9	3.6-5.5 $x10^{12}$/L
Platelets	23	160-400 $x10^{9}$/L
WBC	7.8	4.0-11.0 $x10^{9}$/L
Neutrophils	5.5	2.0-7.0 $x10^{9}$/L
Lymphocytes	1.5	1.0-4.0 $x10^{9}$/L
Monocytes	0.7	0.2-1.0 $x10^{9}$/L
Eosinophils	0.1	0.0-0.7 $x10^{9}$/L
Biochemistry parameters		
Bilirubin	119	1-22 µmol/L
Alkaline phosphatase	55	40-120 U/L
Alanine transaminase (ALT)	21	0-40 U/L
Aspartate transaminase (AST)	64	5-35 U/L
Gamma glutamyl transferase	21	<50 U/L

Initial specimen blood film comment: an occasional spherocyte and a few fragmented forms. There are no platelet clumps or small clots.

In line with our laboratory protocol for severe thrombocytopenia, an urgent repeat specimen was requested. The following day, her blood film contained fragmented spherocytes, fragmented forms and polychromatic cells consistent with microangiopathic haemolytic anaemia (MAHA). Her haemoglobin had dropped to 112 g/L, bilirubin was now 253 µmol/L and the AST was 88 U/L. Other haematology and biochemistry results were similar to those obtained on the previous day. In view of the MAHA, renal functions were performed on the available serum specimens (Table 2).

Table 2. Renal function tests

Parameter	**Initial result**	**Reference interval**	**Subsequent result**
Urea	16.2	3.1-7.5 mmol/L	25.0
Creatinine	0.15	0.04-0.10 mmol/L	0.25

These results indicated progressive renal failure which would have been apparent on initial presentation had the appropriate tests been requested. A provisional diagnosis of haemolytic uraemic syndrome (HUS) / thrombotic thrombocytopenic purpura (TTP) based on these results was made, followed by prompt admission to hospital. Coagulation studies performed subsequent to admission were all normal, ruling out disseminated intravascular coagulation (DIC). A faeces specimen obtained on admission grew Shiga toxin-producing *E coli* O157:H7 (STEC O157) on culture.

She was treated in intensive care with daily plasma exchange transfusions. She also had red blood cell transfusions to keep her haemoglobin >9.0 g/L, kidney dialysis, and potassium supplementation. She made a full recovery and was discharged 15 days after admission.

Discussion

TTP is a rare disorder occurring primarily in adults and is accompanied by the progressive appearance of MAHA, thrombocytopenia, fever, neurologic and renal abnormalities. It has been proposed that a less stringent criterion of MAHA plus thrombocytopenia without an alternative cause be adopted for the diagnosis of TTP (1). Patients with TTP have large multimers of von Willebrands factor (vWF), and have a severe deficiency of a factor cleaving protease, termed "ADAMTS 13" (an acronym for a disintegrin and metalloprotease with thrombospondin - 1-like domains), that is responsible for cleaving the vWF multimers that are synthesised and secreted by endothelial cells. When ADAMTS 13 is not present, the resulting abnormally large von Willebrand factor multimers in plasma have a greater ability to react with platelets and cause the platelet thrombi characteristic of TTP (1). The activity of this protease is normal in HUS. TTP has a high mortality rate if left untreated (90%) but responds well to exchange plasma transfusions and supportive treatment. Complications include: hypertension, acute renal failure, seizures, coma and mortality (2). 85% of adequately treated patients make a full recovery (3).

HUS occurs primarily in children following infection by STEC O157. Risk factors include eating raw or partially cooked meat, drinking contaminated water or unpasteurised milk, and exposure to animals, especially ruminants, and their faeces. The infectious dose of STEC is very low, perhaps as few as a hundred organisms and therefore contaminated meat may not smell, taste or look any different to normal. STEC O157 may produce one or two Shiga toxin/s which is carried by the neutrophils in the blood stream to the glomeruli of the kidneys. The glomerular endothelial cells have 100-fold positive affinity for this toxin and so absorb it, in turn damaging them. Micro thrombi

form with platelet aggregation and consumptive thrombocytopenia (4). Fragmentation of the red cells occurs as they pass through these micro thrombi with the end result of MAHA. Acute renal failure occurs in 55-70% of cases although spontaneous remission is common (4).

Other infectious agents have been implicated in HUS: *Salmonella, Shigella, Yersinia, Campylobacter*, and other *E coli* serotypes (non-O157 STEC). HUS has also been associated with acquired immunodeficiency syndrome, cancer, and chemotherapeutic drugs, as well as familial causes, which may reflect a genetic disposition (4).

Only 5% of children infected with STEC O157:H7 will develop HUS. Isolates producing Shiga toxin 2 (Stx 2) are more likely to cause serious human disease than isolates producing Shiga toxin 1 (Stx 1). Our microbiology department routinely cultures faecal samples from all children under 12 years old with diarrhoea, and all other patients with bloody diarrhoea on Sorbitol MacConkey Agar to isolate this organism. Over the period of 01/01/2006-to 31/05/06 eight positive cultures of STEC O157:H7 from children were identified. To our knowledge, none of these children have developed HUS.

Conclusion

This patient could have been diagnosed immediately had a more complete analysis been performed, with benefit for this patient as an early diagnosis is essential for a good outcome. To highlight the difficulty in this case history, our patient's initial presentation can be compared to the usual laboratory findings.

This patient was not anaemic, whereas the usual presentation is haemolytic anaemia. She did not have a neutrophilia as is normally present in HUS, and had very minimal red cell changes rather than the classic fragmented spherocytes of MAHA. Thrombocytopenia was present. The clinical particulars recorded on the laboratory request form did not include her gastrointestinal symptoms and renal functions were not requested. Patients normally have bloody diarrhoea but her faeces specimen was described as formed and of normal appearance.

Protocols now in use in our laboratory

- Biochemistry now alerts Haematology in the case of a high bilirubin (>30 µmol/L) and/or raised AST (>50 U/L) in the absence of other abnormal liver enzymes, and renal functions are performed if not already requested.
- Haematology will alert Biochemistry in every case of MAHA and arrange addition of renal functions. If a faeces specimen has been submitted, Microbiology is asked to check the cultures for STEC O157: H7.
- Microbiology will inform Haematology of any new case identified of STEC O157:H7. If an EDTA specimen is available, a blood film will be made and examined for red blood cell changes and renal functions will be added to any serum specimen.

The major outcome of these findings is that co-operation between departments can help ensure an early diagnosis in this rare condition. A diagnosis can be hidden away, but with careful team and detective work it can be discovered with positive outcomes for the patient.

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Answers to HSIG questionnaire:

1. Low
2. Any 4 of the following:
   - Hodgkin's disease (HD)
   - Acute leukaemia
   - Non Hodgkin's lymphoma (NHL)
   - Myelodysplastic syndrome (MDS)
   - Essential Thrombocythemia (ET)
   - Chronic Myeloid Leukaemia (CML)
   - Chronic Lymphocytic Leukaemia (CLL)
   - Mycosis Fungoides
3. False
4. Death due to intracranial bleeding associated with thrombocytopenia
5. Cyclophosphoamide, vincristine, procarbazine and prednisone
6. False
7. Death, dysmorphism and behavioural changes
8. True
9. Thromboembolism and placental infarction
10. Possible to attain remission from acute leukaemia and deliver normal infant baby.

Mycosis fungoides is not a fungal infection

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Abstract

We present a case study of mycosis fungoides (MF) on a patient that presented to her doctor with itchy skin lesions of one month duration in October 1996. MF is a non-Hodgkins cutaneous lymphoma. It is difficult to diagnose due to its overlap in clinical and histological appearances with other non specific inflammatory conditions, which can be hard to interpret in the early stages of disease. MF progresses through three phases, initially with premycotic red patches, then infiltrative plaques and finally tumour nodules.

Laboratory tests that can be carried out to aid in the diagnosis of this disease include routine histology, immunohistochemistry (IHC), T-cell gene rearrangement studies, and surface marker studies. In this patient the T-cell gene rearrangement studies were negative, and the surface marker studies inconclusive. The following IHC stains were performed, leucocyte common antigen, CD45RO (T-cell) and CD20 (B-cell). These stains showed the majority of infiltrating cells present to be leucocytes of T-cell origin.

Material was reviewed by two international dermatopathologists who concur with the histological diagnosis of mycosis fungoides. Diagnosis was based on a combination of clinical appearances, histological appearances and IHC.

Key words: mycosis fungoides, cutaneous T-cell lymphoma, Pautrier's microabcesses, mycosis cells

N Z J Med Lab Sci 2006; 60 (3): 99-101.

Introduction

Mycosis fungoides (MF) is not a fungal infection as the name might suggest. It is a T-lymphocytic lymphoma that primarily involves the skin. The name mycosis fungoides refers to the mushroom-like appearance of the tumour type-lesions seen in latter stages of disease. It is a fatal skin disease, with fungous tumours, much pain and is debilitating in its last stages. It is a rare low grade malignancy which occurs in approximately 1 in 345 000. It classically affects individuals in the fourth to sixth decades, although any age can be affected. This disease has a preference for covered sites and may be widespread.

We present a case study of MF giving diagnostic background clinically and histologically while considering the pitfalls of differential diagnosis. This case study was originally compiled in 1997 for presentation at the South Island Seminar, with an update in August 1997 when it was presented at the NZIMLS meeting in Wellington. Methods mentioned were current at that time but have since been superseded in some instances.

Case study

In October 1996 a 65 year old female patient presented to her GP with itchy generalised skin lesions, which had been present one month with some associated bruising. Vasculitis was queried. A biopsy was taken from the left thigh. The histology showed a loose polymorphous infiltrate of lymphocytes in the dermis and epidermis. Overall, the picture was inflammatory but lacked spongiosis, which is a typical feature of inflammation. Pautrier's microabcesses were apparent (Figure 1). These are groups of neoplastic T-cells within nonspongiotic intraepidermal vesicles. Some lymphocytes have convoluted nuclei.

It was decided that the histological pattern present in the lesion may be seen in subacute dermatitis, a drug reaction, or in the early stages of MF. It was suggested that the patient be referred to a dermatologist and that a blood film be reviewed to exclude the systemic presence of Sezary cells (mycosis cells present in the blood). Re-biopsy was recommended, with fresh tissue to be submitted for T-cell gene rearrangement studies and surface marker studies.

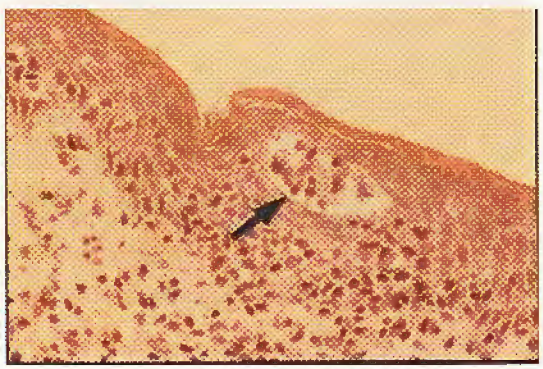
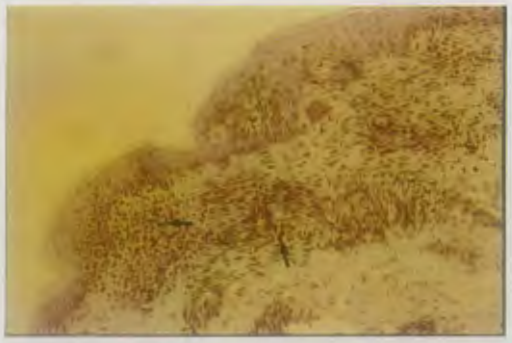


Figure 1

In early November 1996 the patient presented to the dermatologist querying a differential diagnosis of mycosis fungoides papular and plaque form, lymphomatous papulosis, or vasculitis. The lesions were described as haemorrhagic copper red papules and plaques present mainly on the trunk, buttocks and legs of the patient. Pityriasis rosea configurations in parts were also queried. At this point fresh tissue was submitted for surface markers and T-cell gene rearrangement studies.

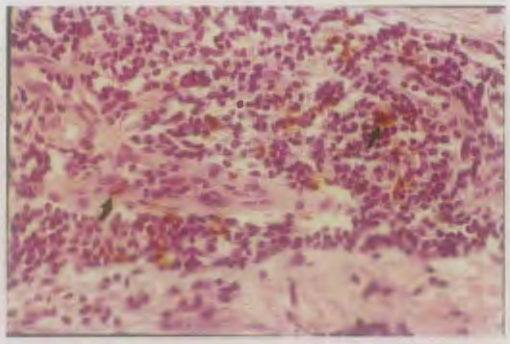
The second lesion had similar histological characteristics to the first. A panel of IHC stains were performed including leucocyte common antigen (LCA) demonstrating leucocytes, CD45RO demonstrating T-cells, and CD20 which demonstrates B-cells (Figure 2). The LCA was

positive confirming that the infiltrating cells present were leucocytes; the CD45RO showed the bulk of these lymphocytes were of T-cell origin, and the CD20 showed presence of some reactive B-cells which would be expected in this type of response.



LCA

CD45RO



CD20

Figure 2. IHC stains

In this particular case the T-cell gene rearrangement studies were negative, due to insufficient DNA, and the surface marker studies inconclusive, rendering these special techniques unhelpful. The case was referred to two expert dermatopathologists who both concurred with the diagnosis of MF. The patient was treated for early stage lesions and at this time is responding well to treatment.

Discussion

MF is a disease which progresses through three phases, the first two of which were queried as part of a differential diagnosis in this patient's case. All three phases can be present simultaneously. The first phase, premycotic red patches, is described as itchy red, purple or brown patches with irregular but well defined borders, and are often scaly. They may resemble other forms of dermatitis including fungal infections and psoriasis. The second phase, infiltrative plaques, is similar but additionally shows a degree of induration. Established lesions may slowly enlarge or undergo atrophy. Partial regression may give them a 'rolled up on itself' or 'creeping outline' and depigmentation can occur in dark skinned races. This phase is the earliest point at which lymph nodes may be involved by the neoplastic process. The third phase, tumour nodules, are seen in the late stages of MF and consist of multiple large, round or irregularly shaped, red brown tumours that are frequently ulcerated. There is usually evidence of involvement of lymph nodes and other viscera such as the spleen, lungs, liver, kidneys, and the gastrointestinal tract in this stage (1-3).

Prognosis

The prognosis for patients with MF varies between individuals; some take a slow, protracted and benign course, while others proceed rapidly to multi-system involvement and disfiguring cutaneous tumours. Over half of patients with mycosis fungoides die within 10 years of the onset of the disease. Topical therapy with steroids or ultraviolet light is often employed to treat early lesions, whereas more aggressive systemic chemotherapy is indicated for advanced disease.

Diagnosis

Histologically MF typically shows an infiltration of the epidermis and upper dermis by neoplastic T-cells, called mycosis cells. They have extremely unusual cerebriform nuclei characterised by marked infolding of the nuclear membrane, plastics are usually required to demonstrate this feature. The presence of Pautrier microabcesses are also diagnostic of this disease, these consist of mycosis cells located within nonspongiotic intraepidermal vesicles (Figure 1).

Epidermotropism would also be apparent; this refers to the lymphocytes migrating towards the epidermis as seen in the patient's H&E (Figure 3). In 90% of cases of patch/plaque MF the neoplastic lymphocytes are CD4 antigen positive T-cells with the alpha beta form of the T-cell receptor. In addition they have the phenotype of memory T-cells, expressing low molecular weight LCA. These features can be demonstrated using T-cell receptor studies and surface marker studies in combination with IHC. In this case the former two techniques proved unhelpful, the IHC sections for LCA and CD45RO were positive (Figure 2) indicating that the bulk of the infiltrating cells present were leucocytes of T-cell origin (1-3).

Figure 3. Epidermotropism

Conclusion

In conclusion, the difficulty in diagnosing MF is due to the overlap in the early stages with non specific inflammatory conditions. Like most diseases there is no single definitive distinguishing feature and it is not always possible to demonstrate features that may be present. Communication of all the relevant clinical information is very important for consideration of the 'whole picture'. In this case the bottom line diagnosis was given by the pathologist's eye and the dermatologist's clinical impression.

Addendum August 1997

Apparently all is not what it seems! The patient responded more quickly than expected to treatment and the diagnosis was queried by the clinical team. In December 1996 further lesions were biopsied with the overall opinion being, that it was possible a cutaneous T cell lymphoma could present with some of these patterns, although perivascular predominance would be unusual. Reactive conditions which could produce these appearances would include pityriasis lichenoides et varioliformis acuta (PLEVA) or a drug reaction.

As further investigations were made a full clinical picture was obtained. It is now apparent that some weeks after helping to clear out garden and compost, overnight the patient suddenly developed thick spots all over her chest, upper thighs, and back. The patient felt this looked unsightly but was not particularly itchy. She saw her GP and Bentnovate ointment was prescribed which helped and the lesions gradually faded but could still be observed. There is no history of further lesions developing, and clinically there is no evidence of any new progression. In reviewing this information the pathologists involved concede that it may not be but are not convinced that it definitely is not MF.

We have been unable to trace this case further as the patient was transferred to the public health care sector. We did however speak with the patient, who advised us that she had had no further treatment. She has had one recurrence of the lesions. She now uses the Bentnovate cream continually to stop it from happening again. Bentnovate is a strong steroid cream, and is a treatment used for early stage MF lesions; however it is also a treatment for various dermatological conditions.

Addendum June 2006

10 years on the patient is alive, well and disease free. Was this patient one of the luckier ones who has taken a slow, protracted and benign course of disease? There is controversy as to whether MF represents a malignancy from the outset or whether it is a reactive phenomenon that may or may not undergo malignant transformation (1). The original slides did and still do show a histological pattern consistent with a diagnosis of MF. A total of five pathologists reviewed the slides at the time of diagnosis, two of which were international specialists in dermatopathology, all concurred with the diagnosis of MF. Additional specialist tests performed were, T-cell gene rearrangement studies and surface marker studies, however in this patient's case they did not contribute information that was useful for diagnosis.

It is clear that it is prudent to attempt to confirm a diagnosis via methods such as seeking second opinions, consulting specialists, and getting further medical tests. All of which were actively pursued in this case to confirm diagnosis. This leads us to conclude that in the pathology laboratory we can do everything possible to ensure the most accurate diagnosis for the patient, however sometimes we may not get a confirmed diagnosis, even with time. Diagnosis is a team approach; we rely on receiving the clinically relevant details and collating all available information.

Final comments

Some entities can be very difficult to diagnose relying on the histology alone. A number of benign skin reactions can have histology which mimics MF, and can only be distinguished by the clinical history and appearance. The clinical appearance of this patient's lesions fitted with a diagnosis of MF. It wasn't until further history was obtained, which suggested exposure to garden chemicals, that a benign diagnosis was suspected. We are dependent in the laboratory on the clinicians for providing us with details of the appearance and history of a lesion. In the words of Sir William Osler (b.1849-d.1919) "If you listen carefully to the patient they will tell you the diagnosis" which emphasizes the importance of taking a good history.

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Performance of the NZIMLS and the services it provides. Results from a questionnaire

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On behalf of the NZIMLS Council

Abstract

The objective was to learn about members' opinions on the performance of the New Zealand Institute of Medical Laboratory Science and the services it provides.

A 30-question questionnaire was distributed to members through the Journal. Members were asked to rate, on a scale of 0 to 10, the services that the Institute provides, and to rate on the Institute activities that were important to the individual member. Further questions elucidated demographic details and members were invited to comment on any of the above.

Out of a potential pool of 1903 members (as at April 2006), 146 returned the questionnaire giving a response rate of 7.7%. Special Interest Group seminars, continuing education and the CPD programme were seen by members to be very important, while Fellowship and Council governance were less so. Promotion of the profession and sponsorship opportunities by the Institute were rated lowly.

These results, together with the many comments made by members should help the Institute's Council in improving its services to meet the needs of the scientists and technicians who make up our membership and profession.

Key words: activities, education, NZIMLS, questionnaire

N Z J Med Lab Sci 2006; 60 (3): 102-105.

Introduction

The New Zealand Institute of Medical Laboratory Science (Institute) is the professional organisation representing scientists and technicians engaged in the profession and practice of medical laboratory science in New Zealand. In order to fulfil its role of serving the professional needs of its members, the Institute provides continuing education through the Annual Scientific Meeting (ASM), Special Interest Group (SIG) meetings, professional examinations (FNZIMLS, QMLT, QPT and QSST), and the New Zealand Journal of Medical Laboratory Science (Journal). The Institute also provides a Competency and Professional Development (CPD) programme and has representation on the Boards of Study or Management Committees of the three New Zealand universities offering a medical laboratory science degree programme.

In order to gauge the performance of the Institute and the services it provides, Council decided to run a questionnaire on those aspects. Its aim was to use the information gathered from the questionnaire to continue to meet the needs of the scientists and technicians who make up the Institute's membership. We report here the results of this questionnaire.

Methods

A questionnaire containing 30 questions was distributed to members of the Institute through the April 2006 issue of the Journal. In order to improve the response rate, travel/accommodation vouchers were offered as prizes for all eligible returns. A close-off date of 1 June 2006 was set for return of the questionnaire.

In the first section members were asked to rate, on a scale of 0 (poor) to 10 (excellent), the services the Institute provides. These services were the Journal, Council newsletter, SIG seminars, Annual Scientific Meeting (ASM), organisational structure, sponsorship opportunities, promotion of the profession, website, CPD programme, Executive Office, QMLT/QPT examinations, and the NZIMLS Fellowship.

In the second section members were asked to rate (on a scale of 0 to 10) on the above Institute services that were important to the individual member. Added to this was NZIMLS representation on the Batchelor of Medical Laboratory Science (BMLSc) programme management committees. Members were then asked the following: how long have you been a member or associate of the Institute (< 1 year; 1 - 5 years, 6 - 10 years, > 10 years); should the Institute provide CPD records of practitioners to employers; why did you join the Institute (wanted to, employer paid for it, had to because of QMLT/QPT exams, other); and what is your current membership category (Member, Associate, Fellow). Finally, members were asked what additional benefits the Institute could offer its members, what areas the Institute could improve on, and any further comments.

Results are presented as mean scores (out of 10) with 95% confidence intervals (95% CI) and range of values. Statistical analysis was by un-paired student t-test with statistical significance set at the p 0.05 level.

Results

Out of a potential membership of 1,903 (at time of the questionnaire), 146 members returned the questionnaire giving a response rate of 7.7%. Of these, 25 were Associates, 118 were Members, and 3 were Fellows. Table 1 shows the mean scores (with 95% CI and range of values) of the Institute's services rating and the Institute's services of importance to members. For Fellowship, only responses from Members and Fellows were considered (Associates are not eligible to sit the Fellowship examinations). There were statistically significant differences in the mean scores between Members and Associates for two of the questions. Thus, members rated sponsorship opportunities provided by the Institute lower than Associates (mean scores: 6.1 and 7.0 respectively; p=0.018), while Associates rated the CPD programme lower than Members (mean scores: 6.5 and 7.2 respectively; p=0.02).

For the rest of the questions there were no significant differences in mean scores between Members and Associates (data not shown).

12 respondents had been a Member/Associate for < 1 year, 53 for 1 to 5 years, 15 for 6 to 10 years, and 66 > 10 years. When asked, should the Institute provide the CPD records of practitioners to employers, 97 (66.4%) replied yes, 49 (33.6%) replied no or did not answer. Reasons for joining the Institute revealed that 85 (58.2%) wanted to, 35 (24.0% because their employer paid for it, 14 (9.6%) because of QMLT/QPT exams, and 10 (6.8%) for other reasons (mainly CPD). Two did not reply to this question.

Table 1. NZIMLS services and activities ratings

NZIMLS services rating	Mean score	95% CI	Range of scores
Journal	7.0	6.7-7.3	0-10
Newsletter	6.8	6.5-7.1	2-8
SIG seminars	8.5	8.2-8.8	2-8
ASM	7.7	7.4-8.0	3-10
Organisational structure	7.1	6.8-7.4	1-10
Sponsorship	6.3	5.9-6.7	0-10
Promotion of profession	5.9	5.5-6.3	0-10
Website	7.6	7.3-7.9	1-10
CPD programme	7.1	6.8-7.4	1-10
Executive office services	7.3	7.0-7.6	0-10
QMLT/QPT exams	7.5	7.1-7.9	1-9
Fellowship	6.1	5.6-6.6	0-10

NZIMLS activities of importance	Mean score	95% CI	Range of scores
Journal	7.5	7.1-7.9	0-10
Continuing education	8.5	8.2-8.8	0-10
Council governance	6.9	6.5-7.3	0-10
ASM	7.8	7.4-8.2	0-10
Special Interest Groups	8.8	8.5-9.1	0-10
Promotion of profession	8.7	8.4-9.0	0-10
Website	8.3	8.0-8.6	0-10
CPD programme	8.5	8.2-8.8	0-10
QMLT/QPT exams	7.7	7.2-8.2	0-10
Fellowship	6.1	5.5-6.7	0-10
Representation on BMLSc courses	8.4	8.1-8.7	0-10

As well as asking to rate the various NZIMLS activities, members were invited to comment on the Institute's services. Below is a summary of comments made.

How do you rate the quality of the journal?

From 21 comments, 6 were positive. Others wanted more articles with scientific content, more social news, more relevant information about the NZ laboratory scene, and have Council members' details and contact information published regularly.

How do you rate the Council newsletter?

From 8 comments, 4 were positive. Comments were made about the content, and others wanted more information on changes in the laboratory scene.

How do you rate the SIG seminars?

From 21 comments, 6 were positive. Comments were made about cost, advertising, location, and lack of information relevant to smaller laboratories. One was under the impression that SIG's were not provided by the NZIMLS.

How do you rate the ASM?

From 18 comments, 4 were positive. Comments were made about cost, lack of opportunity to attend, and some felt its scientific content too high powered. One suggested SIG meetings move back to the ASM.

How do you rate the organizational structure of the NZIMLS?

From 5 comments only 1 was positive. Comments were made about lack of information about the structure, function, and communication with members.

How do you rate sponsorship opportunities?

From 9 comments only 1 was positive. Most asked "what sponsorship". Others said it was not publicised enough.

How do you rate the promotion of the profession?

Of the 21 comments made, all were negative. Most felt that Council was not doing enough to promote the profession to the public, schools and District Health Boards (DHBs). Others felt that the profession was undervalued, and that the "technologist' label was still very strong.

How do you rate the NZIMLS website?

From 10 comments, 5 were positive ranging from excellent to user friendly. Others found it hard to get on, and difficulties with dial up.

How do you rate the CPD programme?

This question received the most number of comments, namely 39 of which 13 were positive. Comments were made about points allocation, its compulsory nature, the requirement to take notes at the meetings, difficulty of obtaining points for part time staff, need for more programmes to obtain points, and need for the NZIMLS doing more to help members obtain CPD points.

How do you rate the services provided by the Executive Office?

From 8 comments, 4 were positive. Three members stated they did not know what services were provided by the Executive Office.

How do you rate the QMLT/QPT exams?

Most of the 15 comments were positive. Some wanted them to be brought into the NZQA framework, and others complained about the delay in receiving certificates.

How do you rate the Fellowship?

From 13 comments, 2 were positive (current Fellows). Comments were made that it was not recognised outside of the profession, lack of recognition by employers, no longer relevant to new graduates (rather do a Masters or PhD), and that to obtain Fellowship was a complex pathway.

How important is publication of the Journal?

From 7 comments, 4 were positive (CPD opportunity created by the journal-based questionnaire). One member commented that the Journal and the CPD programme were the only services of value run by the NZIMLS. Others wanted more content, ease of publication (automatic acceptance of submitted papers), and frequent updates on the NZ laboratory scene.

How important is provision of ongoing education?

From 10 comments, 5 were positive. Some members wanted on-line programs and provision of programmes by employers, others complained about the compulsory nature (for CPD).

How important is NZIMLS Council governance?

Two comments were made. One suggested the NZIMLS merged with the MLSB to save fees, and the other commented that the NZIMLS should up its profile.

How important is the ASM?

From 11 comments, 7 were positive. Comments were made about cost, access for junior staff, that it should not conflict with SIG meetings, relevance of presentations, and whether it should be reduced to a bi-annual event.

How important are SIGs?

From 13 comments, 11 were positive. SIGs were generally considered to be important. Some commented that the main focus of SIGs should be relevance, access and frequency.

How important is promotion of the profession?

From 9 comments, 4 stated that this was important, but could be improved. Most of the comments focussed on the failure of the NZIMLS to promote the profession to the public and to secondary schools. It was also considered important that the profession has a more public face.

How important is the website?

From 6 comments, 3 said it was important and were positive about how good the NZIMLS web site is.

How important is the CPD programme?

From 9 comments, 6 thought it was very important, but the mechanics are difficult, i.e. good idea, bad execution. One commented that the CPD programme does not make a good bench worker, while 2 thought that it was a waste of time going to meetings, and were negative about the programme's compulsory nature.

How important are QMLT/QPT exams?

From 8 comments, 6 stated these exams were very important, one thought it had limited quality and one commented that the laboratory scientist may be an endangered species now that technicians are registered.

How important is Fellowship?

Three comments were positive, one questioned its relevance and one thought the quality of some Fellows to be light.

How important is NZIMLS representation on BMLS programmes?

Nine members thought this was important in order to satisfy industry needs and insuring relevance. One commented that both the course and the graduates were getting worse each year.

What other benefits could NZIMLS offer members?

- Educational opportunities, more opportunities to gain CPD points, CPD incentives (prize for highest number of points each year), more workshops, recommended reading, book reviews, on-line programmes.
- Discount membership if article published in journal, cheaper conferences / SIG's. Life membership after 30 years?
- Discount health insurance, shopping, and legal advice.
- Issue APC's, regulate registration of scientists and technicians. Help acquire registration for MLS overseas e.g. UK.
- Earlier timetable of conferences, SIG's etc.
- SIG talks on website, overseas research / news relevant to us. Interesting cases from other labs on website or in journal.
- Work with union to improve conditions / pay, etc.
- Promotion of profession at schools and in the wider community. Become involved and more public in political issues affecting lab workers, e.g. current contracting.
- Free membership, on-line education, more CPD opportunities, promotion/branding of profession as scientists, not technologists.
- Continue to focus on on-going education of members and promotion of profession to public. Increase the publicity about the profession.
- On-line education and employment of an education officer.
- Insurance / travel / fly buy / discount schemes from large retail outlets / benefits.
- Scholarships or grants for further education other than fellowship exams / thesis, e.g. PhD, Masters programme.
- Encourage or create opportunities for younger members to contribute to NZIMLS activities like organising SIG meetings.
- Closer relationships with similar organizations like the AACB.
- Journal articles on-line.
- On-line educational opportunities for CPD points for long distance learners or part-timers.
- Need to be more pro-active in supporting the profession, where has the NZIMLS been in the current changes.
- Updates on the website on progress of current contract negotiations between laboratories and DHB's.
- Other items of interest, communications regarding health or of laboratory relevance or of interest to members.
- NZIMLS needs a greater profile as does the profession.
- By proactively supporting the profession. Where have the NZIMLS been in the current changes, I have seen more letters from the RCPA!!

Are there any other areas which NZIMLS could improve?

- Media coverage for lab issues (as above), promote profession (11 requests for this)
- Improve education available for mortuary techs and other minority sciences.
- Recognition for technicians, promotion of graduates as good scientists.
- Need the journal to show more of people that work in profession.
- Better communication, NZIMLS regional reps should visit each lab annually.
- Website should have interesting cases, journals, presentation etc. Site for learning with specific topics in all disciplines. Provide on-line quiz for CPD points.
- Give SIG conveners a booklet on how to run SIG meetings, i.e. venue booking, etc.
- Booklet or letter to new members outlining what NZIMLS does for them, including what benefits for a person going on to Fellow or Life Member, and how to achieve these levels.
- Local seminars more frequent for specialist groups.
- Initially CPD registration was very bad, not too sure if it has got better
- CPD education.
- Promotion and helping with CPD.
- Improve CPD website.
- CPD for part-timers.
- Council ought to up date members more frequently and be in more regular contact, especially local reps, and have council news in the Journal.
- Expand on-line education.
- Promotion of profession at DHB level, be more pro-active.
- More opportunities to publish papers in Journal.
- CPD, more on-line education resources, better use of membership database to record members CPD points from their registration and attendance at seminars, conferences etc.
- Have annual SIG meetings for all disciplines.
- Introduce profession at secondary school level.
- Revamp CPD.
- Doing a great job already.
- Closer support of members and issues of topical interest.
- Provide information on expanding changes in science / methods / techniques / - more relevant education.
- More seminars.
- Continue to promote profession and be more supportive of students and courses.
- By providing suitable programme for BSc graduates to train to become BMLS - the current one is unsatisfactory and reflects poorly

on our training institutes concerned.
- MLS profile needs to be improved.
- Journal should regularly have council members contact details and a list of current MLS discipline textbooks to be published in Journal.
- Take a more pro-active and public stand.
- More communications between NZIMLS / moderators and examiners when setting exams.

Any further comments?
- Doing great job in difficult environment, well run organization, keep it up, thank you very much to those who hold office and work on our behalf.
- OK job but could do better. More to encourage life membership.
- Get more professional, get QTA into NZQA framework.
- Could work for benefit of MLS more in terms of salary, holidays, conditions etc.
- Journal excellent, consider a section covering areas of interest to lab technicians and phlebotomists.
- Keep up with CPD to raise standard of profession.
- Find that AUT students far ahead in practical work. Students should be encouraged to have more hands on at work.
- Have main conference every 2 years only.
- Does it really matter; we'll all be redundant soon anyway?
- Know little about NZIMLS as I am a new members, not much information sen
- NZIMLS and NZCS meeting ought to be held at same time.
- Very positive. Big improvements - well done. Many thanks. Positive NZIMLS. Doing a great job. Pleasure to belong to a well organized professional body. Very positive about the CPD and Jillian excellent. Great work, many thanks. Appreciate hard work by NZIMLS council members.
- Wake up! You have missed the boat in too many areas. Laboratory staff are not united but split into at least two camps and the old adage "United we stand...." could have helped in the current restructuring. Also put my number on this form, but feel it is going to bias a lot of people from saying what they really want to if then do not have anonymity!
- Need to be more visible and effective voice of membership.
- Need to provide a pathologist assistants exam.
- The profession is at a watershed and NZIMLS needs to communicate an innovative and contempory strategy to its membership.
- Assistants still feel like a 2nd class lab worker even though we teach and correct MLS mistakes. Need a bridging programme for lab assistants to MLS's especially for part-time workers.

Discussion

Results from this questionnaire show that that SIG seminars, continuing education, and the CPD programme were seen by members to be very important, while Fellowship and Council governance were not generally so. Promotion of the profession and sponsorship opportunities by the Institute were rated lowly. The quality of the many services the NZIMLS provides generated mixed responses, some rating various services highly, while others rated some poorly.

There are some limitations to this study. Firstly, the response rate was very low (7.7%) and thus may not necessarily reflect the opinions of the majority of the members. It could be argued that the non-responders (92.3%) are more or less happy with the current state of affairs, or that they are indifferent. Another limitation is that specific questions can generate biased opinions. However, comments ranged from extremely positive to extremely critical.

From the many comments made, some few key points stood out. One is that members still confuse the different roles of the NZIMLS, the Medical Laboratory Science Board (MLSB) and the Union. For instance, one member stated that the NZIMLS could work for the benefit of members more in terms of salary, holidays and working conditions. This is the role of the Union, not the NZIMLS. Another wants the NZIMLS to issue APCs and regulate registration of members. This is the role of the MLSB. A recent Editorial in the Journal has illustrated the key roles of the NZIMLS and of the MLSB (1).

Another key point that emerged is that the majority of members who commented negatively on the role the NZIMLS plays in promoting the profession. Most feel that the NZIMLS is not doing enough to promote the profession to the public, schools and DHBs.

It also appears that CPD is a controversial topic and members feel that the role of the NZIMLS is to facilitate the accumulation of points by enabling members to have on-line educational opportunities, host, sponsor and organize seminars and conferences, and to make the CPD process as simple as possible.

There have also been quite a few suggestions made by members in what they feel what additional services the NZIMLS should be offering for its members or in which areas it can improve. They range from sensible suggestions, such as scholarships and grants for further formal education, closer relations with other organizations such as the AACB, and on-line educational opportunities for CPD points.

Although the response rate was disappointing, the results from this questionnaire will help and guide the NZIMLS Council in improving its services to meet the needs of the scientists and technicians who make up our membership and profession. It would be of interest to repeat a similar survey of members at some point in future to gauge whether any Council implementations have worked, and to identify new concerns or requirements in the ever changing scene of medical laboratory science.

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[Reprinted from the Journal of the New Zealand Association of Bacteriologists, 1949; Vol. 4, No. 1, pages 1 - 4]

MASSIVE EXCHANGE TRANSFUSION IN A PREDICTED CASE OF HAEMOLYTIC DISEASE OF THE NEWBORN

P.H.Curtis

(From the Pathology Department, Cornwall Hospital, Auckland)

The following is a brief report on a case of Rh incompatibility encountered in this Hospital, where Wiener's technique for massive exchange transfusion was successfully applied.

It is felt to be of some interest, as transfusions using this technique are not very frequently performed in this country, and as the Laboratory has an important part, not only prior to and after, but also during the exchange transfusion itself.

It also serves to illustrate the importance of routine Rh typing in the ante-natal clinic in order that a full and early investigation may be made on all cases of suspected Rh involvement.

Case History

Genotypes of Parents:

Mrs. W., Group A, cde/cde.

Mr. W., Group A, probably cDe/cde, but could be cDe/cDe.

The first pregnancy terminated in a normal full-term male, who is still living. This was followed by a miscarriage at 61/2 months, then two full-term stillbirths (no details available), and a further miscarriage at 3 months.

Present Case: Mrs. W. was referred to this Laboratory for Rh investigation as she had a history suggestive of Rh incompatibility. She was found to be Rh negative and from then attended the ante-natal clinic at this Hospital. Further investigation showed Mr. W. to be Rh positive, and in view of the above history was likely to be homozygous -- no A-B-O incompatibility existed.

In the thirty-first week of gestation a plasma conglutination test for Rh antibodies showed a titre of 128. The titre steadily rose to 512+ a week prior to delivery.

Exchange Transfusion

Owing to the increasing titre of Rh antibodies and blocking antibodies (the latter formed by far the greater proportion), it was planned to terminate the pregnancy some four weeks before full term and carry out an immediate exchange transfusion, as it seemed extremely unlikely that the foetus was Rh negative, but the membranes ruptured spontaneously in the thirty-third week.

It was later thought that a stillbirth would result as no foetal movements or heart beat were evident for the next two days. However, a spontaneous, normal, rapid delivery at 4.30 a.m. on the third day resulted in a live female child, which, although some six weeks premature, appeared in good condition - weight, 4 lb,11 oz. No evidence of hydrops could be seen and the liver and spleen were not palpable (see laboratory findings).

Immediately approximately 700cc. of Group O Rh negative (D negative) blood was bled from an orderly living in the Hospital, into a minimum quantity of glucose citrate anticoagulant (120cc.), and the transfusion was commenced at 6.15 a.m.

The left saphenous vein was exposed and a small cannula introduced. Using a 20cc. all-glass syringe and two-way tap, 100cc. of blood, and 0.1 cc. of heparin were run in. The left radial artery, which had by then been exposed, was partly severed and the blood allowed to run directly into a small bowl, from which it was poured into a graduated cylinder. Some difficulty was experienced at the start in getting the arterial blood to flow freely, but this was soon overcome when the heparin took effect. Calcium gluconate was injected in four doses (5cc. 10%) at equal intervals throughout the transfusion to offset hypocalcaemia due to the infusion of sodium citrate in the blood (1).

From the start of the transfusion the haemoglobin fell from 16.5gms./100cc. to 10.5gms half-way through. It then rose again

steadily to 13.0gms. at the end. This was probably due to two main factors, first, at one point the outflow exceeded the intake owing to repeated gumming-up of the syringe plunger, and, secondly, the haemoglobin content of the infused blood was slightly lower than that of the baby's. The former was overcome by applying a trace of sterile liquid paraffin to the plunger and by repeatedly changing the syringe.

When 700cc. of blood had been bled from the baby, the artery was ligated and a further 100cc. of blood infused. In all, 700cc. of blood was withdrawn and 829cc. in glucose citrate replaced.

A Coomb's test performed before the transfusion showed the baby's cells to be strongly sensitised and gave a negative result at the conclusion. It was still negative 36 hours later.

The baby showed what appeared to be a trace of jaundice at the commencement but this faded early in the transfusion. From laboratory findings the jaundice was probably deeper than observed as the latter was recorded under artificial lighting conditions. Twitching of the face muscles was twice noted but stopped immediately after an injection (I.V.) of 5cc. of 10% calcium gluconate. Oxygen was given when the haemoglobin fell to 11.0gms.

The patient returned to the ward in good condition in spite of the operation having taken 33/4 hours. By evening it had become deeply jaundiced, but this faded completely within 48 hours.

Discussion

It is generally agreed that the time of the transfusion could be considerably reduced mainly by experience in technique, early heparinisation (0.2cc. of heparin 15 mins. Before performing the arteriotomy) and by maintaining a faster rate of infusion of blood.

Possible fatal effects from haemorrhage caused by the use of heparin must not be overlooked, but to date no fatal cases have been reported where this technique was used for transfusion.

Laboratory Findings

Mrs. W. Antibodies (using plasma conglutination technique):

When first tested for complete and blocking antibodies (31st week of gestation) a plasma conglutination test gave a titre of 128. The titre steadily rose to 512+ a week prior to delivery.

5 days postpartum the titre was 8060.

12 days postpartum the titre was 10,240 (complete antibodies, titre 320). Patient discharged.

From a study of the genotypes it would appear that Mrs. W.'s serum contained anti-D antibodies (complete and blocking) of high titre.

Breast milk which was found to contain antibodies, titre 2048, was fed to the baby twice on the third day but was then discontinued.

Cord Blood:

Haemoglobin 8.5gms./100cc.
Icterus index 40 units.

Baby W.:

At delivery: 4.30 a.m. - Rh positive (D+ve), Coomb's test positive. Haemoglobin, 16.5gms. /100ccs. R.B.C., 3.4 million/cmm.

After Exchange Transfusion, 10 a.m. same day - Coomb's test negative. Haemoglobin, 15.0gms. /100ccs. R.B.C., 6.4 million/cmm. 5 p.m.: Haemoglobin, 21.5 gms. /100ccs. R.B.C., 7.1 million/cmm.

Tenth Day After Delivery had settled to: Haemoglobin varied between 16-17gms./100cc. R.B.C. varied between 5-6 million/cmm.

At no time did the normoblast count rise above 10 per 100 leucocytes.

It was hoped that tests for the sensitisation of the baby's cells could have been carried out during the transfusion as a matter of interest in order to assess the actual exchange, but this proved impossible at the time. It is not essential but is undoubtedly of interest.

Wiener considers that such a technique gives up to 98% exchange of blood, but other workers think this figure is too high.

Commentary

It is essential that all necessary apparatus be ready well in advance to assist in the smooth running of the operation.

Fresh Rh negative blood should be used so that little as possible degeneration of red cells occurs prior to infusion.

The anticoagulant for the donor's blood should contain a minimum of sodium citrate as hypocalcaemia may result. Prophylactic doses of 10% calcium gluconate (5cc.) will prevent this.

There was a marked discrepancy between the haemoglobin and red cell count taken at 4.30 a.m., prior to the transfusion, due to icterus, but as a spectrophotometer was not available it was impossible to estimate the haemoglobin accurately.

Although 100cc. of blood replaced over and above that removed is 50cc. more than advocated, the arterial blood loss into the sterile guards could only be assessed, and this amount extra was considered to be safe on that account.

Summary

1. An operation for massive exchange transfusion on a newborn premature infant has been briefly described, and the part played by the laboratory outlined.
2. From the clinical and laboratory aspects the massive exchange therapy in predicted haemolytic disease of the newborn by the above technique was found to be simple technically and highly effective clinically.

Acknowledgements

The case quoted is by kind permission of Dr. J. A. Oddie, Medical Superintendent, Cornwall Hospital. I wish to thank Dr. R. H. T. Holmden for permission to describe the operation and Dr. Lindsay Brown, pathologist, for his valuable suggestions. The genotyping was performed by the Commonwealth Serum Laboratories of Australia.

Reference

1. Wiener, A.S., Wexler, I.B., and Shulman, A.-Am. J. Clin. Path., 18:2, 141, 1948.

NZIMLS President's Report - 2006

For those of you who have already read the annual report you may have noticed that 2005/06 has been a very active year for the Institute and that the finances of the Institute are looking better than they have for a while. These are of course correct; however, there are other matters in the report that perhaps deserve special mention.

Over the past year the New Zealand Institute of Medical Laboratory Science (NZIMLS) has maintained contacts with both the Australian Institute of Medical Science (AIMS) and the Institute of Biomedical Science in the UK (IBMS). In last year's report I mentioned progress with changes to the procedures in the UK for the registration of New Zealand trained medical laboratory scientists (MLS). Unfortunately this has not progressed as speedily as we had hoped. Toward the end of 2005 we received unofficial notice that NZ registered MLS would be considered more favourably for UK registration. Since this time we have heard nothing and the experiences of a number of New Zealand MLS who have gone to the UK in the meantime lead us to believe that little has changed. Despite several attempts to communicate on this matter we have had little success so far.

During the year the NZIMLS met with the Medical Laboratory Science Board (MLSB) together with the heads of the New Zealand BMLSc degree programmes. This continues to be a useful meeting during which issues of training and university accreditation are usually discussed. In addition, to this formal yearly meeting the Institute often acts as a source of advice in submissions to the MLSB on MLS regulation and other matters affecting the profession. Contact between the two bodies has increased over the past years as the MLSB has implemented changes brought about by the HPCA Act.

Currently, the Institute has 1690 MLS and technicians enrolled in its CPD programme. Most of those enrolled in the programme have also enrolled as members of the NZIMLS. With the completion in December 2005 of the first full year of the CPD programme, the CPD programme auditors provided a useful report to council in April 2005. Of the 231 (13.2%) of the practitioners audited in the process, 95.7% of points claimed were verified by IANZ. This level of compliance is viewed by Council and the Institute auditors as commendable for the first year of the programme. The report has confirmed that most MLS are committed to the concept of competence and continuing education in the profession. The audit process and the accumulation of information about activities eligible for CPD points during the 2004/05 year, forced a few small tweaks to the programme for the 2006 year. These have been circulated in the newsletter and have been posted on the website for reference for 2006. The overall acceptance of the programme has been very satisfying which has been in part been due to the work of the Institute's CPD programme coordinator. Jillian Broadbent has done an excellent job of promoting the programme and has put a lot of effort into making contact with as many practitioners and laboratories as possible. The CPD programme is something the members of the NZIMLS should feel proud of, with its development and maturity well ahead of most other programmes used by other professional bodies and registration authorities in New Zealand. It may even the lead the world with its innovative web based approach and its place in the regulation of the medical laboratory science profession in our country.

The Institute's website has been an area of continued development in the last year. The data from the usage of the site shows high activity not only from within New Zealand but also from overseas visitors. During the last year Council approved modifications to the site to improve the way in which practitioners manage their CPD points. In addition to this, members are now able to download articles published in the Institute's Journal, obtain syllabi for the Institute's technician examinations and download examination papers for previous year's examinations. Use of the forum has been slow to get started, however, there is now a growing few who find this a useful means of having their say about medical laboratory science issues. The employment section of the site which is provided free of charge to MLS employers in NZ, is attracting a growing number of employment agencies and overseas enquiries. In 2005/06 the site placed 60 advertisements for companies looking for laboratory staff. The provision of online continuing education for the profession remains a strong focus for the Institute. At its last meeting Council approved a proposal for the development of a medical laboratory science classroom to be incorporated into the website. This development will offer modules for each of the medical laboratory science disciplines using a quiz-style multi-choice question/answer approach and work toward this goal is currently underway and will continue through 2006 and into 2007.

Staff retention, career progression and promotion are ongoing issues for the profession. In 2005 Council initiated enquires with the New Zealand Clinical Training Agency (CTA) about support for clinical research in diagnostic laboratories. Currently there are few opportunities for career progression in the sciences and too few BMLSc graduates undertaking post-graduate qualifications. Some health professions are CTA funded for post-graduate qualifications and there is a chance that MLS may also be eligible. Success with this initiative hinges upon strong support from employers and Council is currently working on this. With a secured source of funding for part-time research, it is hoped that some laboratories will be more able to support career progression in the sciences.

In addition to this, Council is also watching overseas developments in which laboratories are turning toward MLS for greater involvement in areas of the laboratory once deemed the domain of the pathologist. In Queensland the State Government has approved programmes to train scientists in surgical grossing and post mortem work, as pathologist numbers in the state continue to decline. Next semester the Queensland University of Technology commences a Post Graduate Diploma of Surgical Grossing. Plans are afoot to offer similar programmes in other disciplines such as microbiology, clinical biochemistry and haematology through the Queensland University of Technology. In the UK the training of biomedical scientists to become clinical scientists and specialist diploma holders in some of the disciplines is already underway. In some areas training is part of a joint venture between the Royal College of Pathologists and the Institute of Biomedical Science. These programmes are being met with mixed support from pathologists but the need to provide continued laboratory services for the future is the main driver. These are issues relevant also here in New Zealand and Council will be keeping a watch on future proceedings, especially those in Australia.

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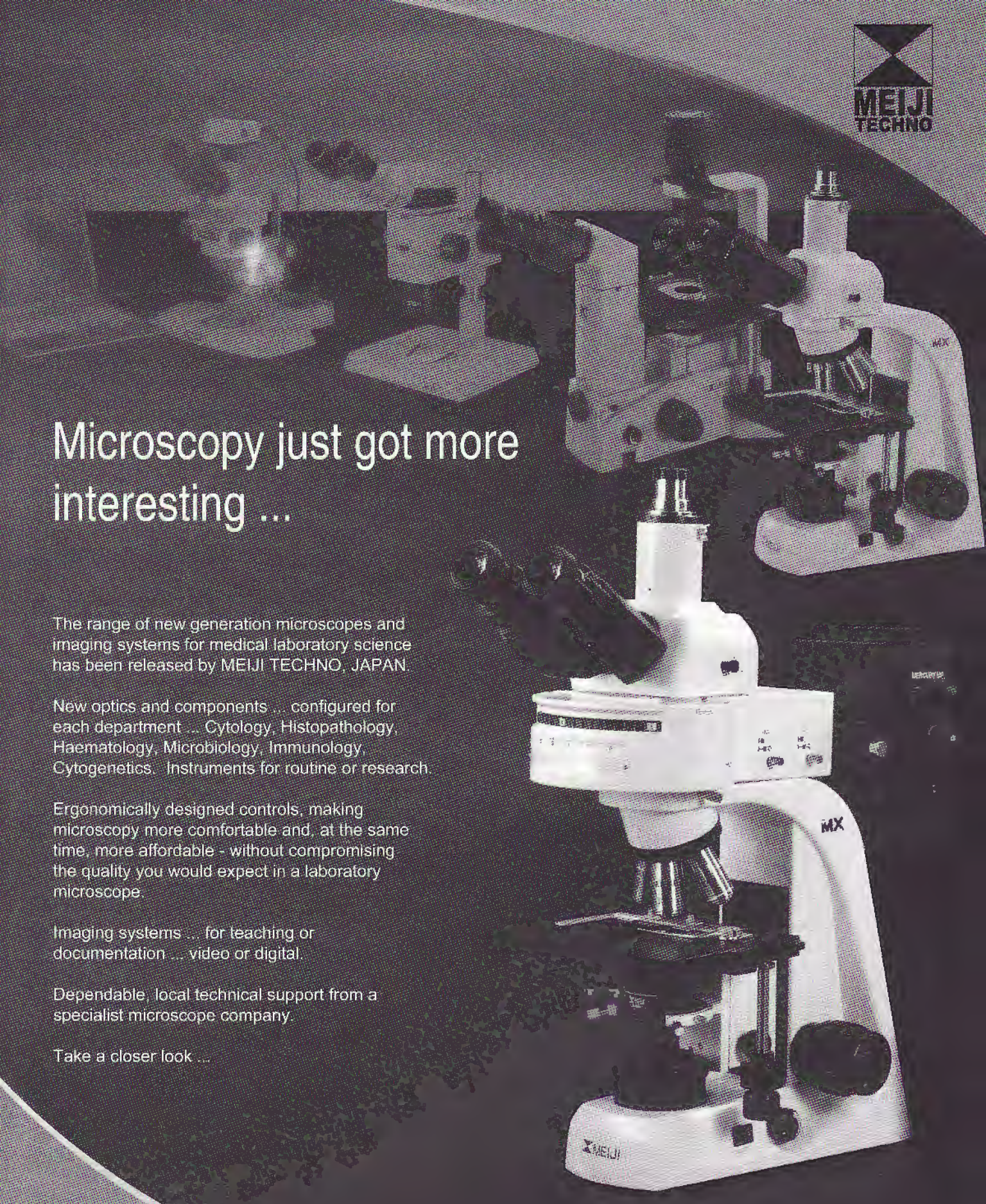

Microscopy just got more interesting ...

The range of new generation microscopes and imaging systems for medical laboratory science has been released by MEIJI TECHNO, JAPAN.

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take a closer look

For those not already aware, staff of the Executive Office has had to deal with a big increase in membership and CPD enrolments over the past two years. In addition, changes to the Institute's accounting systems, invoicing of NZIMLS membership, the CPD programme, and a big increase in numbers sitting the Institute's technician examinations have also contributed to the workload. There has also been a steady increase in the number of Special Interest Group activities as well as increased numbers attending the meetings. Each of these activities has combined to stretch the resources of the Executive Office at times and Council intends to address these issues in the upcoming year.

In my President's report of the activities of the Institute in 2005 I stated that "those who work in the profession of medical laboratory science know that change is an integral part of the profession". At that time I was referring to historical changes dating back to the inception of the Institute and the days of the New Zealand Association of Bacteriologists. Little did anyone realise (most of all myself) how prophetic these words would become for the medical laboratory profession in the year ahead. In this, the 60th year of the NZIMLS, laboratory services have come under attack in many parts of the country. The drivers for change appear to have the goal of forcing down the costs of pathology services thus freeing up health dollars to spend in other areas. This should come as no great surprise; however, this time around changes have been on a scale not seen before. In the past various DHB's and Government have opted to tamper with the provision of services by privatising public hospital laboratories, restricting access to community referred laboratory testing and hospital work, removing important tests from the schedule, and more recently shutting down laboratories completely. The current treatment of laboratory services by the DHB's currently threatens the world class service that exists in this country. In recent times the Institute has responded to this dilemma by writing to the Minister of Health, making a press release stating the profession's concerns over the changes and the impact upon the profession, and written to each of the DHB's Chief Executive Officers and Chairmen of the DHB's. In addition, there have been radio interviews with the President and the opportunity to talk to the media on a growing number of occasions about the ongoing developments. There may be some among the profession who feel that Council has been slow to respond, however in defence it can be stated that it has sometimes been challenging to make statements on the proceedings that have not reflected emotion and presented conjecture. This has forced a focus on the issues of scientist training which have not been viewed by the media as sufficiently newsworthy in the hype of the last months. The message that the quality of New Zealand's laboratory services is now at real threat appears to be now getting through to the public. Comments made by ourselves and others that were dismissed initially as "sour grapes" are now receiving a second consideration and may provide opportunity for the profession to explore in future public statements. The events of the past months have indeed been challenging for Council, however, I now feel as though our comments are increasingly being sought and our profile is increasing.

In closing it is pleasing to see the state of the current accounts of the NZIMLS and the overall positioning of the Institute. These are I no small part due to past and present Councils, Fran van Til and the team at the Executive Office, Rob Siebers, Ann Thornton and Trish Reilly from the Journal, and Jillian Broadbent as CPD programme coordinator. In addition to these, there are many others who have worked behind the scenes organising conferences and SIG meetings etc. I finish with the comment that the profession has continued to be well served by many over the past year!

Chris Kendrick
NZIMLS President

Napier 2006 NZIMLS Conference

The developing lab world - sea, sun, fun and romantic nights - yeah right!

This session was held on the final morning of the conference where personal insights into working in medical laboratories throughout the Pacific and Asia were given. Ron Mackenzie, Chairman of the PPTC gave an outline of how the PPTC was set up to bring Pacific Island country laboratory workers to NZ for short term training. He spoke of monetary assistance from NZ Ministry of Foreign Affairs and Trade, NZ Red Cross and the NZIMLS, the latter he said should take pride in helping lab services in the Pacific.

Marilyn Eales' talk was entitled "A tale of two countries - When is Aid effective?" The two countries she spoke of were Fiji and Papua New Guinea where Marilyn spent time working in hospital laboratories. Marilyn first spent time in Fiji as a VSA tutor Technologist in 1969 at the CWM Hospital. She said Fiji can now be very proud of its lab services and its training programmes. Marilyn also spoke of her time in Papua New Guinea between 1971 and 1974 and the setting up of a School for Health Sciences, which, after enthusiastic expats left, unfortunately did not live up to expectations.

Mike Lynch's talk was how laboratory staff could get to work for the World Health Organization. Mike had worked for the WHO as a Laboratory Specialist in 1989-1990. He mentioned the WHO website which shows different scientific grade vacancies. He said the main attribute of people needed, is to be able to turn a hand for doing anything in a laboratory

Nicky Beamish's talk was entitled "Emails from the Pacific" In 2000 Nicky went to Papua New Guinea working in Rabaul and East New Britain as a VSO volunteer for two years. Her job description was to supervise and train lab technicians in 10 different laboratories many of which were remote, rough and basic, some having water for two hours per day and power for only one hour per day. After returning to NZ and working in Wellington Medical Laboratory Nicky went to Palau in 2004 as an advisor and trainer for the laboratory in Koror. There she found the laboratory to be well equipped and doing a broad range of testing. The 10 lab staff had good technical skills but some lacked background knowledge. Nicky ran workshops for the staff in blood bank, health and safety, quality assurance and parasitology. Since she has returned to live in Wellington, the laboratory has moved a long way forward and is continuing to do so.

Tirath Lakshman spoke of his role as the blood bank EQA Co-ordinator for the PPTC. His talk mentioned three laboratories that are part of PPTC EQA programme and gave numbers of staff in each of the labs, how many blood groups are done each day, how many units were collected and different blood components held in the blood bank.

Vanessa Thompson's talk was entitled "Heaven on Earth". Vanessa spoke of her time working in Nepal in the late 1990s where she was involved with a TB and leprosy project, setting up a laboratory national quality assurance programme, maintaining and fixing equipment and training lab staff. Vanessa completed her Fellowship of the NZIMLS there which involved writing a book on blood cell differential counts. In July 2005 she visited Tibet where she ran a three week course in blood cell morphology. This involved teaching students how to take blood, make stains, prepare and stain blood films and do differentials. Vanessa's differential book has now been translated into Chinese through the help of AusAid.

John Elliot spoke about the PPTC currently and in the future. John introduced the six Pacific Island Laboratory Technicians who are attending a PPTC blood bank course in Wellington and had travelled to Napier to attend the conference. He said the main principles of the PPTC were still the same as when the Centre was set up in 1980 - appropriate, affordable and sustainable and the main objectives of the Centre were in laboratory training, the EQA programme and consultative work. John spoke of the TB EQA programme in association with the WHO and SPC where the PPTC reviews TB smears from Samoa, Tonga, Kiribati, Tuvalu and the Cook Islands and more recently from Binh Dinh Provincial Hospital in Vietnam. John also spoke of his recent time in Vietnam working with the Vietnam Health Trust setting up an introductory course in laboratory management and quality systems based on ISO 15189. He also spoke of the PPTC's involvement with a distance learning programme and the setting up of a Certificate in Medical Laboratory Technology which will be a one year course free of charge to students from 11 Pacific countries. As part of the contract with WHO the PPTC will be required to investigate the possibility of a tertiary educational institution providing credits for the course.

Unfortunately there was insufficient time for the panel discussion and question time which had been advised would take place.

Blood bank technology course 14 August - 8 September 2006

This course was held during August and September with six participants attending. The participants attending were Tuitoma Arobati and Bernard Tatireta from Kiribati, Silivia Rosova from Suva, Fiji, Puipuia Alaelua from Samoa, Evelynn Tomokane from Palau and Rosely Livae from the Solomon Islands. John Dagger from the Wellington Blood Centre was their tutor who gave them valuable information to take back for their countries Blood Service. The PPTC is very grateful to the Wellington Area Centre of the NZ Blood Service for again running the training programme and especially John Dagger for all his hard work. As mentioned above the participants travelled to Napier to attend the NZIMLS conference. Rosely Livae from Gizo Hospital in the Solomon Islands was sponsored to attend the Blood Bank Course by the Hawke's Bay Branch of the New Zealand Red Cross and after the NZIMLS conference had finished Rosely along with the other

participants of the course visited a deer farm of one of the members of the Hawkes Bay Red Cross where they had close up view of farming in NZ and had afternoon tea with members of the branch.

Regional Workshop "Labnet 2006 and Stop TB Meeting Noumea New Caledonia 31 July - 4 August 2006.

John Elliot and Christine Story from the PPTC attended these two meetings which were held at the SPC headquarters and IRD in Noumea. These meetings were valuable in being able to meet up again with laboratory staff from around the Pacific. A full report of these meetings will appear in the next 'Pacific Way" column.

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HSIG questionnaire

Haematology
Special Interest Group

Journal article:
Hematological malignancy and pregnancy: a single-institution experience of 21 cases. Journal of Clinical Laboratory Haematology 2006; 28, 170-176.

Questions:

1. What is the incidence of haematological malignancies during pregnancy?
2. List any four haematological malignancies associated with pregnancy?
3. True or False, A human foetus is most vulnerable to teratogenic factors or agents during the first and second trimesters?
4. Patient 4 was treated with chemotherapy, what was her final outcome and the cause(s) for it if any?
5. What does the drug COPP stand for?
6. True of false, Does the drug ABVD stand for - nitrogen mustard, vincristine, procarbazine and prednisone?
7. What are the 3 embryotoxic or tetatogenic effects of chemotherapeutic drugs?
8. True or false, Danazol is a drug suspected of having a teratogenic effect on humans?
9. What 2 conditions have a greater chance of occurring in a pregnant woman with primary thrombocythemia?
10. Why does chemotherapy during the second and third trimester possibly not require a termination in pregnant woman with acute leukaemia?

Answers on page 98

New Zealand Institute of
Medical
Laboratory
Science

NZIMLS Fellowship

Members of the NZIMLS may not be aware of a recent change to the Fellowship regulations. It is now possible for candidates to be exempted from the Part 1 examination and to obtain Fellowship by Part II if they are holders of an appropriate postgraduate qualification.

Rule 3.17 of the Fellowship Regulations states:

Part 1 by exemption. Candidates applying for Fellowship by examination may be exempted the Part 1 examination if they are holders of an approved postgraduate qualification in Medical Laboratory Science. The course of study must meet the minimum requirement of the equivalent of one year's full time study.

Post graduate qualifications recognised by the Institute, for purpose of exemption to sit the Part 1 examination are:

- ***Fellowship of The Australian Institute of Medical Science (AIMS)***
- ***Fellowship of the Institute of Biomedical Science (IBMS)***
- ***Fellowship of The Australian Association of Clinical Biochemists (AACB)***
- ***A postgraduate qualification in Medical Laboratory Science, or an appropriate postgraduate qualification approved by the Fellowship Committee***

Approval of other qualifications will be at the discretion of the Fellowship Committee

Check out the NZIMLS web site for the full regulations for Fellowship.

Chris Pickett, Rob Siebers, Ann Thornton. Fellowship Committee.

New Zealand Institute of

Medical Laboratory Science

EIGHTEENTH ANNUAL

NICE WEEKEND

Date: 27-29 April 2007

Location: Wairakei Resort

A Transfusion Science Educational Opportunity

Organised by the NZIMLS TSSIG

The NICE Weekend (National Immunohaematology Continuing Education) is an educational meeting for all people working in Immunohaematology and/or blood services. As usual it will be held at the Wairakei Resort Hotel. Registration starts 5pm Friday. Weekend finishes approx. 3.30pm Sunday.

As always, all those who register are required to participate. You must present either a poster, or an oral presentation lasting 2 to 5 minutes, on any topic related to Immunohaematology or blood transfusion. It can be a case study, a discussion, a question, a problem you want others' help with, etc. This will be followed by questions and discussion of the topic you raise. This compulsory participation makes everyone nervous (yes, even the "old hands") but it really is one of the reasons why the NICE Weekend is so successful. There are awards for the best presentation and poster.

The registration fee is $391, reduced to $356 for current financial members of the NZIMLS. Your registration fee entitles you to:

- two nights (Friday 27 April and Saturday 28 April) accommodation on a share twin basis (single room extra)
- breakfast, morning and afternoon teas, and lunches on Saturday and Sunday
- dinner & disco on Saturday night. (Dress theme is 'FANTASY')
- Friday night NICE games - a fun night.

Transport costs will be your own responsibility.

Accommodation on other nights can be arranged by Natalie to get the discounted NICE weekend rate at Wairakei Resort. Please plan to arrive at the venue on Friday evening, as we have a full programme planned.

If this is your first NICE Weekend, we will put you in contact with a "buddy" who can introduce you to everyone, explain anything you don't understand and make you feel at home.

Participant numbers are limited to the 80 registrations. You will be notified when your registration has been received. If you don't hear from us we have not heard from you. As there are limited time spaces for presentations, it is possible you may be asked if you can change your talk into a poster in order to allow another person, or yourself to attend.

Registrations will be accepted on 1st in 1st served basis. You may get your registrations in and then arrange payment and abstract to be sent ASAP, by 30th March 2007

If you have any questions contact

Natalie Fletcher
Tokoroa Hospital Laboratory
Ph: 07 886 1818
Email: fletchen@waikatodhb.govt.nz

New Zealand Institute of

Medical Laboratory Science

NICE WEEKEND

Date: 27th April - 29th April 2007
A Transfusion Science Education Opportunity

Location: Wairakei Resort
Organised by the NZIMLS TSSIG

PAPER OR POSTER PRESENTATION

Paper Presentation _	Poster Presentation _
Title:	
Equipment required: Data projector (PowerPoint) laptop provided _ Overhead Projector _ Slide Projector _	
A brief abstract of your presentation MUST be sent by 30th March 2007!! Please email your abstract if possible to fran@nzimls.org.nz	

NICE Weekend Queries to Natalie Fletcher, 07 886 1818, 027 243 8683, or fletchen@waikatodhb.govt.nz

New Zealand Institute of

Medical Laboratory Science

NICE WEEKEND

Date: 27th April - 29th April 2007
A Transfusion Science Education Opportunity

Location: Wairakei Resort
Organised by the NZIMLS TSSIG

REGISTRATION FORM

Name:		
Laboratory:		
Laboratory Address:		
Email:	Telephone:	Fax:
Do you agree to your email address being published in the NICE Weekend Booklet Yes _ No _	Will you be leaving the weekend early on Sunday? Yes _ No _	Will you be attending the NICE games on Friday night? Yes _ No _
Is this your first N.I.C.E. Weekend?	Yes _ No _	

	Cost	**Amount Paid**
Registration Fee	$391	$
Or for NZIMLS members	$356	$
Private Room Surcharge: (The Private Room Surcharge is payable only if you wish to have a room to yourself). I wish to share a room with	$140	

Payment

1. Please make cheques payable to: NZIMLS Transfusion Science SIG Seminar

2. Visa: ρ Card No. _____/_____/_____/_____

   Card Holder

   MasterCard: ρ Amount $

   Expiry Date Signature

Please forward completed form, with payment to: NZIMLS, PO Box 505, Rangiora. If paying by Credit Card, delegates can either choose to mail this form, or fax to 03 313 2098.

Journal-based questionnaire

Journal-based questionnaire for this (August 2006) issue

Below are the questions from the August 2006 issue together with the correct answers.

The NZIMLS provides the CPD programme, not the MLSB.
True

The NZIMLS issues the Annual Practicing Certificate
False. The MLSB issues the APC.

Together with other insects such as spiders, house dust mites belong to the class Arachnida.
True

Blomia tropicalis is the dominant house dust nite species in New Zealand.
False. Blomia tropicalis is the dominant house dust mite species in tropical and semi-tropical areas. Dermatophagoides pteronyssinus is dominant in New Zealand.

Double-monoclonal antibody ELISA remains the gold standard for measuring Der p 1.
True

Synthetic pillows contain significantly higher levels of house dust mite allergens than feather pillows.
True

House dust mite allergens are present in high quantities in human hair.
False. Human hair contains very low quantities of house dust mite allergens.

Increasing exposure to microbes switches the immune system from the predominantly Th1 to the allergic Th2 pathway.
False. Decreased microbial exposure switches the immune system from Th1 to Th2.

In the Historical Article, using the macro method the whole procedure of obtaining actual pH and Standard Bicarbonate and Base Excess takes 12-13 minutes.
True

Capnocytophaga canimosus is a fastidious, thin Gram-negative rod.
True

Journal-based questionnaire for this (November 2006) issue

Below are 10 questions based on this issue of the Journal. The answers can be found anywhere, thus read the entire Journal. The questions are in the format of **True/False.**

The site for submitting your answers will remain open until 5pm on Friday 1 December 2006 after which it will close. You must get at least 7 questions right to earn 5 CPD points. You will be notified once the Editor and Deputy-Editor have checked your answers (about mid-December).

1. PCR is a rapid and reliable method for detecting HSV infection.
True **False**

2. Sixty-five specimens from cutaneous and genital sites were found to be HSV positive.
True **False**

3. HSV is the most frequently detected virus in most clinical laboratories
True **False**

4. Traditionally, EIA has been the gold standard in the diagnosis of infections due to herpes simplex virus.
True **False**

5. EIA had a significantly higher detection of herpes simplex virus rate than both cell culture and PCR.
True **False**

6. Patients with thrombotic thrombocytopenic purpure have large multimers of von Willebrands factor.
True **False**

7. Only 10% of children infected with STEC O157:H7 will develop haemolytic uraemic syndrome.
True **False**

8. Mycosis fungoides is a T-lymphocytic lymphoma.
True **False**

9. Over half of patients with mycosis fungoides die within a year of onset of the disease.
True **False**

10. Many members of the NZIMLS still confuse the different roles of the NZIMLS, the Medical Laboratory Science Board and the Union.
True **False**

Recent abstracts from articles published in the *British Journal of Biomedical Science*, the official publication of the Academy Of Medical Laboratory Science (UK)

Skippen I, Shemko M, Palmer C, Shetty N. Laboratory diagnosis of bloodstream infections caused by extended-spectrum beta-lactamase-producing E. coli and Klebsiella species. Br J Biomed Sci 2006 ;63(1): 1-4.

Extended-spectrum beta-lactamase (ESBL)-producing organisms are resistant to the third-generation cephalosporins commonly used as empirical therapy for a wide range of serious infections. It is therefore important for laboratories to offer reliable ESBL detection methods. This study compares two combination disc methods (Oxoid and Mast Diagnostics) containing cepodoxime with and without clavulanate with Vitek 2 for routine detection of ESBLs in Escherichia coli and Klebsiella spp. isolated from blood cultures. From December 2003 to April 2005, a total of 58 potential ESBL-producing isolates (resistant to cefotaxime and/or ceftazidime) by BSAC disc susceptibility were tested by the combination discs and Vitek 2. The Advanced Expert System, a feature of Vitek 2 reports possible mechanisms of resistance, based on interpretive reading of MICs. This study detected 7.4% more ESBL-producing isolates by Vitek 2 than by Oxoid disc testing (95% CI: 0.15-14.7%; $P < 0.2$) and 31.6% more ESBL-producing isolates were detected by Vitek 2 than by Mast disc testing, (95% CI: 16.2-46.96%; $P < 0.001$). Batch-to-batch variation was evident in disc performance for both disc types. Thus, use of appropriate controls is recommended when testing by the combination disc methods. Although no phenotypic test is 100% sensitive and specific, the Vitek 2 was a reliable system for ESBL detection; however, it is expensive and interpretation of results can be confusing to inexperienced users. Further studies to compare Vitek 2 with cefotaxime and ceftazidime combination discs may reveal disc methodology for ESBL detection to be a more reliable alternative than using cefpodoxime combination discs alone.

Henriques M, Azeredo J, Oliveira R. *Candida albicans* and *Candida dubliniensis:* comparison of biofilm formation in terms of biomass and activity. *Br J Biomed Sci* 2006; 63(1): 5-11.

Candida albicans and C. dubliniensis are two species responsible for oral candidiasis, especially in immunocompromised patients. Microbial infection is preceded by adherence and biofilm formation. Biofilm formation represents the most common form of C. *albicans* in the oral cavity and is considered to be one of the most important virulence factors. In this study, the biofilm formation ability of C. *dubliniensis* was compared with that of C. *albicans* in terms of biomass (quantified using crystal violet) and activity (assessed by formazan salts formation). Both species formed heterogeneous biofilms; however, species and strain variations were seen in the quantification of biomass and activity. There was no correlation between pseudohyphae formation and biofilm formation capability.

Mahomoodally MF, Fakim AG, Subratty AH. Stimulatory effects of Antidesma madagascariense on D-glucose, L-tyrosine, fluid and electrolyte transport across rat everted intestine, comparable to insulin action in vitro. *Br J Biomed Sci* 2006; 63(1): 12-7.

Medicinal plants are believed to be an important source of potential therapeutic agents. This study investigates the effects of Antidesma madagascariense (AM) extract on the transport of D-glucose, L-tyrosine, fluid and electrolytes (Na+ and K+) across rat everted intestinal sacs. These sacs were mounted in an organ bath containing Krebs-Henseleit bicarbonate (KHB) buffer. Experimental findings showed that incubation with graded aqueous AM extracts above 0.375 mg/mL significantly ($P < 0.05$) stimulated the mucosal disappearance and serosal appearance of glucose and fluid. The concentration of glucose accumulated in the intestinal tissues also increased significantly ($P < 0.05$) compared to that found in the controls. Transport of the amino acid L-tyrosine was not significantly enhanced ($P > 0.05$) when incubated with increasing concentrations of AM extract. Effects on electrolyte (K+ and Na+) transport were assessed. Na+ uptake and transport was significantly enhanced ($P < 0.05$) when incubated with 0.75 mg/mL AM extract; however, K+ transport was not significantly enhanced ($P > 0.05$). For comparison, insulin (1 and 2 units/mL) was incubated in the mucosal solution. Aqueous AM extract produced similar stimulatory effects on the transport of glucose, fluid and Na+ as were found with insulin. It is hypothesised that bioactive phytochemicals such as flavonoids, alkaloids, leucoanthocyanins, phenols and saponins from AM leaf extract might interfere with the Na+/glucose carrier, thereby enhancing the transport of glucose, Na+ and fluid across rat everted intestinal sacs. Thus, AM may represent a possible alternative dietary supplement for the treatment of type 2 diabetes.

Skaik YA, Overfield J. Detection of red cell antibodies: comparison of two low ionic strength diluents. *Br J Biomed Sci* 2006;63(1):18-20.

Various low ionic strength diluents are used routinely for red cell alloantibody detection in the antiglobulin test to increase the rate of antibody association to antigen, thereby allowing a reduction in the incubation time while achieving optimal agglutination. Two commercial low ionic strength diluents (DiaMed ID-CellStab and Inverclyde LISS) were assessed using the DiaMed-ID LISS Coombs' microtube column system, to assess whether or not the choice of diluent influences red cell antibody detection. Effects of two low ionic strength diluents after 15-min incubation were assessed in 150 samples containing a wide range of typical red cell alloantibodies. Inverclyde LISS gave significantly higher reaction strengths in 25% of samples when compared with the same red cells suspended in ID-CellStab. Variation in reaction strengths ranged from 1+ to 2+, using Inverclyde LISS versus CellStab. Of 131 red

cell alloantibodies directed against Rh, Kell, Kidd and Duffy antigens, Inverclyde LISS detected 90% after 15-min incubation, whereas 83% were detected with CellStab. This study suggests that Inverclyde LISS provides better red cell alloantibody detection than does ID-CellStab, and this may be due to the higher ionic strength of ID-CellStab.

Mboto CI, Davies A, Fielder M, Jewell AP. Human immunodeficiency virus and hepatitis C co-infection in sub-Saharan West Africa. *Br J Biomed Sci* 2006; 63(1): 29-37.

Co-infection with human immunodeficiency virus (HIV) and hepatitis C virus (HCV) is becoming a major global problem, leading to increased morbidity and mortality in developed countries. Co-existence in sub-Saharan West Africa of a high prevalence of HIV and HCV, which share similar behavioural risk factors and modes of transmission, must be seen in the broader context of an emerging third epidemic of HIV and HCV co-infection, as many factors that may affect the spread of HIV and HCV co-infection are endemic in the continent, including host factors such as sexual behaviour, presence of other sexually transmitted diseases, female and male circumcision status, percutaneous and perinatal exposure, and poverty. This review examines the epidemiology, risk factors and transmission of HIV and HCV co-infection and draws attention to the possible emergence of an epidemic of HIV and HCV co-infection in the region.

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Kader AA, Angmuthu KK, Kamath KA, Zaman MN. Modified double-disc test for detection of extended-spectrum beta-lactamases in Escherichia coli and Klebsiella pneumoniae. *Br J Biomed Sci 2006;* 63(2) :51-4.

This study evaluates the performance of a modified double-disc test (MDDT) for the detection of extended-spectrum beta-lactamases (ESBLs) in clinical isolates of *Escherichia coli and Klebsiella pneumoniae*. Ninety-six isolates of *E. coli* and 40 *K. pneumoniae* are studied for ESBL production by the National Committee for Clinical Laboratory Standards (NCCLS) combination disc tests and MDDT A total of 112 (82%) isolates (80 [83%] *E. coli,* 32 [80%] *K. pneumoniae*) were positive for ESBL by MDDT compared to 102 (75%; 72 [75%] *E. coli* and 30 [75%] *K. pneumoniae*) by the NCCLS method. In 10 (7.4%) isolates, ESBLs were detected only by MDDT Twenty-four (17.6%) isolates were negative for ESBL by both methods. The protocol described in this study provides a more sensitive approach than does the NCCLS method for ESBL detection in *E. coli* and *K. pneumoniae*.

Nzeako BC, Al Daughari H, Al Lamki Z, Al Rawas O. Nature of bacteria found on some wards in Sultan Qaboos University Hospital, Oman. *Br J Biomed Sci* 2006; 63(2): 55-8.

This study aims to determine what objects lying in the hospital environment or brought in from outside contribute to the introduction of bacteria associated with nosocomial infections. One hundred swab specimens collected from children's toys, sinks, door handles, telephone handsets and flowers brought into the hospital were plated on different culture media. Colonial growth on the media was purified and identified subsequently using standard bacteriological methods. Of the 100 samples cultured, 61 (61%) grew a range of bacteria including *Pseudomonas aeruginosa* (n=14, 23.0%), Acinetobacter spp. (n=13, 21.3%), Serratia spp. (n=9, 14.7%), *Staphylococcus epidermidis* (n=9, 14.7%), *Stenotrophomonas maltophilia* (n=4, 6.6%), *Staphylococcus aureus* (n=4, 6.6%), *Enterobacter cloacae* (n=3, 4.9%), Pantoea sp. (n=2, 3.3%), Chryseobacterium sp. (n=2, 3.3%) and Klebsiella pneumoniae (n=1, 1.6%). Although all the Serratia, Enterobacter, Klebsiella and Pantoea species isolates showed varying degrees of resistance to gentamicin, ceftriaxone, cefuroxime and cefotaxime, all were resistant to ampicillin. Chryseobacterium and Stenotrophomonas species isolates were resistant to amikacin, imipenem, gentamicin and ceftazidime, to which only three isolates of Pseudomonas species were resistant. All the staphylococcal isolates were susceptible to methicillin. Although there has been no major outbreak of a nosocomial infection in the hospital, it is strongly recommended that effective control measures (e.g., sampling the hospital water supply, disinfecting children's toys, use of appropriate hand washing and checking some of the disinfectants for presence of bacteria) are needed. These measures are necessary to ensure that the antibiotic-resistant strains identified in this study are not allowed to spread in the hospital.

Silvestre D, Lopez MC, March L, Plaza A, Martinez-Costa C. Bactericidal activity of human milk: stability during storage. *Br J Biomed Sci* 2006; 63(2): 59-62.

Human milk provides infants with defensive factors against many illnesses. This study aims to analyse global bactericidal activity in fresh human milk and evaluate its stability in relation to milk manipulation and its possible alteration following refrigeration. Nineteen milk samples (mature milk) from 19 healthy women are analysed. Viability testing involving a strain of *Escherichia coli* NCTC 9111, serovar O111: K58(B4):H- was used to determine the bactericidal effect of human milk. Degree of bacteriolysis is calculated as the difference between *E. coli* counts in controls and in milk samples, expressed as a percentage of the control sample counts. An evaluation of the effect of refrigeration at 4-6 degrees C after 24, 48 and 72 hours, and at -20 degrees C for seven days on bactericidal capacity is made. Bactericidal activity was detected in all milk samples analysed (77.33 +/- 15.14%). This activity persisted after refrigeration for 48 hours and after freezing for 10 days, but showed a significant decrease after refrigeration for 72 hours. In conclusion, maternal milk has bactericidal capacity, providing defence and protection against infection for newborn infants. This property can be altered during the storage of milk. Consequently, if storage in excess of 48 hours is required, freezing is preferable to refrigeration.

Aritomi T, Sekizuka T, Imamaki R, Murayama O, Millar BC, Moore JE, Matsuda M. First restriction and genetic mapping of the genomic DNA of urease-positive thermophilic campylobacters (UPTC), and small restriction fragment sequencing. *Br J Biomed Sci* 2006; 63(2) :63-7.

A restriction and genetic map of urease-positive thermophilic campylobacter (UPTC) CF89-12 genome DNA is constructed using a pulsed-field gel electrophoresis procedure after digestion with SalI and SmaI and Southern blot hybridisation. Each of the six gene fragments (flaA, glyA, lysS, recA, sodB and ureAB) selected are mapped in only a fragment on the restriction map. Three DNA fragments for rrn operon

probes are mapped in multiple regions on the map. When two SmaI-digested neighbouring small fragments hybridised with rrn probes are cloned and sequenced, a total sequence length of 7487 bp is determined. In the sequence, part of the pnp gene (734 bp) bearing a p-independent transcriptional termination region, a cluster of five tRNA genes including the putative promoter region, a hypothetical Cj0171-like 507-bp sequence containing an internal termination codon, and a part of the rrn operon including the putative promoter region (4700 bp) are identified. The 507 bp sequence carried both putative transcriptional promoter sequences, including a ribosome binding site upstream of the ATG start codon and a characteristic G9 structure, and a possible p-independent transcriptional termination region. A hypothetical Cj0170-like 204-bp sequence containing an internal termination codon also occurred, overlapping partly with the Cj0171-like sequence. Based on nucleotide sequence alignment analysis between the UPTC rrn operon examined here and the previously reported one, two different 16S-23S ribosomal DNA (rDNA) internal spacer regions are shown to exist.

Woodland JG. CDX-2 and MIB-1 expression in the colorectum: correlation with morphological features of adenomatous lesions. *Br J Biomed Sci* 2006; 63(2): 68-73.

Tumours of the gastrointestinal (GI) tract, of which 70% arise in the colorectum, are a major cause of morbidity and mortality worldwide. Transformation from normal to malignant mucosa is a multistep process involving specific gene mutations and is called the adenoma-carcinoma sequence. Histologically, adenomas are of three types (tubular, tubulovillous and villous) and the extent of mucosal cellular abnormality of three grades (mild, moderate and severe). Cellular proliferation is a marker of malignant potential in many tissues. In the colon, cellular proliferation is partly controlled by the CDX-2 gene, a homeobox gene expressed in differentiated cells of the intestine that has proto-oncogenic potential in murine models. In the stomach, CDX-2 is expressed in intestinal metaplasia and decreasing expression through tumourogenesis shows its tumour suppressor potential. Down-regulation in colorectal cancer cell lines is also observed. This is a retrospective study of colorectal adenomas, and haematoxylin and eosin (H&E) and immunocytochemical staining for CDX-2 and MIB-1 (a cell proliferation marker) are performed on each case. Comment is made on the morphological features (adenoma type and dysplasia severity) and the grade of CDX-2 and MIB-1 expression. This study showed that dysplasia severity is linked to cellular proliferation (P=0.011) but adenoma type was not (P=0.54). CDX-2 was not linked to the morphological features discussed (P=0.11 and P=0.16) and CDX-2 and MIB-1 expression showed no correlation. Increased cell proliferation (MIB-1 expression) was seen in increasingly dysplastic adenomatous lesions of the colorectum. CDX-2 had no link to morphological features or cell proliferation of the dysplastic mucosa.

Morsi MI, Hussein AF, Mostafa M, El-Abd E, El-Moneim NA. Evaluation of tumour necrosis factor-alpha, soluble P-selectin, gamma-glutamyl transferase, glutathione S-transferase-pi and alpha-fetoprotein in patients with hepatocellular carcinoma before and during chemotherapy. *Br J Biomed Sci* 2006; 63(2): 74-8.

Hepatocellular carcinoma (HCC) is an environmentally related cancer, with both viral and chemical carcinogens involved in a multistage process. To date, it has been difficult to detect the asymptomatic precursor lesions in early HCC. Therefore, the majority of HCC patients are not amenable to therapy, as they are detected at late stages. To evaluate the significance of tumour necrosis factor-alpha (TNF-alpha), sP-selectin, gamma-glutamyl transferase (GGT), glutathione S-transferase-pi (GST) and alpha-fetoprotein (AFP) in the diagnosis and follow up of HCC patients during chemotherapy with adriamycin, 45 subjects (15 healthy volunteers, 15 with benign liver diseases and 15 HCC patients) are studied before and during chemotherapy (three cycles of intravenous adriamycin). HCC patients had significantly higher serum levels of TNF-alpha, sP-selectin, GGT, GST and AFP Serum levels of GGT and GST were significantly higher in HCC patients with poorly differentiated tumours than in patients with well- and moderately differentiated tumours. Treatment with adriamycin for three cycles produced a significant decrease in TNF-alpha, sP-selectin and GST. Thus, it is concluded that GST is a superior diagnostic indicator and may be a prognostic marker in HCC patients.

Sanchez-Zeco MP, Hernandez L, Eiros JM, Negredo A, Fedele G, Tenorio A. Detection and identification of orthopoxviruses using a generic nested PCR followed by sequencing. *Br J Biomed Sci* 2006; 63(2): 79-85.

Some orthopoxviruses are considered to be potential biological weapons. After the smallpox eradication campaign ended, routine vaccination was stopped around the world. Consequently, a significant portion of the population is now completely unprotected from infection by variola virus and related orthopoxviruses. Some of the symptoms associated with non-variola infections can be similar to smallpox, causing alert and panic situations. These infections should be considered as real public health concerns, so suitable tools for their differential diagnosis are needed. This study aims to devise a simple and easy-to-perform method that is able to detect and identify any orthopoxvirus that might cause infection in humans. In addition, the similarity of the different genes in the genomes of several species of orthopoxviruses is investigated, and orthopoxvirus-universal primer pairs in the tumour necrosis factor receptor II homologue gene are designed, taking full account of nucleotide similarity. A strategy is devised for their sensitive, rapid and cost-effective detection and identification, based on a nested PCR followed by sequencing. The efficacy of the method is tested with samples sent by the European Network of Imported Viral Diseases as part of two external quality control assays. All human orthopoxviruses assayed were detected and identified.

Hardey SP. Appearance of bacteriology in the British medical school curriculum. *Br J Biomed Sci* 2006; 63(2): 90-8.

Published histories of bacteriology concentrate on the scientific concepts, exemplified by Louis Pasteur and Robert Koch. Arguably, the early British bacteriological studies are headed by Lord Lister, whereas other notables such as Ronald Ross, Robert Bruce and Patrick Manson are honoured for their discoveries of 'tropical' microbes, accomplished abroad. What then was happening in Great Britain? The introduction of bacteriology into the medical school curriculum is examined according to the published lectures in The Lancet between 1889 and 1901 and the dates are reviewed in light of other published sources. The names of the people delivering bacteriology at the medical schools in Great Britain and Ireland provide a guide to the relevance of crediting Lister as the leading light for microbiology in the UK. The diversity of names and backgrounds suggests that a critical reassessment of the perceived late and limited start of UK medical bacteriology is needed.

Abstracts of oral and poster presentations at the NZIMLS ASM, Napier, August 2006

Editor's note: Any abstract containing the phrases: "Results will be presented" or "Results will be discussed" have been omitted, or have had these (or similar) phrases deleted as they are not informative to the reader.

Oxygen therapeutics - an overview
Dr Ken Burhop. Baxter Healthcare Corporation, USA

The perioperative period following a high blood loss surgery and the immediate period following traumatic haemorrhagic shock are believed to share the common sequela of inadequate tissue perfusion and tissue dysoxia. Currently, there are a number of products that function primarily as temporary volume expanders, and thus, attempt to transiently increase blood flow to tissues (e.g. a number of different crystalloids and colloids). However, there is still a great deal of morbidity and mortality observed in both of these clinical settings. For the past several decades, numerous companies have pursued different research strategies to develop, manufacture and market an effective alternative to blood transfusion for the treatment of trauma and blood loss in surgery patients. One approach in particular that has been pursued is the development of haemoglobin based oxygen carrrying solutions (HBOCs). Several companies are in different stages of evaluation and development of these products, including one company that is in late phase clinical testing. Research has shown haemoglobin therapeutics have a unique combination of oxygen carrying capacity, coupled with volume expansion properties that make them an exciting new class of therapeutic agents for potential use in a wide variety of clinical disease conditions arising from inadequate oxygen delivery or tissue perfusion. Within the HBOC category, different sources of haemoglobin have been evaluated and a number of different strategies have been developed in an attempt to modify the native haemoglobin molecule in such a manner that it may better serve as a 'red cell substitute'. The main strategies evaluated in this area include intramolecularly crosslinking the haemoglobin tetramer, intermolecularly polymerizing several haemoglobin tetramers together, 'decoration' of the haemoglobin tetramer with other molecules, a combination of polymerization and decoration, and finally, encapsulation of the haemoglobin into liposomes. Site directed mutagenagenesis of the haemoglobin molecule via recombinant production technology is the newest approach. Each of these approaches has certain unique issues associated with it that will be addressed. Aside from the recombinant technology approach, the majority of approaches described above do not, however, affect the intrinsic chemical properties of the haemoglobin molecule and the haemoglobin solutions are still capable of extravasating from the vascular space, albeit, potentially at a slower rate. Almost uniformly, infusion of these different HBOC's into certain animal species and man has been reported to cause a number of other negative physiologic effects, such as adverse effects on the gastrointestinal system and vasoactivity. The prevailing hypothesis for the mechanism of most of these physiologic responses is scavenging of NO by haemoglobin secondary to extravasation of the haemoglobin into parenchymal tissue. Some background on haemoglobin-based oxygen carrying solutions in general will be provided. In addition, some of the unique testing issues faced as part of the product development cycle and the current status of clinical trials and the clinical indications being pursued in the field will be reviewed.

D-dimer testing in thrombosis - problems and pitfalls
Dr Paul Harper. LabPLUS, Auckland Hospital

The d-dimer assay is widely used in the assessment of suspected venous thromboembolic disease. It was initially introduced as an exclusion test, where patients with a negative result are assumed to have a low probability of thrombosis. In clinical studies d-dimer assays have been reported to give a high sensitivity and negative predictive value, but in practice there are many difficulties using these tests. First there is no international standard available. Various methods have been used to produce one but these have problems with reproducibility and do not reflect the clinical picture. Second, quality assurance programmes, such as Neqas, have shown poor performance of these tests to the extent that clinical interpretation of results can be different on the same sample. There are also problems with its use in clinical practice. D-dimers vary considerably with age. We reviewed over 6000 d-dimer results from a hospital and community laboratory using the vidas d-dimer test. Our results showed that the median d-dimer concentration increased with age (16 to 40 yrs: 294ng/ml, 40 to 60 yrs: 387ng/ml, 60 to 80 yrs: 854ng/ml, >80 yrs: 1397ng/ml) and altered the assay specificity making it a very poor test in older patients. In clinical practice there has also been a trend to use the assay as a diagnostic test rather than an exclusion test. This may have a place in practice but has not been validated in clinical studies.

Newborn metabolic screening programme 2006
Dr Dianne Webster. Auckland Hospital

Purpose: The purpose of the newborn metabolic screening programme (NMSP) is the reduction of morbidity and mortality due to inborn errors of metabolism (single gene defects which result in absence of critical enzymes).

Methods: NMSP currently screens for seven conditions, PKU, MSUD, galactosemia, biotinidase deficiency, cystic fibrosis, congenital hypothyroidism and congenital adrenal hyperplasia. Expanded screening utilises tandem mass spectrometry to measure aminoacids and acylcarnitines to allow screening for fatty acid oxidation disorders, aminoacidopathies and organic acidemias. NMSP records have been reviewed for historical, present and future screening.

Results: New Zealand had arguably the first national screening programme in the world. Although the present screening technology is current, most screening programmes in developed countries now use tandem mass spectrometry to screen for additional disorders. All current screening has high sensitivity and specificity (generally greater than 99%) and high predictive values. The current programme significantly benefits approximately 30 babies per year. Introduction of new screening to New Zealand is a complex process in both financial and political terms and the NMSP has achieved the purchase of an instrument, ministerial signoff in principle and is awaiting ministerial signoff of an implementation plan. It will increase the specificity of current programmes as well as allowing for additional disorders.

Conclusions: The introduction of expanded screening will benefit about ten extra babies per year and will bring the NMSP into line with all the Australian programmes.

More challenging thyroid cases
Dr Chris Florkowski. Canterbury Health Laboratories

The advent of more sensitive TSH assays has enabled the distinction between euthyroidism and hyperthyroidism and strategies have evolved based upon initial measurement of TSH alone, with follow up T4 and possibly T3 measurement if TSH falls outside the reference range. This has the potential to miss central (pituitary) hypothyroidism, given that the majority (84%) of these patients have normal TSH1. A UK survey2 suggested that 60% of such cases would be missed by a TSH only approach. Debate has focused on reference intervals for TSH, with a biologically rigorous approach3 favouring a range from 0.40-3.77 mU/L. Others have argued4 that the upper limit for TSH should be 2.5 mU/L given that 95% individuals have TSH below this level and with implications that those above be classified as sub -clinical hypothyroidism. Counter arguments5 have been that excessive numbers would be so classified and that there is no evidence for improved outcomes with T4 treatment. Eminent bodies have not achieved consensus on this, although some guidelines offer good practical solutions. Standard comments cover most patterns of commonly encountered thyroid function tests. Some patterns are not easily explained, for example raised thyroid hormones with non-suppressed TSH. Once artefact is excluded, the main differential diagnosis is between TSH-secreting pituitary adenoma (very rare) and generalised resistance to thyroid hormone (GRTH)6. Definitive diagnosis often invokes extensive and often inconclusive investigation6. We have recently developed an approach based on mutational analysis of the thyroid hormone receptor gene and identified a number of NZ kindreds with GRTH7, potentially obviating the need for more detailed investigation.

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Perspectives in the management of HIV
Dr Richard Meech. Hawke's Bay Hospital

The global burden of HIV continues to rise and is not expected to stabilise for a decade or two yet. New Zealand figures reflect this situation, showing a rise for each of the last three years, up by 17% comparing 2004 with 2005. Men who have sex with men (MSM) remain the largest risk group, with the average age for new infections being 37 years, and most of these are infected within New Zealand. For heterosexual transmitted HIV, in contrast, most transmission occurs overseas (88%). During 2005, six cases of mother-to-child transmissions (MTCT) occurred, four within New Zealand. The public health issues these figures challenge us with are (i) for MSM, risk takings vs condom fatigue, (ii) for New Zealand travellers, ignorance (or naivety) regarding the global transmission of HIV as a heterosexual STI, and (iii) for MTCT, the need to implement a maternal HIV testing programme. On thetreatment front, the introduction of Highly Active Anti-Retroviral Therapy (HAART) from 1995 onwards has driven down AIDS defining conditions, and mortality. The issues that emerge are two-fold; (i) maintaining adherence to drug regimens that have significant toxicity (lipodystrophy, mitochondrial toxicity, lipid disorders), and (ii) managing virus that has developed resistance mutations that accumulate over time and are transmissible. Understanding the biology/pathophysiology of HIV has led to the development of exciting new drugs such as Integrase inhibitors, or the family of drugs collectively known as 'entry inhibitors'. Exciting as such developments are, the best approach remains prevention of infection, which can be refined only through improving our understanding of human behaviour.

Some disorders occurring in neonates and children
Gillian Rozenberg. Prince of Wales Hospital, Sydney

Many of the disorders occurring in neonates and children are age-related. Being aware of these disorders is a prerequisite to the issuing of clear, concise haematology reports by the morphologist. Disorders occur in all three-cell lineages namely red cells, white cells and platelets. Those occurring in the red cell line include:

- Occult haemorrhage prior to birth
- ABO incompatibility
- Rh Haemolytic Disease of the Newborn
- Erythroblastosis foetalis
- Oxidant haemolysis

Those occurring in the white cell line include:

- Transient Abnormal Myelopoiesis (TAM)
- Kawasaki disease
- Bordetella pertussis
- Acute Lymphoblastic Leukaemia

While those occurring in the platelet line include:

- Destructive thrombocytopenia
- Reactive thrombocytosis

These are but a few of the disorders occurring in each cell lineage.

Diamond- Blackfan anaemia - a case study
Michelle Masters. Hawke's Bay District Health Board

Diamond-Blackfan anaemia is also known as congenital erythroblastopaenia, and is often diagnosed in infancy, with 65% of sufferers demonstrating anaemia by the age of 6 months. Over 90% of sufferers will be diagnosed by 1 year. Initially the earliest manifestation is pure red cell aplasia, with reduced reticulocytes, macrocytosis and anaemia. As the disease progresses there may be a reduction in neutrophils and or platelets, with eventual pancytopaenia. There is an increased incidence of Acute Myeloid Leukaemia. The prevalence of Diamond-Blackfan Anaemia is 5-7/100,000 live births; 3/4 of cases are sporadic, the remaining are inherited in an autosomal dominant fashion, although in some families the inheritance is recessive. The defect is found in stem cells of colony and blast forming units of erythroid cells which are decreased in number and insensitive to the actions of erythropoietin and IL3. The disease was first described in 1936 by W H Joseph, and then again by L K Diamond and K D Blackfan in 1938.

This case study will focus on a nine year old girl recently moved to Hawke's Bay, with an apparently worsening anaemia. The patient is of small stature compared to her peers, and of pale complexion. The subject was diagnosed by the age of 18 months, after a professor took a keen interest in her medical history. Two bone marrows were performed to rule out leukaemia. Treatment has only now been undertaken, with her paediatrician very surprised that she has managed to do so well for so long without any chemical assistance.

Holotranscobalamin as a predictor of vitamin B12 status
Terry Pry. Abbott Diagnostics

Serum levels of vitamin B12 are routinely used to appraise haematological abnormalities (anaemia and macrocytosis) and psychoneurological disorders. Early diagnosis of vitamin B12 deficiency is crucial due to the potential for irreversible neurological damage. Unfortunately, significant overlap of normal and abnormal vitamin B12 serum levels occurs leading to its poor positive and negative predictive value. Vitamin B12 is protein-bound in serum to either Haptocorrin (80%) or Transcobalamin (20%). Holotranscobalamin (Holo-TC) represents the biologically active fraction of vitamin B12 that is available to all cells. Recently, Holo -TC testing has emerged as a potential improved predictor of vitamin B12 status.

Making brain out of blood and muscle
Edwina Mandisodza. Hawke's Bay District Health Board

Stem cells are a special kind of unspecialised cells that have a unique capacity to renew themselves indefinitely and give rise to specialised cell types such as muscle, blood or nerve cells. These features enable the stem cells to generate replacements for cells lost through normal wear and tear, injury or disease; for example, bone marrow-derived stem cells contribute to replacement of cells lost through normal senescence or degeneration in blood and skin. Under certain physiologic or experimental conditions, stem cells can be induced to become cells with special functions, such as insulin-producing cells of the pancreas, heart muscle cells, or new body organs can be engineered These cells are broadly classified as embryonic or adult stem cells (ASCs). Embryonic stem cells (ESCs) originate from the blastocyst (inner cell mass of an early embryo) and adult stem cells are found among specialized cells in tissues of an organism of any age. Because of the origin of ESCs, which implies destroying embryos and cloning concerns, their use provokes ethical and religious controversies. ASCs on the other hand are less controversial. ASCs exhibit a phenomenon known as plasticity, which gives them the potential to form cell types of completely different tissues, for example, bone marrow cells becoming brain cells or myocardial cells and liver cells that can be made to produce insulin. This lends them the promising and exciting potential for wide applications in regenerative medicine.

Quantitative acid-base physiology
Dr Peter Lloyd. Hawke's Bay Hospital

Acid-base physiology has advanced to today's quantitative predictive model. The major conceptual breakthrough was in 1981 by Canadian physiologist Peter Stewart. The Australian veterinary physiologist, Peter Constable has since made vital contributions to our understanding and to the practical application of Stewart's theory. Body fluids contain several interacting factors, including strong ions (>99% dissociated, e.g. sodium, potassium, chloride, lactate), weak acids (examples include albumin, other plasma proteins, phosphate: these incompletely dissociate to achieve equilibrium with other factors), CO2 (dissolves according to Henry's Law, then participates in an equilibrium reaction with bicarbonate as described by the Henderson-Hasselbalch Equation) and hydrogen ions (concentration one millionth that of the other factors). Three factors are independent: strong ion difference (SID), which is the sum of the concentration of strong cations (in mEq/L) minus strong anions; total weak acid concentration, Atot; and PCO2. Biological fluids obey physicochemical laws, including conservation of mass and charge and the law of mass action. Each of these laws can be expressed as an equation. A system of simultaneous equations enables us to solve for hydrogen ion concentration (activity). Stewart's original system resulted in a complex polynomial equation. In some brilliant work published in 1997, Peter Constable made some simplifying assumptions, resulting in a quadratic equation whose solution is readily obtained. The graph depicts the relationship between the three independent factors and plasma acidity. As a result of Constable's work we can now accurately predict the acidity of plasma from the concentration of proteins, electrolytes and PCO2. When a discrepancy exists between the predicted and measured acidity, we can calculate the concentration of unmeasured anions to account for the difference.

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Using antibiotics smartly
Dr Richard Doehring. Medlab Hamilton

Rapidly increasing resistance to antimicrobials creates urgency in finding ways to use what we have left most effectively, and in ways which do not further accelerate the loss of antimicrobial utility. In-vitro measures of antimicrobial activity, combined with knowledge of pharmacokinetics - how the drug is distributed in and eliminated by the body, and pharmacodynamics -how the drug exerts both its antimicrobial effect and its toxicity to the patient, can allow more effect to be wrung from an agent, and may also assist in preventing emergence and selection for resistance.

Flies, fingers, fomites, and food
Ben Harris. Southern Community Laboratories

Man's peskiest insect in association with cows, finger lickin' takeaways and BBQ's may well be responsible for more than casual irritation. New Zealand has a very high rate of seasonal, sporadic campylobacteriosis compared to other OECD countries. Can the seasonality of New Zealand cases fit with an explanation of food borne transmission, especially by chicken meat, and where does the fly-transmission hypothesis fit? Campylobacteriosis in New Zealand - food associated rather than food borne?

Microbiological diagnosis of infection in sepsis.
An intensive care Perspective
Dr Louise Trent. Hawke's Bay Hospital

Sepsis is a common reason for admission to intensive care. Preventing, diagnosing and treating nosocomial infection, like catheter related blood stream infection and ventilator associated pneumonia, is also a vital part of ongoing daily patient management. But diagnosing infection in sepsis is not as simple as it may retrospectively seem. Why is it difficult?

· Defining whether a patient has an infection causing their constellation of clinical signs and symptoms can be hard. A positive microbiological culture does not always distinguish a pathogen from a colonising organism.
· Localising the site of infection is not always straightforward. Why is it important to obtain a microbiological diagnosis?
· Intensive care units need to know their local ecology and patterns of antibiotic resistance to guide initial effective antibiotic therapy.
· Early streamlining or de-escalation of antibiotics when a pathogenic organism is identified may help reduce antibiotic resistance.
· Delayed initiation of an appropriate and effective antibiotic early in sepsis increases mortality.

In the future microbiological diagnosis may guide use of adjuvant therapies in sepsis. So why and when do we send you specimens and what do we do with the results? How do we decide when to treat and importantly when not to? Can increased communication between intensive care and microbiology staff result in a decrease in inappropriate specimen processing requests and improvement in diagnosis and treatment of sepsis? Good communication between the microbiology service and the clinical workplace is essential to improving patient care in the sickest of hospital patients.

Perinatal pathology
Dr Jane Zuccollo. Wellington Hospital

Perinatal pathology is a branch of anatomic pathology that specializes in the examination of the embryo, the foetus and the newborn. It is predominantly an autopsy based speciality in contrast to paediatric pathologists who perform both surgical pathology as well as autopsies on infants and children. The role of the perinatal pathologist includes being part of a multidisciplinary feto-maternal medicine team that

care for women with high risk /complicated pregnancies and they are expected to have a good understanding of both obstetric and neonatal practices. The placenta is an integral part of a pregnancy and its examination by the pathologist should be regarded as mandatory when the infant is submitted for autopsy. The placenta should also be submitted for examination by the pathologist in adverse pregnancy outcomes that include premature birth, perinatal asphyxia and maternal complications of pregnancy. The infant autopsy differs from an adult autopsy most obviously in the size of the patient. The loss of a pregnancy or a child is the loss of an expected life and there is an urgency in completing a report as the parents may be already worrying about the next pregnancy. The purpose of the perinatal autopsy is driven in part by the questions - Why did it happen? Will it happen again? Unlike an adult death there is often no clear preceding history and no opportunity to ask the patient how they felt. Histopathologists cannot perform their job effectively without the laboratory team and perinatal pathology is no exception. A diagnosis would not be possible in large numbers of cases without histology. At the time of the autopsy, the pathologist may have a fair idea of the cause of the death but it is commonly the histology that enables the pathologist to conclude the report. Histology is a very important part of the diagnostic procedure. There are a number of instances where the pathologist may request a frozen section during the autopsy - the reason for this is that it may guide me in pursuing certain diagnostic avenues. This has proved particularly effective in determining between an infectious aetiology and a metabolic/other pathology. The latter requires extensive sampling for genetic testing that takes considerable time. The former requires routine sampling only -but more importantly, the pathologist can go back to the parents immediately after the procedure and give them the answer.

Vasoactive properties of haemoglobin solutions: facts, fiction and myths
Dr Ken Burhop. Baxter Healthcare Corporation, USA

A number of different haemoglobin-based oxygen carriers (HBOC's) are currently under development by a variety of companies, with each company using a slightlydifferent technical approach for product development. Almost uniformly, infusion of these different HBOC's into certain animal species and man has been reported to induce varying degrees of systemic and pulmonary hypertension and to cause a number of other negative physiologic effects, such as adverse effects on the gastrointestinal system. These effects are not unexpected, since it is known that an inherent property of all natural (wild-type) haemoglobins is their ability to interact with nitric oxide (NO). Therefore, the prevailing hypothesis for the mechanism of most of these physiologic responses is scavenging of NO by haemoglobin secondary to extravasation of the haemoglobin into parenchymal tissue. To address this issue, the most common product development strategy is the modification of the final haemoglobin product in order to alter the temporal profile of the normal physiologic response(s) to infusion of cell-free haemoglobin. The different approaches being pursued include polymerization and/ or decoration of the haemoglobin molecule to reduce the rate of extravasation and/or addition of other pharmacologically active agents to the haemoglobin molecule itself. However, these approaches do not affect the intrinsic chemical properties of the haemoglobin molecule and the haemoglobin solutions are still capable of extravasating from the vascular space, albeit, potentially at a slower rate. Recombinant technology is the only approach known that can significantly alter the inherent interactions of haemoglobin and NO. Using recombinant technology and mutagenesis of the distal heme pockets of recombinant human haemoglobin, it has been possible to construct a series of haemoglobin variants with reduced NO reaction rates. Substitution of certain amino acids into the heme pockets of and subunits reduced the rate constants for reaction with NO by up to 30-fold relative to wild-type haemoglobin. The systemic hemodynamic responses to these haemoglobins were reduced and the magnitudes of the responses were correlated with the rates of NO scavenging. Therefore, it appears that there are now available viable approaches to modify the intrinsic vasoactive properties of haemoglobin and produce improved, second generation haemoglobin products.

Enforcing specimen labelling standards - Waikato Hospital experience
Mary-Ann Janssen. Waikato Hospital

A DHB-wide policy on minimum standards for labelling of laboratory specimens (and completion of laboratory request forms) was implemented in December 2004 at all Waikato DHB Hospitals. Monitoring of unlabelled, mislabelled and wrong patient labelling errors, demonstrated no reduction in errors rates following implementation of the policy. In April 2006 under the direction of the Clinical Board, the laboratory at Waikato Hospital undertook to strictly enforce the minimum requirements detailed in the policy. This approach showed significant benefit within the first month with reduction in the numbers of serious errors. This gain was, however, not without pain.

Safe use and work practices for laminar flow and biological safety cabinets
Andrew Bryan. Airpro Scientific

It is important to consider what level of containment your application requires when selecting containment equipment for your laboratory. There are four 'biosafety levels' that correspond to combinations of laboratory practices and techniques, safety equipment and facilities, and these levels dictate what level of biohazard containment is appropriate. Another consideration is what you are aiming to protect, i.e. Do you want product protection, operator protection, environment protection, or combinations of these? Biosafety Level 1 encompasses practices, equipment and facilities for working with defined and characterised strains of viable micro-organisms not known to cause disease in healthy adult humans. This is the lowest level of containment and work is generally conducted on open benchtops using standard microbiological practices. Special containment equipment is neither required nor generally used. Personnel have specific training in the procedures conducted in the laboratory and are supervised by a scientist with general training in microbiology or a related science. Biosafety Level 2 encompasses practices, equipment and facilities for work done with a broad spectrum of indigenous moderate-risk agents present in the community and associated with human disease in varying severity. It differs from biosafety level 1 in the following ways:

- Laboratory personnel have specific training in handling pathogenic agents and are directed by competent scientists.
- Access to the laboratory is limited whilst work is being conducted.
- Extreme precautions are taken with contaminated sharp items.
- Certain procedures in which infectious aerosols or splashes may be created are conducted in biological safety cabinets or other physical containment equipment.

A class I or class II biohazard safety cabinet is highly recommended for work involving these agents. Biosafety Level 3 encompasses practices, safety equipment and facilities appropriate for work done with indigenous or exotic agents with a potential for respiratory transmission which may cause serious and potentially lethal infection. More emphasis is placed on primary and secondary barriers to protect personnel in the contagious area, the community, and the environment from exposure to potentially infectious aerosols. A Class I or Class II biohazard safety cabinet is required for work involving these agents. Biosafety Level 4 encompasses practices, safety equipment and facilities appropriate for work done with dangerous and exotic agents which pose a high risk of life threatening disease. These may be transmitted via the aerosol route, and for which there is no available vaccine or therapy. Members of the laboratory staff have specific and thorough training in handling extremely hazardous infectious agents and they understand the primary and secondary containment functions of the

standard and special practices, the containment equipment, and the laboratory design characteristics. They are supervised by competent scientists who are trained and experienced in working with these agents. Access to the laboratory is strictly controlled by the laboratory director. The facility is either in a separate building or in a controlled area within a building, which is completely isolated from all other areas of the building. A specific facility operations manual is prepared or adopted. A Class III biohazard safety cabinet is required for work involving these agents.

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Biological safety cabinet or blind sense of confidence

Mary Ann Janssen. Waikato Hospital

Class I Biological Safety Cabinets (BSC) offer operator and environment protection. Class II BSC also protect both the operator and the environment but in addition offer product protection. Annual Recertification confirms the correct functioning of a cabinet with testing including measurement of face velocity, checking the integrity of the HEPA filter and checking airflow patterns. This testing does not, however, measure how the cabinet is working in its particular location. There are a number of environmental factors that can reduce the effectiveness of the BSC and therefore compromise operator safety.

Development of lymphoma classification from Malpighii to WHO and beyond

Dr David Ellis. Adelaide

The last 20 years have seen a dramatic change in the way we classify, and therefore diagnose lymphoma. Two decades ago, the International Working Formulation enabled diagnosis and management on the basis of H&E sections alone, with no mandatory requirement for immunophenotyping, molecular studies or any other ancillary investigations. The concept of categorisation by 'clinicopathological entities' defined by clinical features, morphology, immunophenotype and more recently, genotype, began with the Kiel, and Lukes and Collins classifications in the late 70's; becoming fully expressed in the REAL and subsequently WHO classifications. Multi-centre reviews have demonstrated the clinical relevance of this approach and other studies have shown that it can be applied in a diagnostic setting with good inter-observer variation for most categories. Despite rapid acceptance in its present form, the WHO classification is under pressure to evolve further and a revised WHO classification is expected within the next 2 years. Certain WHO 'entities' are known to be quite heterogeneous both clinically and biologically. In some of these, such as anaplastic large cell lymphoma and extranodal marginal zone lymphoma, the molecular events underlying the disease are becoming better understood, leading to further refinement and sub-categorization. Thus, the classification can be expected to grow organically, by the addition of further hierarchical layers, rather than by radical restructuring. Frustratingly however, some categories such as diffuse large B-cell lymphoma have thus far resisted efforts at meaningful subdivision based upon morphology or immunopheno type alone, and most of the recent insights in this area have come from microarray analysis. The lack of intrinsic grading within the WHO classification is a further source of criticism. Apart from the grading of follicular lymphoma (the scientific validity of which remains unproven), our range of prognostic indicators and biomarkers is limited. In 1999, the Director of the NCI in the USA issued a challenge: (The Director's Challenge), *'...intended to lay the groundwork for changing the basis of tumour classification from morphological to molecular characteristics.'* The rapid expansion in molecular studies which followed, particularly gene expression profiling, is adding greatly to our understanding of the molecular events in lymphomagenesis; at the same time identifying new prognostic indicators and therapeutic targets, yet the WHO classification, thus far, remains the primary guide to lymphoma management. Since it reflects ultimately, the structural and functional expression of protean genetic abnormalities and their interactions, the essential form of the WHO classification is likely to be reinforced, rather than relegated, by a molecular framework. The classification will adapt and grow as further subtypes, identified by molecular or proteomic analysis, are added as deeper layers of taxonomic complexity, but we are unlikely to see a purely molecular classification of lymphoma in the near future.

Is there a place for postgraduate qualifications in medical laboratory science?

Associate Professor Mike Legge. University of Otago, Dunedin

Medical laboratory science has evolved from an 'apprentice-based' training system to a formal University degree. Over the last 15 or so years we have witnessed the emergence of University graduates with little 'on-the-bench' training into a profession which has historically prided itself on the traditional knowledge based system. Over time the new generation of medical laboratory scientists will replace the traditionally trained scientists, but is this good for the profession, will this new generation of scientists feel they have a place in diagnostic pathology? Historical evidence clearly demonstrates that medical laboratory scientists are good at their chosen professional discipline and the in-house training placed an emphasis on sound professional practice. University degrees have changed this emphasis by providing a 'ticket' qualification with deeper scientific knowledge, a more flexible qualification but less emphasis on the traditional bench skills based tuition. Linked with this development came the possibility of post-graduate qualifications such as Diplomas, MSc and PhD and an associated higher level of research training. The paradox is how can academically competent medical laboratory scientists with higher degree qualification aspirations fit into a profession, which has not traditionally been focused on research or higher degrees? With the advent of CPD and the recent changes to the health professional legislation it is timely for the medical laboratory science profession to consider the role of the graduate workforce and where post-graduate qualifications fit in the profession as this will define the future of medical laboratory science in diagnostic pathology.

Emerging Gram negative resistance

Dr Tom Gottlieb. Concord Hospital, Australia

'It was the best of times. It was the worst of times'. Microbiology is finally reaping some of the promises of the molecular era. The detection of resistance is increasingly more genotypic and in epidemiology there are improvements in molecular typing methods. There is increased understanding of pharmacodynamic principles guiding antibiotic therapy. Yet the ability to put these into use is becoming more limited. Resistance among *Enterobacteriaceae* and non-fermenting Gram negative bacteriasuch as *Pseudomonas* and *Acinetobacter* is ever-evolving, and is a major problem particularly affecting inpatient care. The 'seed' for this is extensive antibiotic use, acting as a promoter of antibiotic resistance. The 'setting' is often in the specialised units, such as Intensive Care, Transplantation and Burns Units. Here, creditably, patients with severe illness survive longer than ever. However, clinical imperatives and empiricism largely guide antibiotic prescribing which remains largely subjective. Prescribers rarely distinguish colonisation from infection. Prescribing is often dependent on habit, whim, or fears of worsened outcome in an (broad-spectrum) antibiotic void. It is amplified by a lack of new antibiotic classes to counteract emerging resistance, reduced research dollars for antibiotic development and instead heavy promotion of the remaining antibiotics. In crowded hospital units, with high concentration of antibiotic use, and limitations in effective infection control, endemicity of antibiotic resistant Gram-negative bacteria - including several forms of ESBL (TEM, SHV, CTX) and

metallo-enzyme (MBL) producing *Enterobacteriaceae,* multi-resistant *Pseudomonas aeruginosa,* carbapenem-resistant *Acinetobacter baumannii,* Quinolone resistant GNRs - are an increasing reality. This feeds the spiral of antibiotic use and resistance.

Sensitivity of methods used in New Zealand laboratories to identify ESBLs
Helen Heffernan. ESR, Porirua

Purpose: The methods used to identify extended-spectrum - lactamases (ESBLs) need to be appropriate for the types of ESBLs that are currently prevalent in a country or area. The aim of this study was to assess the sensitivity of the methods being used in New Zealand laboratories to identify ESBL-producing *Enterobacteriaceae* (ESBL-E).

Methods: The methods used to screen for and confirm ESBLs were ascertained using a questionnaire. The most common methods were then assessed using a test panel of ESBL-positive *E. coli, Klebsiella,* and other *Enterobacteriaceae,* including *Enterobacter, Serratia and Citrobacter freundii.*

Results: Aztreonam (6 mg/L) blood agar, the medium most frequently used to directly screen clinical specimens for ESBL-E, had poor sensitivity (61%) for ESBL-positive *E. coli* and *Klebsiella.* Multiresistance, a pattern of 2nd-generation cephalosporin resistance and co-amoxiclav susceptibility, synergy between a 2nd-generation cephalosporin and clavulanate, and the CLSI disc screening test, were commonly used methods of screening isolates for ESBL production. A pattern of cephalosporin resistance and co-amoxiclav susceptibility was not a sensitive screen, as 31% of ESBL-positive *E. coli* and 18% of *Klebsiella* were co-amoxiclav resistant. Similarly, synergy between 2nd-generation cephalosporins and co-amoxiclav was not a sensitive screen, especially for *Enterobacteriaceae* other than *E. coli* and *Klebsiella.* The CLSI screening test had good sensitivity except with ceftazidime as the sole screening agent. The CLSI disc confirmatory test and the double-disc synergy (Jarlier) test were the most common confirmatory methods. These tests, using cefotaxime and ceftazidime (and a disc spacing of 20 mm in the Jarlier test), identified all ESBL-positive *E. coli* and *Klebsiella*. In species that also produce AmpC - lactamase, there was a moderate increase in the sensitivity of these confirmatory tests when they were extended to include a 4th generation cephalosporin.

Conclusions: Most laboratories in New Zealand use sensitive methods to confirm ESBL production. However, the methods used for initial screening of clinical specimens and isolates are less sensitive, which suggests ESBLs may often go undetected.

Multi drug resistant ESBL organisms-impact and management in Hawke's Bay
Barbara McPherson. Hawke's Bay District Health Board

Hawke's Bay Hospital has experienced an ongoing incidence of new isolates of multi drug resistant (MDR) Extended Spectrum Beta Lactamase (ESBL) *E. coli* organisms within the last five years. Compared to other ESBL producing organisms, the organism in HB Hospital is highly resistant to cefataxime and ceftazidme. It carries other plasmid mediated antibiotic resistant factors, which result in it being resistant to Gentamicin, Tobramycin, Quinilones and other antibiotics. The first isolates identified were in clinical specimens but since a screening programme was initiated in 2002 most isolates have been reported as colonised only. Since November 2005 increasing numbers of MDR ESBL *Klebsiella pneumoniae* colonisation have been identified along with smaller numbers of other MDR gram negatives i.e. *E. cloacae.*

Testsafe - Auckland regional results repository
Dr Ross Boswell. Auckland

Reports of laboratory, radiology and other investigations for the three DHBs in the Auckland region and from the community laboratory servicing the region are collated in a common repository where clinicians can view them by web browser. The repository has now been used as the sole mode of reporting to Middlemore hospital clinicians, replacing paper reports, for six years. Critical success factors have been found to be the performance and reliability of the repository, and appropriate business rules to direct a report to the correct clinician. The repository maintains a full and open access audit trail that helps to discourage inappropriate use and thereby safeguard patient privacy.

Pharmacogenetics and its current applications
Professor Peter George. Canterbury Health Laboratories

Pharmacogenetics (PGx) is not a new science but the development of simple techniques for DNA analysis has made it technically easy to implement a new paradigm for drug prescribing. It is now possible to prospectively predict both the effectiveness of selected therapies and the probability of adverse reactions, enabling personalised medicine. In some situations the role of PGx is clear and endorsed by the FDA but in others further work is required before it is used routinely. The analysis of TPMT and UGT1A1 is well established but PGx prediction can potentially be based on DNA analysis, enzyme or receptor assay or measurement of metabolites. In other cases such as warfarin or 5 FU, analysis of multiple genes may be required. This may be facilitated by the introduction of commercial assays such as the Roche P450 gene chip.

The...opathies - new classes of disease on the radar
Dr Richard MacKay. Canterbury Health Laboratories

The biological basis of many diseases, both old and new, is increasingly becoming recognised following the rapid advances in molecular biology in the last decade. A lot of 'orphan diseases' are now clearly related to others of a similar type, allowing them to be grouped into a number of hitherto un-described aetiologies, some of which have been suspected for a long time, some of which were not thought of. As a consequence, it is becoming possible to detect biochemical and genetic variations in these diseases, or to understand the biological reason for an old observation. Cystic fibrosis remained a disease of unknown cause until 1989, when the CFTR gene was cloned and the protein subsequently described along with the function, a chloride channel, which accounted for the recognition of the basis for the sweat test. This was followed rapidly by an expanding group of diseases which affect ion channels - the channelopathies - causing a diversity of diseases including heart, skeletal muscle, brain, kidney and others. Deposits of abnormally staining material have been observed in histology samples for many years but the reason for the deposits has never been clear. Many such diseases are now known to be examples of conformational diseases and these can affect the kidney, brain, blood and other systems. The description by Jaeken in 1980 of siblings with a disease caused by deficient N-glycosylation of serum proteins ushered in the congenital disorders of glycosylation which has recently been widened to include a number which affect O-glycosylation, and probably in the future, carboxyl group glycosylation. More recently, new classes of disease include those of filaments, molecular chaperones, chromatin and polyol metabolism. Perhaps these could be termed filamentopathies, chaperonopathies, chromatinopathies and polyolopathies?

ZZAP: what's in a name?
Dr Don Branch. USA

1980 produced the first description of a reagent that can be used to remove autoantibody from direct antiglobulin test positive cells of patients having autoimmune haemolytic anemias to allow for antibody-coated autologous cells to be used in autoadsorption studies looking for underlying clinically significant alloantibodies. This reagent is called ZZAP. ZZAP continues to be used today and has become the 'gold standard' for comparisons of methods for auto- and

alloadsorption techniques in investigations of alloantibodies underlying autoantibodies.

In-Vitro reactions with red blood cells that are not due to blood group antibodies
Jeanette Corle., Diamed Australia New Zealand

Reactions in-vitro that are not due to the presence of an identifiable blood group antibody can be encountered when performing ABO and Rh typings and all forms of compatibility testing. These anomalies can lead to serious errors and delays in the supply of blood for transfusion. The potential causes of these errors and their underlying sources range from HLA types through to 'immune complex' mechanisms implicated by a range of antibiotics to the chemicals and potentiators added to commercial reagents.

Making blood better: leucoreduction and the quest for a safer blood supply
Dr Mark Cortiula. Terumo Corporation

The introduction of technology into blood banking to improve the quality and safety of blood packs is nothing new. Indeed, the field of transfusion medicine has been marked by a number of developments that stretch back to the First World War when Rous and Turner developed an effective sodium citrate anti-coagulant solution that allowed for whole blood to be collected and stored in advance of needs. Since then transfusion medicine and blood banking have been transformed by a series of scientific and technological developments, which include the more recent development of leucoreduction, an increasingly widespread practice that has generated controversy within the transfusion medicine community.

A guide to the treatment of non-Hodgkin's lymphoma - 2006
Dr Simon Allan. Palmerston North Hospital

Non-Hodgkin's lymphoma represents a disease group of many forms, of which there are some more common types. This is a disease group which is increasing in incidence in the Western world for reasons that are not very clear. The main causes of non-Hodgkin's lymphoma are therefore not known. Lymphomas arise from the different lymphocytes which exist within the body, mainly divided along the lines of B and T cell malignancies. There are lower grade lymphomas, producing grumbling disease states which require intermittent treatment over a long period but which are ultimately life-threatening. There are explosive high grade lymphomas which can also be very treatable. In between are a range of intermediate behaviour lymphomas, some with a good prospect of cure and others still of poor prognosis. The identification of the sub-type of non-Hodgkin's lymphoma is therefore quite critical to assessment or prognosis and treatment. Staging of lymphomas is also important to prognosis and treatment implications. Diffuse large B cell lymphoma is one of the commoner sub-types of lymphoma. It is interesting that the main chemotherapy for this has not shown much change over 30-40 years but in recent times the addition of Rituximab to CHOP [Cyclophosphamide, Doxorubicin, Vincristine and Prednisone] chemotherapy has shown significant disease free survival advantage. Rituximab is an antibody against CD20, frequently expressed in B cell NHL. For high risk patients or patients following first relapse then high dose chemotherapy with autologous stem cell rescue can be curative in up to 40% of patients and, therefore, with careful patient selection further advantages may accrue to treating this category of patient. With follicular lymphomas [low grade and more chronic in their behaviour] there have been little changes in overall survival for many decades. There is a hint, however, with recent aggressive interventions of some benefit accruing to the intensive use of chemotherapy in appropriate patients and high dose chemotherapy with autologous stem cell rescue is beginning to demonstrate an advantage for young patients so treated. For the majority of older patients developing follicular lymphoma, however, this remains a chronic disease state requiring intermittent intervention with treatment where and when appropriate for symptom control. The category of mantle cell lymphoma remains an enigma. There are reasonably high response rates with a variety of chemotherapy/ Rituximab interventions but median survivals tend to remain around the three year mark. Although this group of lymphomas is increasing it remains a very treatable group of malignancies. It certainly represents a challenging and varied group of malignancies.

Blood and bone marrow morphology of common B- and T-cell lymphomas
Sue Webber. Waikato District Health Board

The WHO classification of lymphomas represents a list of entities that can be identified separately on the basis of their clinical, morphological and/or cytogenetic features. The lymphomas are first divided broadly into B-and T-cell groups. The B-cell lymphomas are grouped into those with peripheral blood involvement, plasma cell neoplasms, extranodal lymphomas, nodal lymphomas and lymphoproliferative disorders of uncertain malignant potential. The T/NK-cell lymphomas are similarly grouped into those that tend to involve the peripheral blood, cutaneous lymphomas, other extranodal lymphomas, nodal lymphomas and a single entity of uncertain lineage. Examination of the morphology of cells in well stained peripheral blood and bone marrow films is the first diagnostic procedure. Details which are useful in the identification of cell types include: cell size, nucleo-cytoplasmic (N/C) ratio, regularity or irregularity of the nuclear outline, the characteristics of the cytoplasm such as the presence and length of any villus formation, the degree of basophilia, the presence or absence of cytoplasmic granules, the degree of nuclear chromatin condensation and its pattern, and the prominence, frequency and localization of the nucleolus. Bone marrow infiltration is frequently present in lymphoproliferative disorders. Three major patterns of infiltration can be seen either alone or in combination. They are designated (i) interstitial, (ii) focal and (iii) diffuse (or packed). Such patterns are important in the differential diagnosis and can also be of prognostic importance. B-cell chronic lymphocytic leukaemia (CLL) is the most common lymphoproliferative disorder involving the blood and has typical morphological features, however, if morphology alone is relied on mistakes will certainly be made. There are three types of B-cell Non-Hodgkins lymphoma (NHL) which not infrequently evolve with lymphocytosis which mimics and can be confused with CLL. These are follicular lymphoma, splenic marginal zone lymphoma or splenic lymphoma with villous lymphocytes (SLVL) and mantle cell lymphoma. The incidence of T-cell disorders varies around the world. Overall they are common in Eastern and rare in Western countries. For classification purposes of the T-cell lymphoproliferative disorders it is essential to compound the clinical features with laboratory investigations. The latter should include (i) lymphocyte morphology, (ii) histology of bone marrow and lymphoid tissues, (iii) immunological markers, (iv) cytogenetics - standard and/or FISH, (v) analysis of the T-cell receptor (TCR) chain genes to demonstrate clonality of the T-cell population and (vi) serology for HTVL-1. Careful morphological examination of blood and bone marrow can aid the differential diagnosis of lymphoproliferative disorders.

Integration of morphology, immunohistochemistry, flow studies, and molecular findings
Dr David Ellis. Adelaide

The greater complexity of the WHO classification, in comparison with earlier, primarily morphological systems such as the International Working Formulation, demands greater knowledge and technical expertise from the diagnostic laboratory. Two decades ago, the International Working Formulation enabled diagnosis and management on the basis of H&E sections alone, with no mandatory requirement for immunophenotyping, molecular studies or any other ancillary

investigations. The current, multidisciplinary approach to categorisation adds significantly to the task facing the pathologist, since it requires distribution of biopsy material to all the appropriate specialised laboratories, the gathering of a range of cross-disciplinary information -often from different sources and of varying or unspecified quality, the correlation of all diagnostic findings, deduction of a definitive diagnosis and finally, integration of all the above into a single multi-parameter report.

The 'Q factor' and how to get it!
Wendy Maynard. Hawke's Bay District Health Board

It is widely understood that pre-analytical and post-analytical factors influence the overall quality of results reported by medical laboratories. The processes involved need to be standardised and well understood, so that laboratory staff, especially phlebotomists and specimen reception staff, can add the 'Q Factor'. This will ensure that the right specimen coming from the right patient, going to the right laboratory department, in the right time fame, will have the right test performed, and will get reported to the right doctor. More than just from the necessity to 'keep IANZ happy' i.e. ensure compliance to external accreditation standards, there needs to be an awareness and understanding of how the documentation that litters collection rooms and specimen reception areas in laboratories around the country, if put into practice, does actually help the overall quality of the final result. These manuals are reference books. Use them. But most importantly understand what they are telling you, they may just help you to get the Q Factor!

An extended outbreak of multiply antibiotic resistant E.Coli UTIs amongst the elderly in the South Island
John Aitken. Southern Community Laboratories, Christchurch

It is crucial that the clinical microbiology laboratory provides early and accurate reports about pathogens exhibiting significant antibiotic resistance. Long term care facilities present a particular challenge, and establishment of antibiotic resistant bacteria in a facility results in a significant increase in costs of antibiotic therapy. Flow-on effects of environmental colonization include an increase in infection rates, horizontal gene transfer and increased mortality. Early intervention is an effective strategy in controlling spread. In January 2006, 220 isolates of multiply antibiotic resistant E.coli (MREC) from Christchurch patients were retrospectively examined using PFGE and antibiograms to determine whether there were significant clusters of MREC infection in the Christchurch area. These strains were compared to reference strains associated with an extensive outbreak in the Dunedin region. Of the 220 MREC isolates from the last 4 years, 143 were MREC isolated from patients in the Canterbury area over the last 18 months. Of these 143 isolates of MREC, 55 strains closely conformed to the ESR profile EcA strains associated with the Dunedin MREC outbreak and were designated by us as Group B. Analysis of the data indicated the presence of the Group B MREC in several Christchurch Elderly care establishments. On initial detection of the Group B MREC the establishments were notified and infection control procedures put in place. Occupants of one facility were screened for carriage of Group B MREC as a method of assessing effectiveness of control measures. Rapid laboratory and infection control response has also proved effective in the control of extended spectrum beta lactamase (ESBL) producing organisms. Laboratory detection and response to outbreaks associated with MREC involve considerable expense, both in time and follow-up. No funding is currently available for this task and most efforts to contain spread remain regional and variable in technical scope. Early warning, education of staff and implementation of appropriate protocols are essential to prevent establishment of MREC in long term care facilities.

An outbreak of Gentamicin-resistant S. aureus infections in a neonatal unit
Dr Mark Jones. Wellington Hospital

In April 2004 Gentamicin-resistant Staphylococcus aureus (GRSA) was isolated from superficial infections in two babies in the Regional NICU. By September 22 babies had acquired GRSA and phage typing showed this to be a single strain. Twelve staff members were nasal carriers. Early attempts to contain and limit the outbreak primarily involved improving compliance with hand hygiene. This was partially successful at first but, later, many adverse factors contributed to failure of control. During the Summer of 2005 three babies developed GRSA septicaemia and died, and a further 40 babies developed skin sepsis with this isolate. Stringent infection control was applied and the practical aspects focused on:

- Early recognition of skin infection in babies.
- Hand hygiene and skin care in staff.
- Eradication of nasal carriage amongst staff.
- Strict cohorting of patients and staff.
- Contact isolation precautions.

Compliance with these measures was immediately successful and over the next four months only three further babies acquired GRSA before the outbreak was terminated.

Bad bugs, no drugs
Dr Maria Shvab. Hawke's Bay Hospital

Antibiotic resistance is a natural phenomenon. Resistant strains of microorganisms have been noted as the antimicrobial discovery progressed. It is undeniable and documented by multiple experiments that the use (and overuse) of antibiotic agents contributes to development of resistance. Antibiotics are frequently used as 'drugs of fear' - fear of clinicians to fail to provide what is believed to be the state-of-the-art medicine. The development of newer antibiotics, in part, responding to the emergence of resistant microorganisms, has resulted in a sense of complacency on the part of the general public and medical care providers. Now, with clear indications of a decline in the pharmaceutical industry's interest in anti-infective research and at a time when multi-drug resistant microorganisms continue to be reported, it is very important to emphasize the prudent use of the available agents to fight these microorganisms.

Causes of mild lymphocytosis
Ian Morison. Southern Community Laboratories

Mild lymphocytosis is a common problem but the majority of patients have a benign cause. From our experience of performing lymphocyte marker studies in a community setting, we detect numerous small clonal populations but a greater number of benign, insignificant causes. Rationale triaging of abnormal cases prior to performing lymphocyte marker studies is important but is difficult to achieve. Smoking is the commonest cause of and is associated with an increase in CD4 T cells and B cells, and the association with neutrophilia may be a clue. Unnecessary studies in hyposplenism (CD4, B cells) can be avoided by film examination. Severe stress is associated with a T cell lymphocytosis. We have seen marked polyclonal B cell lymphocytosis after high dose steroid therapy. In older patients, chronic proliferations of CD8+ T cells (LGLs), associated with previous CMV infection, are common. Since they tend to have chronic indolent behaviour, there is no need to detect this group. Chronic natural killer cell disorders have similar behaviour. The most common clonal abnormality is Monoclonal B-cell Lymphocytosis, the precursor to CLL, which occurs in 5.5% of patients > 65 years. Although MBL (CLUS) is common, it cannot be dismissed as unimportant since it is indistinguishable from small lymphocytic lymphoma with minimal blood involvement.

Orbital myeloid sarcoma and acute myeloid leukaemia in a child
Vanessa Thomson. Hawke's bay District Health Board

A case study of a 2 year old girl presenting with hypertropia of sudden onset. A biopsy was taken and sent to the histology department. A full blood count was taken and sent to the haematology department. Examination of the blood film revealed 34% blast cells and a diagnosis of Acute Myeloid Leukaemia. The histology biopsy showed a tumour composed of a relatively uniform population of immature cells with large nuclei and scanty cytoplasm in keeping with a myeloid sarcoma, blastic type. Orbital myeloid sarcoma typically presents in children (average age 7 years) and can occur up to a year before leukaemia is diagnosed but usually presents up to two months before diagnosis. In children it is more common in Acute Leukaemia. Acute Myeloid Leukaemia is responsible for 10-15% of childhood leukaemia's and leukaemia is responsible for 2-6% of orbital tumours in children. Differential diagnosis includes malignant lymphoma, rhabdomyosarcoma, neuroblastoma and other childhood tumours. Immunohistochemistry, bone marrow investigation, cell markers and cytogenetics are helpful in identifying Myeloid Sarcoma and Acute Myeloid Leukaemia.

Tuberculosis - watching resistance develop
Dr Rod Ellis-Pegler. Auckland

A Filipino man with lupus erythematosus on steroids develops M.tuberculosis infection of his thoracic spine. During treatment he develops central nervous system disease and in that site alone, some resistance. His treatment is complicated and accompanied by major side effects. He eventually recovers taking oral moxifloxacin and rifampicin predominantly, augmented by intraventricular levofloxacin and amikacin. Isolates at various time points are genetically identical but rifampicin resistance develops in one of those isolates during treatment.

Cardiac markers and the diagnosis of heart disease - Troponin update
Associate Professor Hans Schneider. Alfred Pathology Service, Australia

Over the last ten years Troponin, either measured as Troponin I or T, has become the biomarker of choice for the detection of cardiac injury. This has been because of the unique isoforms of Troponins that are present in cardiac tissue but are absent in all other tissues. Consequently Troponin assays offer improved sensitivity over CK-MB. Troponin assay formats typically utilise chemiluminescence and two or more monoclonal antibodies to different parts of the Troponin molecule. The technology allows a washing step between binding of the first monoclonal antibody and detection with the second antibody. Work towards standardisation of Troponin I assays has progressed with a single reference material comprising a complex of Troponin C with I and T now commercially available from the National Institute of Science and Technology in the USA. However, Troponin I assays are only harmonised, not standardised, and numerical values can still significantly differ between assays. The time course of Troponin release after onset of chest pain leaves a gap of 4 to 8 hours requiring repeat testing in patients who present with acute chest pain if the first result is negative. Currently there is no optimum marker identified that can fill this window. Half life of Troponin I after the peak ranges between 14 and 80 hours, as seen in our laboratory. The importance of absolute Troponin levels has been shown in a number of prospective trials. These show that even small rises in Troponin in patients presenting with unstable angina are associated with increased mortality at later time points and increased risk of AMI. This has encouraged development in the Troponin assay area with different manufacturers trying to improve the sensitivity of the assays in second and third generation assays. Results from prospective trials show that some assays have advantages over others by identifying about 10% to 15% of additional patients who are at risk of having adverse outcome. Recently, negative interference due to autoantibodies to Troponin has been described by a Finnish group. The extent of this problem is currently unclear and it remains controversial whether lower levels of antibodies against Troponin can decrease the early sensitivity of Troponin assays as claimed. International guidelines propagated by the National Academy of Clinical Biochemistry (NACB) ask for cutoffs in normals of the 99 percentile and a CV of the assay of 10% at that level. Currently few assays fulfil these guidelines. The 99 percentile cutoff is probably more important than the 10% CV of the assay in situations where both requirements cannot be fulfilled. Surveys in Australia show a variety of different cutoffs used by different laboratories using either 10% CV or 99 percentile of normals or even AMI by receiver operator characteristics. This will cause problems when patients move between laboratories using different cut-offs. Current guidelines require turnaround times of less than 60 minutes. This is infrequently achieved by laboratories. The increased sensitivity of the Troponin assay has made us aware that a variety of non-AMI conditions can lead to elevated Troponin levels. These lead to significant confusion in the clinical arena. Furthermore heterophil antibodies can give false positive results. A difference between Troponin I and Troponin T assays seems to be in patients with end stage renal disease. While only about 5% to 10% of patients with Troponin I have elevated levels, 80% to 85% have elevated Troponin T levels. Overall, the introduction of Troponin testing has led to a major advance in the diagnosis of cardiovascular disease in our patients. However, there are ongoing problems with the definition of cutoffs and there is increasing awareness that Troponin levels can be elevated in conditions other than acute coronary syndromes.

An evaluation of ARCHITECT BNP assay
Dr Mohamed Saleem. Canterbury Health Laboratories

B-type natriuretic peptide (BNP) is an important marker in the diagnosis and management of patients with heart failure. An automated immunoassay for BNP has been developed for use in the Abbott ARCHITECT instrument system. We evaluated this assay with respect to precision, analytical sensitivity and its correlation with the AxSYM BNP assay. To evaluate the precision, three control levels were assayed in replicates of two on two separate runs over five days and the total %CV was calculated. Analytical sensitivity or limit of detection was established as two standard deviations of low-level BNP samples above the mean concentration of calibrator A (0 pg/mL). Calibrator A was run in replicates of twenty on three separate runs. Three plasma pools of low-level BNP were also run in replicates of five in three separate runs. The correlation between ARCHITECT BNP and AxSYM BNP was determined by testing 98 samples (3.8 -3445 pg/mL) and performing Passing and Bablok regression analysis. The %CV for the low (94 pg/mL), medium (497 pg/mL) and high (3387 pg/mL) controls were 2.9%, 3.8% and 2.5% respectively. Measured values were Cal A (0.1 pg/mL) and LOD (1.94 pg/mL). The Passing and Bablok regression analysis between ARCHITECT and AxSYM BNP showed a slope of 0.8427 (95% CI: 0.8000 -0.8852) and a correlation coefficient of 0.97 (95% CI: 0.95 - 0.98). The Abbott ARCHITECT BNP assay is a precise method for measurement of BNP with a total %CV < 5% and correlates well with the Abbott AxSYM BNP assay.

Highly deceptive lipoproteins
Max Reed, Southern Community Laboratories

High density lipoproteins (HDL) are involved in the uptake and transport of cholesterol from peripheral cells to the liver. As low HDL cholesterol levels are associated with an increased risk of coronary heart disease (CHD), they are routinely used in the assessment of CHD risk. The New Zealand Guideline Group (NZGG) recommends assessment of CHD risk for asymptomatic men from 45 years of age and for asymptomatic women from 55 years of age, utilising a fasting lipid profile containing HDL cholesterol. However, a common method of analysis for HDL cholesterol may be unpredictably affected by the

presence of paraproteins, which are more prevalent in the population recommended for screening by the NZGG.

Can an oxygen therapeutic ever be commercialized?
Dr Ken Burhop. Baxter Healthcare Corporation, USA

Introduction: There is an immediate, critical need to effectively re-establish oxygen delivery to tissues in the setting of acute blood loss in order to avoid the mortality and morbidity consequences of haemorrhage. The current standard of care is to transfuse blood for this purpose. However, there are a variety of reasons why this is not always desirable (e.g., transfusion reactions, pathogen transmission, compromised immunity). For this reason, several haemoglobin and non-haemoglobin based carrier solutions were developed to enhance oxygen delivery to tissues and to reduce or avoid the need for blood transfusions. However, since the explosion of product development programs in this area in the 1980's, most development programs in this area have either been stopped and/or are facing significant delays. Prior to approval and wide spread commercial use, these products will all need to overcome significant technical and regulatory hurdles.

Preclinical testing: Most of the first-generation haemoglobin therapeutics were designed more than 25 years ago, and subsequent preclinical and clinical testing has identified several issues with their use, including pulmonary and systemic vasoactivity, extravasation, serum enzyme increases, adverse effects on gastrointestinal motility, generation of myocardial lesions, and potential interactions between haemoglobin and endotoxin. Successful product development will require a new therapeutic candidate to address all of these issues, with myocardial lesions being one of the most difficult to resolve.

Clinical testing: Clinical trials of oxygen therapeutics will require performing studies against blood, for which there is no precedence. Designing and executing clinical trials in the complicated settings of trauma may require waiver of informed consent. Clinical trials in surgery, where blood is considered the 'gold standard', will be difficult, and surrogate endpoints will likely not be acceptable. Other unique clinical trial design challenges include binding of a coloured solution with pharmacologic activity, ethical issues surrounding randomization against placebo controls, and the co-administration of other fluids.

Commercial sale: If approved, these products will ultimately face a number of interesting commercial issues, such as how would a company price these products against blood (e.g., how do you price a product that is viewed as 'free/donated', what is the true 'cost' of blood, and is all blood 'created equal'?). These products will likely face a number of production issues (e.g., if derived from human blood, will the blood have to be of a specific country origin?). Raw material supply could also be an issue for human derived products (e.g., with current blood shortage issues, will there be enough blood to supply requirements or will you have to collect blood specifically for the production of these products?).

Conclusion: While oxygen therapeutics can provide an essential component to enhance blood conservation and are complementary with other blood saving regimens, significant hurdles must still be overcome before any product is approved for sale/use.

Message from the BIN(H)
Lyn McMillan. Canterbury Health Laboratories

The purpose of a recent visit to Viet Nam was to carry out an assessment of the Blood Donor and the Blood Transfusion Service in the central coastal province of Binh Dinh. This New Zealand Viet Nam Health Trust (NZVNHT) project was at the request of the Binh Dinh Department of Health. New Zealand has had a long association with this area of Viet Nam. During the war years (1963-1975) large numbers of mostly civilian doctors, nurses and technicians served for short periods in Qui Nhon at what is now the Province Hospital. In the aftermath of the Viet Nam war relations were disrupted as the Vietnamese rebuilt their country. The association was re -established during the 1990's with New Zealand aid support for Volunteer Service Abroad (VSA) and the NZVNT. The trust was formed by health professionals who spent time in the region during the Viet Nam war. Their aim was to help improve health services in Viet Nam - and in particular Binh Dinh province. The trust has undertaken many projects including setting up a medical laboratory, training specialist staff and providing equipment upgrades.

From compliance to quality
Don Mikkelsen, Branko Vidakovic. LabPLUS, Auckland Hospital

Historically the challenge in medical laboratories was the production of an accurate and precise laboratory result that was clinically meaningful. The overwhelming body of medical laboratory literature continues to be focused on the development of or the improvement of tests for diagnosis or monitoring of illness or treatment. It would seem from the above that the demand for service from laboratory users (clinicians) continues to be for new and or better tests. A survey of the complaints about service delivery at LabPLUS, Auckland City Hospital received from clinicians paints a very different picture. 33% of the complaints received were about an inadequate turnaround time for results. Furthermore, of the over 150 complaints analysed, not a single complaint was about unsatisfactory result quality. Our understanding of the process and flow of specimens and work in a laboratory is rudimentary in comparison to that of the science and clinical interpretation of results. This is evidenced by the very poor performance of laboratories against industry standard turn around time specifications. The National Academy of Clinical Biochemistry has set a target turn around time for Troponin of 60 minutes from sample collection to result availability. Data from LabPLUS shows that our Median Turnaround time in 2005 was 50 minutes but our 95th percentile was 180 minutes. Working with techniques learned from LEAN and Six Sigma, LabPLUS has been able to improve Turnaround times for a number of key analytes significantly. Improvements in Specimen Services have reduced the 95th percentile for registration of Potassium from >60 minutes to less than 45 minutes and there has been a 50% increase in the number of samples registered within 20 minutes.

Mast cell leukaemia - case study
Sarah Hardingham. Hawke's Bay District Health Board

A 78 year old male presented with a history of prostate carcinoma and a low platelet count (PLT = 107). A Bone Marrow (BM) aspirate and trephine was performed to establish whether the low platelet count was attributable to either infiltration of the BM or the effect of the hormonal antineoplastic drug regime. Following the BM investigation, the patient was diagnosed with Mast Cell Leukaemia. Mast Cell Leukaemia (MCL) is a rare variant of Acute Myeloid Leukaemia (AML). MCL may occur de novo, or as a complication of systemic mastocytosis or urticaria pigmentosa. However, systemic mastocytosis may also terminate in other variants of AML, and MCL must be differentiated from other leukaemia's. MCL diagnosis maybe confirmed by Bone Marrow aspiration, cytochemistry, immunochemistry and the utilisation of electron microscopy.

Mycobacterium engbackii isolated from an immunocompetent patient with chronic olecranon bursitis
Esther Lau, Medlab South

Mycobacterium engbackii was recovered from the aspirate and tissue sample from a previously healthy adult. *Mycobacterium engbackii* is a newly identified non-tuberculous *Mycobacterium*. It most closely resembles the *Mycobacterium* non-chromogenic group. It was isolated by culture method and confirmed by 16srRNA PCR. Invasiveness was apparent by histopathology examination.

Pandemic influenza: how good are our surveillance networks?
Dr Lance Jennings. Canterbury Health Laboratories

The globalisation of the Avian Influenza A (H5N1) virus and associated occurrence of human infections, continues to ensure that the real threat of another human influenza pandemic remains. At the same time, seasonal influenza outbreaks and epidemics pose on-going risks to community human health causing a substantial burden of illness, hospitalisation and mortality. The confirmation of influenza activity in many countries relies on active surveillance networks, integrated into the WHO Global Influenza Surveillance Network. Knowledge of the presence of influenza is of value to primary and secondary health care clinicians as it can assist the accuracy of their clinical diagnoses. It can also assist clinical decisions on infection control, specific antiviral chemoprophylaxis or treatment, and public health interventions such as vaccination. The optimal use of rapid influenza tests for influenza diagnosis in these settings, can also be guided by surveillance. However, should the H5N1 virus begin to exhibit characteristics of adaptation to humans and an increasing frequency of human to human transmission, or another novel virus emerge, are the current surveillance networks sensitive enough? What surveillance will be required to monitor the entry and spread of a novel virus in a country?

A case of Stevens Johnson syndrome
Jackie Wright. Canterbury Health Laboratories

First described by Stevens and Johnson in 1922, Stevens Johnson syndrome (SJS) was originally thought to be an infectious disease. It has been since shown to be a hypersensitivity reaction to various triggers which include both microorganisms and antibiotics. SJS presents as severe bullous erythema multiforme, with buccal, genital, and/or ocular involvement. Differential diagnosis involves excluding a physical cause (burns), and infectious processes such as Staphylococcal scolded skin syndrome and toxic shock syndrome. Treatment is supportive: pain relief, fluid replacement, nasogastric feeding, and prompt withdrawal of the trigger if this can be identified. The mortality rate is reported to be 3% -15%. Worldwide the incidence is rare and why SJS occurs is yet to be determined, but a genetic cause has been mooted.

Technologies and chemistries used in molecular diagnostics
Tom Berkovits. Abbott Molecular Division

Over recent years major achievements have been made in diagnoses of disease in order to improve patient management, especially in the area of molecular diagnostic technology. Molecular technologies have evolved from non-amplified methods to target-amplified end point methods with EIA or chemiluminescent detection to real-time PCR. RealTime PCR is a closed homogeneous reaction system in which amplification and detection occur simultaneously, which makes the technology easily automatable. It lends itself easily to multiplex testing, and the performance of real-time PCR technology is significantly improved over traditional end-point PCR or non-PCR technologies in terms of sensitivity, dynamic range and precision. RealTime PCR quantitates the initial amount of target template most specifically, sensitively and reproducibly. The fluorescence is emitted and monitored during the reaction as an indicator of amplification production during each PCR cycle in real time. Designing assays for the Clinical Molecular Diagnostic Lab is quite challenging because they must address very different requirements. Sometimes they need to detect and quantitate genetically diverse viruses, such as HIV, HCV and HBV, other times they need to detect single nucleotide polymorphisms (SNPS), or single base changes. In one case, you want the assay to tolerate genetic diversity; in the other case, you want it to discriminate genetic diversity. When it comes to selecting the target region for an assay, probe and primer regions must be approached somewhat differently. To enable amplification for genetically diverse targets, the primer region must be highly conserved. When it comes to selecting the appropriate probe region, it makes a big difference whether the design is intended to discriminate or tolerate. Different technologies (FRET Probes, Linear Probes, Molecular Beacons, TaqMan Probes) can assist in the design and success or failure of an assay. The philosophy that Abbott Molecular uses is based on using the right technology for each individual application. New advances improve mismatch tolerability and in some cases dramatically improve subtype and genotype detection, making choice of probe technology critical to the success of an assay, be it a commercial or home brewed test.

Comparison of the Roche Cobas Amplicor CT/NG PCR and the new Roche Cobas TAQMAN Chlamydia trachomatis Real-time PCR assays for the detection of Chlamydia trachomatis DNA in 200 samples from patients attending sexual health clinics
Kevin Barratt. Waikato Hospital

The Roche Cobas Amplicor CT/NG PCR assay has been used at Health Waikato Laboratory since 1998 for the detection of urogenital Chlamydia trachomatis. The diagnostic performance of the Roche Cobas Amplicor CT/NG PCR assay and the new Roche Cobas TAQMAN Chlamydia trachomatis Real-time PCR assay were compared for the detection of Chlamydia trachomatis DNA. First-void urine (FVU), endocervical or urethral swab specimens were collected from 200 patients attending sexual health clinics and tested using both assays. Agreement was seen in 197 of the 200 specimens tested. Of the discrepant results two were negative by Cobas Amplicor CT/NG and positive by Cobas TAQMAN. A third sample was inhibitory using the Cobas Amplicor CT/NG assay and negative/non-inhibitory using the Cobas TAQMAN assay. The two samples found positive using the Cobas TAQMAN assay alone were confirmed positive using an in-house PCR assay targeting a different region of the Chlamydia trachomatis cryptic plasmid. The new Cobas TAQMAN assay was found to be straightforward to use and resulted in fewer problems with PCR inhibition compared to the Cobas Amplicor CT/NG assay.

Recent advances in HCV and HBV diagnostics
Dr Scott Muerhoff. Abbott Diagnostics

Hepatitis B viral mutants can emerge in patients as a result of selection pressure, for examp le, following HBV vaccination or HBIg immunotherapy or from antiviral therapy. Immune selection for HBV mutants with altered HBsAg epitopes allows the mutant virus to propagate in the presence of a neutralizing immune response which reduces the wild type virus to undetectable levels. These mutated HBsAg antigens can present as false negative results in some immunoassays. Abbott Laboratory's automated immunoassays detect the majority of the known HBsAg mutants including the most common mutant, Gly145-Arg. An understanding of immunoassay reactivity with HBsAg mutants is the key to establishing an appropriate testing algorithm for HBV. Infection with hepatitis C virus (HCV) typically results in a window period during which antibody response is not detectable yet viremia can be confirmed via RT-PCR. The recent development of HCV core antigen assays has allowed the detection of core antigenemia during the preseroconversion window period. Based on seroconversion panel testing, the sensitivityof the prototype Architect HCV core antigen assay demonstrates sensitivity very close to the performance of nucleic acid testing. This new assay provides a method for detecting HCV infection much earlier than with conventional antibody assays and provides a less-expensive alternative to NAT. Combination of the core antigen test with the Architect HCV antibody assay has resulted in an assay that detects both markers of infection while significantly closing the seroconversion window period. The HCV Ag/Ab combo assay has utility in both diagnostic and blood screening laboratories.

Cervical smears and positive predictive values
Reena Ramsaroop. Diagnostic Medlab

Cytology laboratories are monitored by a number of performance indicators. The quality control procedure should monitor the ability of screening test results to accurately detect malignant change and pre-malignant diseases that have a high probability of progression to invasive cancer. It should appropriately reassure women without neoplasia. One of the more consistent meaningful indicators is the positive predictive value. The PPV is defined as the number of histologically confirmed high grade lesions diagnosed on cytology, i.e. the accuracy of cytology predicting a HGSIL. Histology is used as the gold standard to calculate PPV but sampling and technique limits accuracy.

Qualitative review of outcomes in woman with abnormal glandular cells of Pap smears
Dr David Roche. Southern Community Laboratory

Abnormal glandular cells are an uncommon finding on Pap smears. A group of women were identified who had smear results of atypical, dysplastic, or malignant glandular cells. Outcomes included smear and biopsy followup. The outcomes included normal findings, LSIL, HSIL, endocervical adenocarcinoma and endometrial adenocarcinoma. A worrying number had no follow-up recorded who on review had significantly abnormal cells on their smears. Abnormal glandular cells indicate a group of women who have moderately increased likelihood of significant glandular or squamous abnormality.

National gynae cytology training service (NGCTS)
Dr Margaret Sage[1], Judy Cartwright[2]. 1National Gynae Cytology Training Centre and [2]Canterbury Health Laboratories

As most people will be aware, the NGCTS was implemented as a result of the Gisborne enquiry. In July 2005 the contract was awarded by the National Screening Unit, to Canterbury District Health Board, with the first six months of the contract being devoted to the setting up of the service. The training service is a cooperative venture between Canterbury Health Laboratories and MedLab South Ltd.

New guidelines for the management of woman with abnormal smears
Dr Hazel Lewis. National Cervical Screening Unit

In early 2005 a multidisciplinary guidelines development team (GDT) was established by the NCSP to review new evidence and advise on what changes (if any) would be required to the 1999 Guideline for the Management of Women with Abnormal Smears. The GDT comprised two gynaecological oncologists, three colposcopists, one general practitioner, one consumer, two epidemiologists and two pathologists. The New Zealand Guidelines Group was asked to identify and review published studies relevant to a number of clinical questions. In addition, a comprehensive search was made of all guidelines for management of abnormal smears, published since the 1999 New Zealand guideline. The GDT agreed to use the recently published 2005 Australian guideline as a key resource to inform its recommendations. Three meetings were held during September, October and November 2005 to consider the summary of evidence statements for each question and develop recommendations based on these summaries. In some instances where evidence was inconsistent, recommendations were developed by discussion, considered judgement and consensus. One of the options for change being considered is for the management of women with low grade abnormalities. In order to inform the recommendations of the GDT the NCSP was asked to review data on the NCSP-R to assist with determining the optimal timing of recall following a first abnormal low grade (LSIL or ASCUS) smear.

HPV vaccination as a promising new strategy for cervical cancer
Professor Eduardo Franco. McGill University, USA

Universal deployment of organized or opportunistic screening with Pap cytology has been the primary reason for the substantial reductions in cervical cancer morbidity and mortality in high-income countries during the last 50 years. However, in many low-income countries Pap cytology screening is yet to be effectively implemented or has failed to reduce cervical cancer rates to an appreciable extent. Cervical cancer thus remains a critical public health problem that is second only to breast cancer in overall disease burden for women throughout the world. Global incidence estimates indicate that approximately 470,000 cervical cancer cases and around 230,000 deaths occur annually. One of the greatest cancer research advances of the past decade has been the accrued evidence that human papillomavirus (HPV) infection is a necessary cause of cervical cancer. This discovery has led to new research fronts on the prevention of cervical cancer: immunization against HPV and screening with HPV testing. Prophylactic vaccines against HPVs 16 and 18 are currently at advanced stages of clinical testing in adolescent and young adult women. Made from viral capsid proteins, these vaccines induce strong protective antibody response. Recent research on the safety and efficacy of candidate prophylactic HPV vaccines have shown very promising results with nearly 100% efficacy in preventing the develo pment of persistent infections and cervical precancerous lesions associated with HPV types 16 and 18, the two HPV types included as immunogens. Such studies have formed the basis for licensing of candidate vaccines by the major pharmaceutical companies in the next two years, Merck and GSK. Ongoing phase III studies are likely to corroborate the preliminary findings from the latter trials concerning the high vaccine efficacy against high-grade preneoplastic cervical lesions. Mathematical models of the potential impact of HPV vaccines have also suggested a substantial public health benefit to be derived in most geographical areas.

Efficacy of HPV testing in cervical cancer screening
Professor Eduardo Franco. McGill University, USA

Of all malignant neoplastic diseases, cervical cancer is the one in which public health prevention initiatives have been the most successful in the western industrialized world. Widespread programmatic or opportunistic screening with Pap cytology has likely contributed to reducing about three-fourths of the cervical cancer burden in high-income countries during the last 50 years. In spite of its success, however, Pap cytology has important limitations. Its high false negative rate is its most critical limitation. About one -third of false-negative diagnoses are attributable to slide interpretation errors and two-thirds to poor sample collection and slide preparation. False-negative diagnoses have important medical, financial, and legal implications. In many settings, especially developing countries, cytology-based programs have failed to reduce cervical cancer rates substantially. This state of affairs elicited interest from the medical technology industry in developing new molecular tests with adequate sensitivity and specificity for detecting clinically significant cancer precursors. The elucidation of the causal connection between infection by certain types of human papillomavirus (HPV) and cervical neoplasia has led to the development of tests to detect cervical HPV infection as the necessary precursor event driving cervical carcinogenesis. Tests to detect HPV DNA have the potential to become a useful cervical cancer screening tool either as a standalone approach or in combination with Pap cytology to augment the latter test's efficacy. Several studies have already appeared providing evidence in favour of HPV testing as a potentially superior cervical cancer screening technology when compared with Pap cytology. The first generation of these investigations was based on split-sample designs and cross-sectional assessments of screening efficacy. A second generation of studies is beginning to emerge; using randomized controlled trial designs and short-term follow-up.

The impact of HPV vaccination on cervical cancer screening
Professor Eduardo Franco. McGill University, USA

Recent research on the safety and efficacy of candidate prophylactic vaccines against human papillomavirus (HPV) infection has shown nearly 100% efficacy in preventing persistent infections and cervical precancerous lesions. Licensed HPV vaccines will be available in 2006-07. Although the future seems bright on the prevention front policy makers are strongly cautioned to avoid scaling back cervical cancer screening. The two candidate vaccines, Merck's Gardasil and GSK's Cervarix, do not protect against all HPV types that cause cervical cancer. Although a small degree of cross-protection against other oncogenic HPVs is expected, there is also the potential for the distribution of HPV types in vaccinated populations to change gradually as a reflection of the vacated ecologic niches following the progressive elimination of HPVs 16 and 18. There is also the possibility that the type-specific immunity conferred by vaccination may wane over periods extending much beyond five years. While much is yet to be learned about these and other vaccine-related issues, such as target ages and whether or not men should be vaccinated, it is sensible to consider that existing cervical cancer prevention strategies cannot be cost-effective following the incorporation of HPV vaccination without substantial changes to existing screening policies. Even health-care resource-rich countries will be hard pressed to absorb the high societal costs of vaccination without some form of streamlining or restructuring of their cervical cancer screening programs and management practices. Simply making cytology screening less frequent may not be a viable strategy in light of the potential problems that may plague Pap cytology performance in conditions of low lesion prevalence, which will prevail after successive cohorts are vaccinated. HPV testing has the characteristics that would make it an ideal primary cervical cancer screening test in such conditions. Pap cytology should be reserved for triage settings, i.e., in assisting management of HPV positive cases because it is more likely to perform with sufficient accuracy when lesion prevalence is high, either artificially as in triage, or in unscreened populations. Another key advantage of using HPV testing as primary screening tool is the opportunity to create HPV infection registries with the provision to link test results from the same women over time, thus allowing an efficient and low-cost strategy to monitor long-term protection among vaccinated women.

Review of negative Pap smears in woman with HSIL
Karin Bradshaw. Southern Community Laboratories

Previous negative smears are routinely reviewed in women who have an HSIL diagnosis. Occasionally there are abnormal cells found in retrospect. These false-negative smears have been reviewed and found not to be the same as "routinely diagnosed" positive smears. Differences include fewer abnormal cells, smaller abnormal cells and difficult cell groups. In addition the smears which are confirmed as negative were found on review to be of lower quality than routine smears. Although technically "adequate" they were of lower cellularity and less well-fixed than routine smears.

In summary: False negative smears are more difficult to interpret than "routine" smears. Smear quality may affect the false negative proportion more than previously appreciated, indicating the need for continued smeartaker focus on obtaining an adequate smear.

Assessing new cancer screening technologies: the tyranny of evidence-based medicine
Professor Eduardo Franco. McGill University, USA

Medical progress can no longer be based on individual perceptions and cursory clinical investigation. The randomized controlled trial (RCT) is the only study design that can provide unequivocal evidence for or against therapeutic and public health interventions. Wide scale adoption of the RCT by the scientific community and health technology agencies has changed the landscape of medical training in the last decade. However, we must keep in mind that blind and exclusive faith in the RCT as a paradigm for decision-making can be dangerous. RCTs are frequently conducted among subjects who do not represent the population targeted for the intervention. RCTs can assess the efficacy of a particular intervention but shed little light onto its mechanism or mode of action. Assessing the pros and cons of new cancer screening technologies requires studies that are able to generate high quality evidence for the efficacy and effectiveness of a given intervention. Such studies should also incorporate societal variables. Lessons learned from RCTs must be supplemented with a knowledge base derived from large-scale observational investigations and basic research studies.

Performance of the NZIMLS and the services it provides. Results from a Questionnaire
R Siebers, A Buchanan, R Hewett. NZIMLS

Objective: To learn about members' opinions on the performance of the New Zealand Institute of Medical Laboratory Science and the services it provides.

Methods: A 30-question questionnaire was distributed to members through the Journal. Members were asked to rate, on a scale of 0 to 10, the services that the Institute provides, and to rate on the Institute activities that were important to the individual member. Further questions elucidated demographic details and members were invited to comment on any of the above.

Results: Out of a potential pool of 1903 members, 146 returned the questionnaire giving a response rate of 7.7%. SIG seminars, continuing education and the CPD programme were seen by members to be very important, while Fellowship and Council governance were not. Promotion of the profession and sponsorship opportunities by the Institute were rated lowly.

Conclusions: These results, together with the many comments made by members should help the Institute's Council in improving its services to meet the needs of the scientists and technicians who make up our membership and profession.

New Zealand chlamydia survey 2005
Michael Brokenshire. LabPLUS, Auckland Hospital

A national chlamydia survey was carried out to obtain information about chlamydia testing in New Zealand in 2005. A questionnaire was sent to 53 laboratories (25 public and 28 private). Individual laboratories would not be identified in the results. The questionnaire consisted of a number of questions relating to a variety of topics on chlamydia testing. These included the following: was testing carried out on site or sent away; what was the primary method of testing (NAAT or antigen); was there a secondary method of testing; what were the main specimen types; specific questions relating to NAAT or antigen testing; how many years had the current testing been carried out; questions relating to changing methods; how many specimens were tested; what was the positivity rates; what were the main types of specimens in males and females; what swab collection system was used; questions on use of external or internal QA programmes; and was chlamydia data sent to ESR for national surveillance. Additional comments were invited.

Chronic myeloid leukaemia in a 10 year old boy
Michelle Charles. LabPLUS, Auckland Hospital

A 10 year old boy initially presents with eczema and symptoms of gastroenteritis and asthma, responsive to ventolin, steroids and discharged. Re-presents 3 weeks later with splenomegaly, WCC 376x10E/L, and a full range of myeloid maturation and thrombocytosis consistent with a chronic myeloproliferative disorder. The diagnosis of Chronic Myeloid Leukiamia was confirmed by Philapdelphia Chromosome t(9;22)detection. Chronic Myeloid Leukaemia is rare in

children, and it is important to be diagnosed correctly - particularly distinguishing it from Juvenile Myelomonocytic Leukaemia, for treatment purposes.

My dippy dippy heart
Elaine Booker. LabPLUS, Auckland Hospital

A case of Corynebacterium diphtheriae endocarditis is reported in a 10 year old Samoan boy who presented with congestive heart failure. Large vegetations were present on the leaflets of the boy's aortic heart valve. These were sent for culture. A Gram stain of the tissue grindings revealed the presence of what appeared to be Gram-negative bacilli, however, the sample remained culture negative. 16S ribosomal sequencing was carried out to reveal the causative organism as being Corynebacterium diphtheriae.

The role of the myeloid-lymphoid leukaemia gene (MLL) rearrangement in infant leukaemia: a preliminary study of three cases of infant leukaemia in Auckland City Hospital
Sara Derballa. LabPLUS, Auckland Hospital

Cytogenetic alterations including translocations and deletions involving the 11q23 region have been observed in many haematological malignancies. The characterisation of the 11q23 breakpoint lead to the cloning of the MLL gene found on the breakpoint cluster of chromosome 11q23. The normal MLL gene plays a significant role in developmental regulation of gene expression in normal haematopoiesis, in leukaemia however; this function is subverted by breakage, recombination and chimeric fusion with various partner genes. The MLL mutation is detected in 60-80% of infants with Acute Lymphoblastic leukaemia (ALL) and Acute Myeloid leukaemia and is correlated with a poor prognosis.

The effect of kava consumption on liver enzyme gamma glutamyl transpeptidase
Brijesh Kumar, S Chand, R Singh, B Kumar.
Fiji School of Medicine, Suva, Fiji

Kava refers to the rootstock of the plant Piper methysticum. It has been described as a psychoactive beverage that induces relaxation, improves social interaction, promotes sleep, and plays an important role in the socio -cultural life in the islands of the South Pacific. The aim of this study was to investigate the effect of kava consumption on liver. One of the functions of hepatic cells is to detoxify numerous ingested substances such as alcohol, nicotine, kava and other poisons. The liver enzyme gamma glutamyl transpeptidase (GGT) was selected to determine the functioning of the liver. For this study, a sample size of 89 participants, who were either kava-drinkers or non-kava drinkers, was selected. As alcohol also increases the GGT level, participants who consumed alcohol were excluded. GGT levels were measured using the Hitachi 917 analyzer. It was observed that 40% of the kava consumers had high GGT levels compared to only 2% of the non-kava consumers. It was also observed that 60% of the kava consumers whose GGT were not elevated had their GGT near the higher limits of normal range. This indicates there is a relationship between GGT level and kava consumption. Additionally it was seen that as the duration of kava consumption increased, the likelihood of elevated GGT levels also increased. The increase in GGT levels was also observed to be dependent on the amount of kava consumed. This was a pilot study which did reveal a relationship between kava consumption and increased GGT levels.

Identification of cryoprotectant aldehydes and their removal by thiol scavengers
Mike Legge, M Byers. University of Otago, Dunedin

Cryopreservation has become an important technique for the storage of cell lines as well as for gametes and embryos. Although most cell lines generally survive the cryoprotection process, certain lines demonstrate poor recovery and in particular mammalian oocytes are especially sensitive to significant damage to cryoprotectants and the cryopreservation process. Previously (Karren and Legge, Human Reproduction, 1996: 11, 2681-2686) we identified that aldehydes are formed in the cryoprotectant solvents dimethyl sulphoxide (DMSO), 1-2.propanediol (PROH) and glycerol by non-enzymatic reactions and that these compounds could be removed by treating with free thiol agents.

L-cysteine improves survival and growth of human peritoneal mesothelial cells (hPMC) after freezing
Mike Legge, SD Bird. University of Otago, Dunedin

The archiving of cell lines is achieved by cryopreservation, and the successful thawing and recovery in culture. However, certain cell lines either fail to recover in culture post-thaw or fail to recover their full phenotype. This post-thaw recovery problem restricts the successful archiving of some tissue and cell lines as well as the development diagnostic techniques in-vitro. One such cell line which exhibits poor recovery post-thaw is human mesothelial cells (hPMC). Cells exposed to L-cyteine post-thaw demonstrated significant ($p<0.001$) survival over the non-exposed cells with rapid recovery of cell morphology. A dose response of L-cysteine demonstrated that 0.25 to 0.5mmol.L(-1) was optimal for normal growth and that higher concentrations were toxic. Using an optimized culture system [M199,10% fetal bovine serum, L-cysteine 0.25mmol.L(-1)]; tritiated thymidine incorporation was significantly higher ($p<0.001$) in the optimized culture system than in the control (no L-cysteine). From this data we conclude the addition of L-cysteine enhances the recovery of hPMC cells following cryopreservation by both the removal of non-enzymatically formed low molecular weight aldehydes and the maintenance of intra-cellular redox status.

Audio-visual training in Point of Care testing
Mehran Zareian. Waitemata District Health Board

Point of Care Testing is a rapidly growing area, both within and outside the hospital environment. To ensure competency of the users, it is necessary to have a regular re-certification process. This can be laborious and a repeat training session of the original content may not be the answer! At Waitemata DHB, the process has been designed to provide maximum assessment with minimum effort. A year after the original training, staff are sent multiple-choice competency forms to complete for each instrument or process. Successful completion will merit recertification for a further 12 months. If, however, there are areas of concern in the response, then a refresher will be necessary. This may be difficult to arrange although it would only take a short time to resolve, particularly for staff who work weekends and overnight.A pilot scheme has been initiated at WDHB, which involves the production of audio-visual training. This has been processed in-house and has been made available using a progressive strategy. The use of a MS PowerPoint add-on, called 'MS Producer', has enabled the simultaneous broadcast of video and slides. A study is due to follow to identify the benefits of using this tool compared with video or personal refresher sessions. Other clinical areas have shown interest in the scheme, as a similar process may be of benefit to them.

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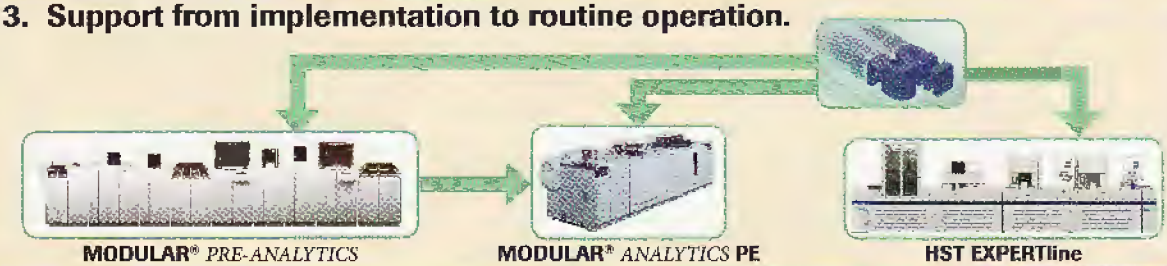

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