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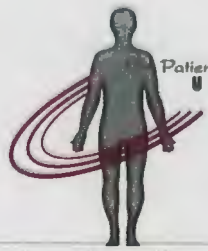

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Point-of-Care

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Editorial: Registration, annual licensing/certification and ongoing competence

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NZ J Med Lab Science 2000; 54(2):43

Laboratory performance at Good-Health Wanganui and Gisborne, have raised public concerns over the performance of health professionals and served to highlight aspects of the laboratory's role in disease diagnosis. In light of these developments it is relevant to consider that as recently as 1997-1998 the profession of Medical Laboratory Science was battling the threat of de-registration in New, Zealand. Extensive written submission, and lobbying by the profession's representatives managed to convince the bureaucrats of the need to retain registration of Medical Laboratory Scientists/Technologists (MLS). The outcome of the review, of registration signalled that a number of changes were likely in any amendments made to the MLS regulations. The most important of these related to the composition of future Medical Laboratory Technologist's Boards.and changes to annual licensing of MLS.

Political pressures during the term of the first MMP coalition government limited progress on changes to the MLS regulations. Under the current Labour government, there is again momentum to proceed with the changes. Indications are that the multitude of separate legislation used to regulate the registered health groups (including MLS) will be replaced with "blanket-type" legislation (provided agreement can be reached) that could incorporate clauses, specific to the individual professions. Indications are that the regulations governing NZ's General Practitioners will be used as a model for other health professionals. The possible impact of the changes could mean that practising MLS would be required to supply supporting proof of competency as part of continued annual licensing or certification. This is in line with the amendments to the GP's regulations made in 1998 that now requires this group to apply to the Medical Council to practise each year and to provide documentation, supporting competence.

In 1996 the Medical Laboratory Technologist's Board introduced the Maintenance of Laboratory Standards (MOLS) programme for NZ registered MLS. The pilot programme introduced the concept of documentation of continuing education and professional activities. The programme ran over a period of four years and the MOLS activities of approx., 10% of participants were reviewed annually. An audit of the programme released by the MLTB in 1999 showed general acceptance and a high level of MOLS activity among the participants. An independent survey of a group of MLS on the MOLS programme by Lisa Brennan is presented in this issue of the journal.

In April 2000 the NZIMLS introduced the Continuing Professional Development (CPD) programme which is available to all members of the NZIMLS (member category only). The programme is voluntary and rotates over a three-year cycle. Participants accumulate points allocated to a range of professional and related activities, in a manner similar to that used in the
MOLS pilot (see later). The goal is to reach a minimum of 300 points over a consecutive three year period after which successful participants will receive a "time-limited" certificate of attainment. Active participation in the programme requires interaction between the Executive Office of the NZIMLS and those in the programme. Participants are required to supply an annual tally of claims together with supportive documentation, which will be used to update CPD records held against NZIMLS membership details. A record of progress will be issued to each participant yearly.

Promotion and periodic review of the CPD programme will be performed by the NZIMLS. The MLTB will maintain an ongoing interest in the structure of the programme to ensure it continues to meet the requirements of legislation. Once proposed changes to the law have occurred, the MLTB will require evidence of competency prior to the issue of an annual practising license. Those unable to show who fail to demonstrate that they meet the requirements of the CPD programme will not be issued a license to practise and will no longer be able to work as a Medical Laboratory Scientist/Technologist in New Zealand.

The CPD programme has therefore been developed to meet the requirements of projected changes to the regulations governing our profession. The programme has been structured to complement the continuing educational activities of the NZIMLS, scientific meetings of MLS industry and other allied health professionals, and recognises activities that contribute to professional development. The format selected for the programme is consistent with that used by other health professions , and its use as a tool for formal recognition of participation in professional activities will play an important role if future changes to MLS regulations as described in this editorial, proceed to reality.

Part Two of Becoming a Fellow, the Treatise

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NZ J Med Lab Science 2000; 54(2):44-45

Choosing the Subject:

One of the most difficult aspects I found when I decided to write my Treatise was choosing an appropriate subject. I believe it is important to choose a topic that has been the subject of recent research, however this does not mean that you cannot use older references that are related to that topic in order to illustrate the course of the research.

The topic that you choose, however, must have been sufficiently researched to provide you with enough material to complete your treatise. It is no use choosing a topic which is of interest and which has been recently researched if there are only a dozen published papers covering the subject, you will simply not have enough material to allow you to complete your treatise. The best method of discovering how well referenced your chosen subject is, is to use a tool such as MedLine or Ovid, these will give you a list of all the papers published which relate to your topic, although you need to be very specific in your search and look at all the tiles listed as many will not be relevant to your needs.

I work in a crossmatch laboratory and have an interest in platelets. I decided that I would like to write my treatise on some aspect of platelets, however the subject is immense and it took me a long time to eventually decide on what aspects of the subject I would like to cover. The problem I had was that of the many aspects of platelets, many did not have sufficient material available to allow me to complete my paper, but at the same time the subject, as a whole was far too vast to allow me to cover anything in sufficient depth for Fellowship level. I decided that I would like to write my treatise on platelet transfusions and how we may better utilise platelets in the clinical setting. The title of my treatise eventually became " Optimising the Effectiveness of Platelet Transfusion Therapy" and covered a fairly wide range of subjects such as leukodepletion, choice of ABO group, transfusion triggers, alternative treatments and platelet substitutes. In hindsight I found this to be rather an ambitious subject to tackle as it was difficult to balance including all of the aspects I wanted to in sufficient depth. However I must have succeeded in doing so since the Fellowship referees decided that my paper was worthy of Fellowship. But it was an extremely difficult task and if I had to do it again I would narrow down my field of reference.

Writing the Abstract:

Once you have chosen your subject, you need to write an abstract of not more that 500 words to submit to the Fellowship committee. You need to have researched your subject quite extensively before you attempt to write your abstract. Firstly I printed a list of all the references I thought would be relevant to my chosen subject, then went on a search to find them all, this is a very time consuming process and I started in December and finished writing my abstract a week or so before the required deadline. Again, hindsight is a wonderful thing and if I were to have to do it again I would have started much earlier as I believe it would have been much easier to write the abstract after I had written my treatise. My first attempt at writing the abstract resulted in the abstract being about 1500 words long, I was trying to summarize every individual aspect of my topic. In fact it took me about four attempts to achieve the final abstract, which had been cut to 250 words and was a summary overview of what my treatise would cover.

References and writing the treatise:

Before you attempt to write your treatise it is important to be clear about exactly what you are going to write. I read through every reference I had and sorted them into different categories, made a list of every title and numbered them and made a brief summary of what each reference contained. This gave me a quick reference and allowed me to me to easily access any reference I needed. I also wrote a skeleton of what I wanted my final treatise to look like, again this took several re-writes before I was satisfied that I was presenting the information in a clear and logical manner. I had two filing systems for my references, I had the original categorization which contained all the references I was going to use and the second was for all the references I had already used, kept in the same order so that I could find and refer back to them if necessary. Keeping track of the references you have used and inserting the reference into your work is extremely time consuming. I used a computer program called End-Note to organise all my references which certainly made life easier, although it didn't store them in the format required and I had to go through every reference adding bits and changing their format, even then I didn't get them all formatted correctly as the Editor of the Journal found when he edited my treatise. The main advantage of End-Note was that it created a library of my references and made it much easier to insert them into the text. I believe that there are quiet a few bibliography programs available and they can take some of the pain out of compiling a bibliography.

A further tip which may save you time is to ensure you read your most recent references before the older ones. If you read the older ones first and include the information into your treatise you may find that the more recent references may contradict the older information due to more recent advances in research. There is nothing more annoying than spending a few hours researching and writing information into your work only to find that the information is now outdated and you have to start all over again.

Writing a treatise is extremely time consuming and involves a lot of reading and research before you even begin to start the actual writing and my advice would be to start the process as soon as possible. It is not the sort of thing you can leave until a month or so before the deadline and hope to end up with a final product that does justice to the Fellowship. This applies not only to writing the actual Treatise but also to all aspects of the fellowship, from choosing your subject, finding and collating your references and writing your abstract. Having said that, all the hard work leaves you with a great sense of achievement

when you finally have your finished paper all ready to send to the Fellowship committee and especially when you get a letter telling you that it is of sufficient standard for you to be awarded the Fellowship. One final tip before is to ensure that you read and follow the instructions to authors which is supplied by the Editor through the Institute, it will save you time in the long run and make the Editor's a lot easier.

If anyone has any questions they would like to ask me, or wants to talk to me in further details about writing a Fellowship treatise I can be contacted by e-mail on mark.bevan@nzblood.co.nz , it is easier to contact me by e-mail than by phone as I tend not to be in Palmerston North very often at the moment. If anyone wishes to talk to me they can include their phone number in the e-mail and I will get back to them.

Fellowship Workshop Report

With this year being the last window of opportunity for Specialist exam holders to obtain Fellowship of the NZIMLS by submission of a dissertation (Part 2 of Fellowship by examination), it was decided to hold a practical workshop to prepare potential candidates for this route.

Thus over a weekend at the beginning of April, seventeen participants from as far away as Auckland and Invercargill arrived at the Workshop which was held at the Wellington School of Medicine. It was decided prior to the event to spread the lectures over two half days in order not to overload the participants with to much information over a full day. It also gave the participants time to arrive from far afield on the first day of the meeting. As it was several participants had some trouble arriving in time due to weather problems throughout the country playing havoc with airline schedules.

After welcoming participants to the workshop, during which the course outline was explained, Trevor Rollinson as Fellowship Convenor of the NZIMLS gave a brief history of the Institute's Fellowship and the current regulations. He followed this up with a talk on how to plan the treatise.

Paul Campbell, computer specialist at the Medical School, then gave a presentation on how to create graphs and tables and on how to down-load references using computer programs and data bases. Unfortunately, due to technical hitches, he was unable to demonstrate the use of such programs, but nevertheless managed to get the concepts across.

Rob Siebers, Editor of the Journal, then gave a talk on the structure of a treatise with special emphasis on the abstract and the references, areas which frequently contain many errors in submitted publications.

Mark Bevan, a recent successful Fellowship candidate, was scheduled to give a final talk of the day on his experiences on writing his treatise. Unfortunately Mark experienced massive delays on his journey from Palmerston North to Wellington due to a serious traffic accident blocking the main highway for over four hours. However, Mark e-mailed his talk to Wellington that night and was distributed to the participants. It is reproduced in full in this August issue of the Journal as a leading article and is well worth reading by Fellowship candidates as it contains sound advice and many useful tips.

After a delightful meal at an Italian restaurant that night, the workshop resumed on the Sunday morning which was entirely devoted to a practical exercise by the participants. They were split into three groups, each group were then given a published review article on a laboratory related topic minus the abstract. They were then asked to write an abstract on that article, which was at the end of the session was compared to the published abstract. Some interesting results were obtained!

Finally, before departing to their various destinations, a workshop overview and general discussion took place. The participants seem to have enjoyed the experience and they stated that they had benefited from attendance at the workshop. It is hoped that the Fellowship workshop will become a regular feature on the NZIMLS calendar over the coming years. A special thank you to Ross Hewitt and Roche Diagnostics NZ for kindly supporting the workshop, and to Fran van Til for her help in the organisation.

Rob Siebers and Trevor Rollinson

Coeliac Disease: Testing the New Zealand Iceberg

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NZ J Med Lab Science 2000; 54(2):46-48

Introduction

Coellac disease (CD) is a common(1-7)(~1% New Zealand) disease of the upper small intestine resulting from gluten ingestion in genetically susceptible individuals. This leads to malabsorption of several important nutrients including iron, folic acid, calcium and vitamin-D, and an increased risk of lymphoma(8). The long term hazards of CD are reduced if affected individuals are identified and treated by adherence to a strict gluten free diet (GFD). Many patients have minimal symptoms(3) (gastrointestinal symptoms may be absent) making clinical diagnosis difficult. The introduction of several immunological antibody tests(9) have significantly aided in diagnosis, simplifying the screening of at-risk patients. This in turn has helped in unlocking the previously undiscovered "iceberg" of CD sufferers in New Zealand.

Pathogenesis

Coeliac disease is an autoinimune disease caused by intolerance to prolamins, the storage proteins of wheat, barley, and rye; and is triggered by an as yet unidentified factor or factors in genetically susceptible individuals(1). In wheat the toxic prolamin is gliadin, the alcohol soluble fraction of gluten. These toxic agents lead to mucosal inflammation, crypt hyperplasia, and villous atrophy; and upon exclusion of these cereals from the diet, the intestine returns to normal without residual scarring.

The precise pathogenic mechanisms are unknown, but current theories for the cause of the mucosal lesions of coeliac disease revolve around both humoral and cell mediated immune responses.

Humoral immune response

Antibodies to gliadin, endomysium, reticulin and tissue transglutaminase (tTG) are synthesised by the B-cells in the lamina propria of the small intestine. Recently Dieterich and co-workers(10) identified tissue transglutarninase as the target antigen of the endomysial antibody. There is however, no proven pathogenic role for any of these antibodies in the gut, and there have been cases of adults with active CD and negative antibodies at diagnosis. Also hypogammaglobulinemia does not prevent mucosal damage.

Cell mediated immune response

T cell mediated immune response and genetic factors appear to play a larger part in the pathogenesis of CD (11-14). An estimated 10% of first-degree relatives of CD sufferers are diagnosed as having coeliac disease. The HLA-DQ2 and/or DQ8 molecules are expressed in greater than 90% of CD individuals. Complex interrelationships between T cells, HLA-DQ, gluten derived peptides, antigen presenting cells, and tissue transglutaminase lead to mucosal damage by the release of inflammatory cytokines or secondary inflammatory mediators such as nitric oxide(13). Tissue transglutaminase has a direct role in the induction and/or amplification of damage to the gut.

Other factors are involved in the pathogenesis of coeliac disease as not all HLA-DQ 2 or DQ 8 positive individuals develop CD. The non-HLA gene or genes also participates and may be a stronger determinate of disease susceptibility than the HLA locus.

Epidemiology

Reports in the 1950's suggested that the prevalence of CD ranged from about I in 4000 to I in 8000, However, this prevalence was based on clinical interpretation of classical symptoms of malabsorption. This. changed in the 1970's with the rising awareness of the myriad symptoms presented to doctors and the introduction of antibody testing. Several recent studies from Northern Ireland(6) , Sweden(4), America(5), United Kingdom(3) and Italy(7), have revealed prevalence's ranging from 1 in 152 to I in 300. For example, one large study of 17201 Italian school children demonstrated a prevalence of I in 184, and the ratio of previously undiagnosed to diagnosed CD sufferers was found to be 7: 1(7)

In New Zealand the most common cause of malabsorption is coeliac disease. A study in Christchurch has shown the prevalence of CD to lie between 1 in 82 and 1 in 198(1). In Canterbury there has been, since the 1980's, a steady increase in the number of CD patients diagnosed.

Symptoms

A diverse range of symptoms and related signs may be associated with CD(3,7,14) These can be divided into intestinal features and those caused, by malabsorption (Table 1). Many patients (especially in adulthood) have mild or non-specific symptoms, such as fatigue or borderline iron deficiency, or no symptoms at all ("silent"), making clinical diagnosis difficult. Although strongly linked with childhood, coeliac disease often presents later, between the ages of 10-40. Females are more commonly affected than males, especially during the fertile years.

Patients may present with the classic intestinal signs of chronic diarrhoea with bulky, foul smelling, floating stools due to colonic bacterial digestion of malabsorbed nutrients. The consequences of malabsorption include short stature in children, weight loss, severe anaemia, neurologic disorders(15,16) from B vitamin deficiencies, and osteopenia (17,18) from deficiency of vitamin D and calcium.

Severe osteopenia in symptom free adults with a childhood diagnosis of CD have lower than normal Bone Mineral Density (BMD) and an increased risk of fractures(17). After one year on gluten free diet the BMD increases to near normal levels in many patients(18).

Associated diseases

Many diseases and disorders are frequently associated with coeliac disease (l,3,14). Definite associations have been established with dermatitis herpetiformis, certain malignancies(8), Down's syndrome, hyposplenia, serum IgA deficiency, and autoininiune conditions such as Type 1 diabetes mellitus and thyroid disease.

Table 1. Symptoms and signs of coeliac disease.

Common Laboratory findings:

Iron deficiency (with or without anaemia)

Vitamin B12 and/or folate deficiency

Vitamin D and/or Calcium deficiency

Gastrointestinal symptoms:

Recurrent diarrhoea

Abdominal distention, bloating and pain

Constipation

Non-gastrointestinal symptoms:

Recurrent mouth ulcers

Infertility

Pubertal delay

Rheumatic disorders- arthritis, bone pain

Osteoporosis, osteomalacia -lowered bone mineral density

Poor appetite, anorexia, failure to thrive, short statue

Vomiting

Psychomotor impairment

Neurologic disorders - Depression, anxiety, ataxia, epilepsy, migraine

About 90% of patients with the pruritic skin disorder dermatitis herpetiformis also have CD. Coeliac disease is normally niild or asymptomatic in dermatitis herpetiformis sufferers but the skin lesions in most patients respond to gluten withdrawal.

In unrecognised and untreated patients there is an estimated eight-fold increase in risk of upper gastrointestinal malignancies and a 30-fold increase in the risk of a highgrade malignant lymphoma, Enteropathy Associated T-cell Lymphoma (EALT). The risk of EALT falls after several years on a gluten free diet.

Coeliac disease (mostly asymptomatic) has been found in 5-10% of patients with Type I diabetes mellitus. The dietary treatment of both diabetes and CD is complicated and care is needed to maintain control of the diabetes.

Selective IgA deficiency occurs in about 1 in 50 coeliac disease sufferers. Screening for CD is improved by testing for Gliadin IgG antibodies.

Diagnosis

The traditional diagnoses of CD requires the demonstration of severe villous atrophy on initial biopsy, a normal second biopsy after six months on gluten free diet, and a third biopsy demonstrating atrophy following gluten challenge. Such a stringent requirement is seldom required for most patients (>2 years old) with the introduction of reliable screening tests.

Biopsies are invasive, expensive and the interpretations are not without difficulty or problems. They require human tissue to be taken by a gastroenterologist, and a pathologist to view the slide. The interpretations of biopsies are not necessarily consistent between testing centres because they are qualitative and therefore operator dependent. Other causes of villous atrophy need to be considered and excluded, for example, Crohn's disease, giardiasis, Zollinger-Ellison syndrome and tropical sprue.

Despite these difficulties small intestine biopsies at present remains the "gold standard" in CD diagnosis.

Screening tests

Gliadin IgG and IgA, Reticulin IgA, Endomysial (EMA) IgA and, more recently, tissue transglutaminase IgA and IgG antibodies are used to screen at risk patients for CD. There are large differences in the reported sensitivities and specificities of these methods among different laboratories - Table 2 summarises these.

Endomysial antibodies

The Endomysial IgA antibody test has the highest specificity and a positive predictive value approaching 100% in the appropriate clinical setting. The sensitivity is good (>85%) and has been used to detect and monitor CD patients for a number of years. The down side is that it is a labour intensive and relatively expensive immunofluorescence technique requiring primate tissue (monkey oesophagus or human umbilicalis) with operator dependent result interpretation.

Tissue transglutaminase antibodies

The tTG-IgA assay, developed in the late 1990's, is a highly specific and probably the most sensitive CD screening antibody test available at present[9]. Commercial kits in New Zealand use guinea pig antigen preserved in its native state on the walls of microtitre wells. The ELISA format allows for automation, large volume screening and objective quantitative result interpretation. The assay looks promising in monitoring compliance and response of known CD suffers on a GFD[9] but has yet to be fully evaluated. Moderate to high antibody levels are highly suggestive of coeliac disease. Weakly reactive or borderline results should have further investigations such as EMA and gliadin antibodies carried out. There is some debate regarding antigen choice in the assay. It has been suggested that recombinant human antigen assays would increase specificity without a corresponding loss of sensitivity.

Table 2. Sensitivities and specificities of screening tests for CD

Screening tests for CD	Sensitivity.	Specificity
Gliadin IgG	75-85%	70-90%
Gliadin IgA	70-80%	85-95%
Reticulin IgA	25-30%	95-98%
Endomysial IgA	85-95%	97-100%
tTG-IgA	90-100%	87-97%

There are currently no commercial kits available for tTG-IgG. The sensitivity for tTG IgA and tTG IgG antibodies when tested concurrently approaches 100%. Unfortunately non-specific cross reactivity has been reported in the tTG-IgG assay with anti-SSA/Ro sera producing falsely elevated results.

Gliadin antibodies

There are several different commercial and in-house Gliadin IgG and IgA ELISA assays available in New Zealand. The sensitivities and speci-

ficities for Gliadin antibodies are lower than EMA or tTG-IgA and they vary depending upon method, population tested and cut-offs used. Gliadin antibody tests are quantitative, easily automated and less expensive than EMA and tTG assays. Gliadin IgA levels may be used to monitor GFD compliance; a significant fall off in levels is expected after six months. Gliadin IgG levels do not fall to the same degree and are not useful in monitoring diet compliance. Although the gliadin IgG assay suffers from lower specificity and has been reported to have a positive predictive value of only 2%(7), it is useful in identifying selective IgA deficient individuals. Strongly positive Gliadin IgG levels in the IgA deficient patient should be considered for biopsy if there is clinical suspicion of CD.

Reticulin antibodies

Gliadin, EMA and tTG antibody tests have superior sensitivities for CD and have largely superseded the Reticulin IgA assay.

Other non-invasive tests

Biochemical and haematological tests such as calcium, vitamin D, vitamin B12, folate, faecal fat, iron and haemoglobin are used as an aid in CD diagnosis. These tests by themselves however, lack specificity.

Patient Management

The management of CD patients involves the instigation of a gluten free diet, monitoring compliance with serological tests, and if the response is poor, a repeat biopsy.

Modern highly processed food makes diet compliance difficult and advice from a dietician is recommended. A moderate intake of contaminate free oats, a close relative of wheat, barley and rye, is now considered acceptable(1,14). Oats are an important source of fibre and nutrients. Supplementation of deficient nutrients such as iron, folic acid and calcium may be required.

The diet compliance is often most rewarding to the patient in terms of alleviation of symptoms and increased energy in a matter of weeks. The longer-term prognosis is excellent with a lower risk of bone fractures and lymphoma.

Future trends

The search will continue to completely elucidate coeliac disease pathogenesis and use it to uncover immunotherapies. The recent discovery of the dominant gliadin T cell epitope is a step toward the development of an antigen-specific immunotherapy for CD(13,20). This would forever remove the need for gluten free diets.

There will be increased screening of at risk populations in an effort to reduce the long-term health costs, for example, unexplained osteoporosis sufferers(14,18,19). There is ongoing controversy regarding population screening in general. Most debate centres on the availability of both financial and staff resources versus possible longterm benefits.

The Celiac Disease Standardization Group was formed to establish a set of serological standards, clinical standards, and to improve resources for education and research. The introduction of serological standards will improve the consistency of screening tests worldwide.

Conclusions

Coeliac disease is a common, treatable and under diagnosed disease with significant morbidity and mortality. A greater awareness by doctors of the myriad presentations and symptoms of CD, and the increased availability of accurate screening blood tests is continuing to shrink the "iceberg" of coeliac disease suffers in New Zealand.

Acknowledgements

I would like to thank Dr Guy Mulligan and Marie Sutton.

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An Evaluation of the Maintenance of Laboratory Professional Standards (MOLS) Pilot Programme.

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Abstract
The need to ensure the continuing professional development of healthcare professionals has intensified in recent years due to pressures from the public, government and internal professional pressures. In 1995 the New Zealand Medical Laboratory Technologists Board introduced a voluntary, four-year pilot programme called the Maintenance of Professional Laboratory Standards (MOLS) programme. The aim of the programme was to ensure the involvement of technologists in ongoing educational activities that maintain professional standards. This project was undertaken to identify which groups of technologists are and are not participating in the MOLS programme; what educational activities they are attending; what benefits they have received from their participation and problems they have encountered; what resources and employer support they have received and the reasons why some may not be participating.

A self-administered postal questionnaire was sent to 180 randomly selected medical laboratory technologists from the New Zealand register which contained 1272 individuals registered to practise as technologists in this country. Eighty-five completed questionnaires were returned giving a response rate of 48.3%. Twenty-six respondents (31%) were actively participating in the MOLS programme, while 59 (69%) were not. This is a much lower participation rate than the 80% reported by the New Zealand Medical Laboratory Technologists' Board in its 1998 annual report.

Technologists were significantly more likely to be participating in the MOLS programme if they worked more than 20 hours per week, predominately worked the day shift, had staff reporting directly to them or worked in any discipline other than microbiology and/or virology. There was no difference found in the participation rates based on gender, type of laboratory worked in, number of years registered as a technologist or past membership of the Institute Executive, the Board, or a Special Interest Group convenor.

All technologists who had been participating in the MOLS programme for the full four years had achieved the minimum 2500 credits. Fifty-three percent of these credits came from laboratory practise and 29% from attending conferences and seminars. The major problem with participation in the MOLS programme identified by the respondents in this survey was lack of time to attend educational activities. However 31% of programme participants had no problems at all.

The main benefits identified by the respondents was increased clinical and technical knowledge and some participants had introduced new diagnostic tests and techniques into their laboratory as a result of their MOLS programme participation. Twenty-three percent of programme participants had increased their attendance of educational activities during this four-year period, while 42% said they had altered the way the practise as a medical laboratory technologist as a result of participation in the MOLS programme.

The reasons given for non-participation included lack of information about the programme (45%), not compulsory (27%), not relevant to their current work situation (23%) and lack of employer support (6%).

Key Words
Competency, professional development, medical laboratory science

Introduction
It has been estimated that depending on the field of study, the knowledge within that field doubles every three to ten years (1). If this is true, then to remain up to date with current research and developments in their field, professionals must look at life long learning as a practical necessity and not just a desirable goal.

Within the healthcare industry, this commitment to continuing education and a lifetime of learning is not new. Oster in 1905, stated *"the hardest conviction to get into the mind of a beginner is that education upon which he [sic] is engaged is not a college course, not a medical course, but a life course ending only with death, with which the work at a few years under teachers is but a preparation"*. (Cited in 2).

However, it is only recently that the demand to demonstrate the continued competency of healthcare professionals has intensified. This demand has come from a number of areas, both externally and internally. With access to the Internet and other electronic media the general public is now better informed and has a greater access to more health related information than ever before. They are more actively involved in the decision making regarding their health care and are more likely and often encouraged to challenge health professionals. As a result public pressure to ensure the competency of health professionals is increasing (3).

The advent of managed healthcare in America and the greater emphasis worldwide on receiving the best value for the healthcare dollar, are other driving forces for continuing professional competency. Both insurance companies and governments are actively encouraging the evaluation of continuing competency. A 1995 report by The Taskforce on Health Care Workforce Regulation in the United States recommends that *"States should require each board to develop, implement and evaluate continuing competency requirements to assure the continuing competence of regulated healthcare professionals"* (Cited in 4).

Traditionally the health professional registration boards have been involved in the accreditation of individuals. They have been involved in collecting and verifying information on practitioners' training and experience. In New Zealand all health professional registration boards including nursing, physiotherapy, radiology and medical laboratory technology, but excluding medical practitioners, have to date been responsible for setting only the entry level practise standards. Renewal of practising certificates is achieved on the payment of a fee. This system is similar to that seen in many other countries (4). However, even though the registration boards set minimum standards of competency that are necessary to protect the public, there is a growing consensus that an examination after registration does not ensure competence in

perpetuity.

There is also an internal motivation from within health professional organisations to be proactive in demonstrating that its members meet the standards established by their peers. Historically, professional organisations have policed themselves based on the idea that they are the best qualified to set the standards of competency within their discipline (4,5). Therefore health professionals must balance the desire for self-regulation with public accountability.

Also, there is increasing desire and commitment among healthcare organisations to become accredited to various healthcare standards, this has increased the pressure on employers to ensure that their staff perform their duties competently. Most bodies that accredit healthcare have companies in New Zealand, including International Accreditation New Zealand (IANZ) and Healthcare New Zealand and many overseas organisations. For example, the Joint Commission of the Accreditation of Healthcare Organisations (JCAHO) of America and the National Association of Testing Agencies (NATA) of Australia have specific requirements that are aimed at ensuring employee competence. The healthcare organisations must regularly assess the ability of each staff member to meet performance expectations, encourage and support self-development and provide education and training to maintain and improve staff competence.

This is a move away from the view that by holding a current licence to practise an individual is competent. The concept of competence has changed, as now the outcomes of a professional's practise are more important than the qualifications they hold. Therefore competence should be linked to the demonstration of the ability to perform adequately in an individual's required role (6).

Before one can asses the competency of an individual we must be able to define competency. Competence in the health professions requires more than just knowledge. It must include the understanding of knowledge, clinical, technical and interpersonal skills, problem solving and clinical judgement (7). Willis and Dubin (8) classified professional competence into two broad domains of proficiencies and general characteristics. The proficiencies are profession specific and include the knowledge base of the discipline; the technical skills considered essential to the profession and the ability to solve the types of problems generally encountered in the profession. Whereas the general characteristics, refer to the individual's attitudes, personality traits, motivations and values. Hence they argue that competence involves both objective aspects, for example knowledge and manual skills, and subjective aspects like personal attitudes and values.

Perry (9) describes a competency as *"a cluster of related knowledge, skills and attitudes that affect a major part of one's job, that correlates with performance on the job that can be measured by well accepted standards, and that can be improved via training and development"*. He argues however, that many competencies often listed in job descriptions are merely a list of personality traits, for example objectivity, adaptability and intuition, which are either inborn or determined before adulthood. As such, they are not able to be changed significantly through training or other developmental activities. However, personality does have an impact on how a person functions in their role, therefore the focus for competence assessment should be on performance and not personality.

Youngstrom (10) argues that competence is integrative in nature and that competence and practise are inextricably linked. Youngstrom asserts that clinical practise is the context in which competence in the health professions is demonstrated. Hence, as practise is dynamic in nature and is always changing and developing, so also must competence be changing and growing.

The knowledge base on which the health industry is built is expanding at a very fast rate, 1500 scientific articles are published daily (11). Therefore the initial competence of a newly trained healthcare practitioner is not assured over time unless an effort is made to update and to seek new knowledge and then to put it into practise. Also central to the issue of competence is the awareness that one cannot know everything. Practitioners must have sufficient knowledge of their own skills and abilities to recognise when a patient needs to be referred or another practitioner needs to be consulted.

There is no doubt that there is a need for health professionals to be actively involved in continuing education after their initial registration in order to maintain an adequate level of competence. However, it is the demonstration of this continued competence that has been the topic of debate (3,4,12,13). The evaluation of competency involves making conclusions regarding performance. Poor performance can result from situations where there is a lack of continuing education, however there are other causes as well. These may include emotional and physical disability, chemical impairment (for example drug abuse) and unethical behaviour. Hence defining and evaluating competence is not an easy task.

Grossman (4) identifies a number of questions that she thinks should be considered with the regard to the implementation of a continuing competence system.

1. Should the assessment involve the evaluation of discipline specific general knowledge, similar to entry level assessments, or should it be specific to the individual's current practise?

If the purpose of assessing continued competence is to satisfy government and other legislative bodies that all health professionals meet a minimum standard of competency then a general, one assessment for all, measure would achieve this. However, Youngstrom (10) argues that competence relates to a person's ability to adequately perform the required duties of their job. Therefore assessment should take into account the nature of a person's role, whether a generalist or a specialist. Hence a person is not necessarily more competent because they have chosen to specialise within their particular profession or because they hold a position of seniority within their organisation. An individual's competency should be measured against the performance relating to the requirements of the role they currently fill.

2. Should evidence of continuing competence be mandatory or voluntary?

A compulsory approach is much more likely to ensure compliance, however it may be less likely to foster a positive attitude towards continuing education. On the other hand, voluntary participation may not necessarily meet the need to ensure a minimum level of competency among all practitioners. Also if the demonstration of continued competence is made compulsory, this implies an obligation to take disciplinary action whereby a licence to practise may be revoked if evidence of competence is not maintained. This is a deviation from the current practise of many registration boards, which normally operate reactively, taking disciplinary action only when it has been proven that a practitioner has not met the required standards of practise or ethical behaviour.

3. How should continuing competency be measured?

A number of assessment tools have been used to measure competency. These include knowledge based examinations, problem solving examinations, diagnostic tests, patient satisfaction surveys, case studies, educational activities and peer review assessments (4,14). Holmboe and Hawkins (15) in their study of competence assessment methods for internal medicine residents concluded that no single evaluation tool can adequately assess knowledge, skills and attitude. A multifaceted approach should be used and it should incorporate direct observation of the individual performing their duties.

The most commonly used mechanism to demonstrate continuing professional development is the participation in various educational

activities. In this system credits or points are given for each activity attended. Often more credits are given for activities that require more input from the practitioner, for example publishing a scientific paper would get greater recognition than attending a one day seminar. This type of system is used by many health care professional organisations including The Royal College of Surgeons of England, The Australasian College of Pathologists and the Canadian, Australian and New Zealand Institutes of Medical Laboratory Sciences. However this system offers no assessment of the actual performance of the practitioner. It is assumed that participation in these activities will translate into continued competence, an assumption that may or may not necessarily hold true.

The effectiveness of various continuing medical educational activities in the setting of general medical physicians has been studied. The authors concluded that the relatively short (one day or less) formal events, for example conferences and seminars, on their own generally had no effect on performance. However when two or more educational strategies were employed, there was greater likelihood of inducing a positive change in performance. The more successful strategies were the practise enabling strategies, for example patient educational methods, and the reinforcing strategies, like expert opinion leaders. Also group strategies including peer discussions and role-playing tended to be more successful at improving performance. The effectiveness of various educational activities varied greatly; however, when barriers to change were addressed and resources were deployed where needed, then the change appeared to occur relatively frequently (16).

It would appear that the choice of which competency assessment tools to use is difficult. However, in order to be successful they need to be non-punitive, non-threatening, reasonably priced and objective. Presently used methods have their strengths and weaknesses and it is the validation of these methods that has continued to challenge (4).

Aims

In 1995 a four-year pilot programme, called the Maintenance of Laboratory Professional Standards (MOLS) Programme, was introduced to New Zealand medical laboratory technologists. The stated purpose of the programme was to ensure that technologists are involved in a range of ongoing educational activities which maintain professional standards once registration has been granted, so that they may continue to provide the highest quality of laboratory medicine. The MOLS programme involves the allocation of credits for various educational activities of which a minimum of 2500 must be gained in a four-year period. This was a voluntary programme open to all registered technologists.

The aims of this project were:

- To assess the perceptions of the New Zealand registered medical laboratory technologists of the pilot MOLS programme.
- To identify the characteristics of technologists that are participating in the MOLS programme and of those not participating and to evaluate the differences, if any, between these two groups.
- To identify the benefits or otherwise that the participants perceive from participation in the programme.
- To ascertain what educational activities the MOLS programme participants were engaged in and what resources had been spent on attending these activities.
- To identify any problems encountered or any changes that the participants would like to see with regard to the programme.
- To identify what employer support the MOLS programme participants had received.
- To ascertain why technologists are not participating in the MOLS programme.

Methods

To achieve the aims of the research project regarding the pilot Maintenance of Professional Laboratory Standards (MOLS) Programme, a self-administered postal questionnaire was chosen as the assessment tool. Questionnaires were sent to 180 randomly selected individuals from the New Zealand register of medical laboratory technologists which as of August 1999 contained a list of the 1272 registered practicing technologists in New Zealand. Therefore 14.1% of the entire population of registered medical laboratory technologists was asked to participate in this project. A copy of the MOLS credit distribution list (as supplied in the MOLS programme documentation) was included with the questionnaire in order to remind the participants of the method of credit allocation.

The questionnaire was made up of 36 questions that consisted of a combination of closed, tick box type and opened ended questions. The first eleven questions were designed to collect general demographic information regarding the respondents including the type of laboratory worked in, the scientific discipline most often worked in, the gender of the respondents, the number of years since first registration as a technologist, the hours and time of day usually worked, whether they had staff reporting directly to them and had they ever served on the Institute Executive, the Medical Laboratory Technologists Board or as a convenor of a Special Interest Group.

The respondents were asked if and where they had heard of the MOLS programme. If they had not heard of the programme, they were not required to answer any more questions, as the remaining questions all required some knowledge of the programme. The remaining respondents were then asked if they were actively participating in the MOLS programme. This question was included to define the two study groups, those actively participating and those that had chosen not to participate in the MOLS programme. Those respondents that indicated that they were actively participating in the MOLS programme were then asked a number of questions regarding the credits they had accumulated, the resources required to obtain their credits and the benefits and difficulties encountered in the participation in the MOLS programme.

Eighty five completed questionnaires were returned giving a 48.3% rate of return. In some cases results were aggregated due to the low number of responses for a particular question. The Exact Probability Test was used to calculate the probability of occurrence between the two groups, those participating in the MOLS programme and those who are not. This test also determined the significance or otherwise of each result. A significance level of $p = 0.05$ was selected as the level to indicate significance.

Results

Questionnaires were sent to 180 randomly selected individuals listed on the register of medical laboratory technologist. As at 17 August 1999 this register contained 1272 names. Four questionnaires were returned unopened due to incorrect mailing address and 85 were returned fully completed. Therefore the response rate was 48.3% for the survey population or 6.7% of the entire population of registered medical laboratory technologists.

The number of responses received from the eighty-five completed questionnaires was tabulated for each question. This was then divided into two further sets consisting of those participating in the MOLS programme and those who were not participating. A comparison between the number of responses received for these two subgroups and with the whole group was performed to using the Exact Probability Test to determine significance. This comparison was performed for the eleven demographic questions to identify any differences between the medical laboratory technologists that were participating in the MOLS pro-

gramme and those that were not. For some questions there was similar data available about the entire population of active medical laboratory technologists from the Ministry of Health summary of results from the 1998 Health Workforce Annual Survey, an annual survey completed each year by all registered health professionals. Where this information was available, the comparison was carried out between it and the data for all the respondents to that question. This was performed in order to determine if there was a sampling bias in the survey. This data was available by gender, type of laboratory and the discipline worked in.

Demographic Information

Nineteen (22%) replies were received from male technologists and sixty-six (78%) from females. This compares to the 28% of males and 71% of females in the total population of active medical laboratory technologists as given, and it is not significantly different from the population data.

Similarly, there was no significant difference between the respondents and the active medical laboratory technologists with regard to the type of laboratory they were employed in or the discipline they worked in. Sixty (71%) worked in hospital (HHS) laboratories; twenty-one (25%) worked in a community laboratory; one was not working at present and three (4%) worked in a teaching institution or other organisation. This compares with the 63% of active medical laboratory technologist who work in hospital laboratories, 28% in community laboratories and 6% in other types of organisations.

The comparison between the number of respondents and the total population with regard to the discipline worked in is shown in Table 1. Statistically no difference was seen. The replies to the questions regarding the demographic characteristics of the respondents were broken into the two subgroups of those respondents that were actively participating in the MOLS programme and those that were not participating. Twenty-six (31%) of the respondents indicated that they were actively participating in the MOLS programme, while fifty-nine (69%) stated that they were not.

There was no significant difference seen between the participating and the non-participating groups with regard to the type of laboratory worked in. Sixty-nine percent (69%) of non-participants were employed in a hospital laboratory compared to 77% of participants. In the community laboratory the figures were 27% for non-participants compared to 19% for participants and 5% compared to 4% respectively for those who worked in other institutions.

The percentage of males that are participating in the MOLS programme is higher than the percentage of males in the whole population. Thirty-five percent of the programme participants were male compared with 17% of the non-participating group, while 65% of the participants were female compared with 83% of the non-participating group. However this did not reach statistical significance (p=0.0922).

Table 1.

Discipline	Population	Respondents
Biochemistry	17%	22%
Haematology	20%	21%
Microbiology/Virology	20%	21%
Immunology/Trans.Med	15%	9%
Anatomical Pathology	5%	7%
Multiple disciplines	4%	11%
Other	8%	9%

The length of time since registration did not have an impact on whether technologists were likely to participate in the MOLS programme or not. However the scientific discipline that the respondents worked in did. Only one of the twenty-six (4%) MOLS programme participants worked in a microbiology or virology laboratory compared to seventeen (29%) of the fifty-nine non-participants. This means that only 6% of the microbiology / virology technologists surveyed were participating in the MOLS programme, while 94% chose not to. This was highly significant with a p value of 0.0091. No significant differences were found for any of the other major disciplines.

The hours of work of the technologists surveyed influenced their participation in the MOLS programme. Twenty-four (92%) of the twenty-six participants worked greater than twenty hours per week, compared to forty-three (73%) of the non-participating group. This had a high degree of statistical significance with a p value of 0.0006. There was also a significance difference seen with regard to what shift; day, afternoon, night or various shifts; the technologists worked and whether they participated in the MOLS programme. Twenty-five (96%) of the twenty-six participants regularly worked a day shift compared to forty-one (69%) of the fifty-nine non-participants ($p = 0.0052$).

The medical laboratory technologists who had staff reporting directly to them were more likely to be participating in the MOLS programme. Seventeen (65%) of the twenty-six participants had staff reporting to them compared to eighteen (31%) of the fifty-nine non-participants. This was statistically significant ($p = 0.0039$). There was however no statistical difference seen with regard to technologists that had served on the Executive of the Institute of Medical Laboratory Science, the Medical Laboratory Technologists' Board or as a convenor of a Special Interest Group.

Seven of the respondents had not heard of the Maintenance of Professional Laboratory Standards (MOLS) Programme. Of these seven, two had first registered after the introduction of the programme in 1995, the other five had been registered for more than ten years. One of these individuals had staff reporting directly to them. None of these individuals had served on the Institute executive, been a Board member or a Special Interest Group convenor. Five of the seven worked the day shift and in a hospital laboratory and five worked less than thirty hours per week.

Programme Participation / Purpose

Fifty-nine (69%) of the eight-five respondents were not actively participating in the MOLS programme. They were asked to comment on why they were not participating. Of the thirty-six responses received to this question, ten (27%) said that it was because the programme was not compulsory, sixteen (45%) required more information about the programme and how it functioned, eight (23%) because it was not relevant to their current work situation and two (6%) because they did not have the support of their employer.

Thirty-eight replies were received to the question regarding the purpose of the MOLS programme. All respondents stated that the purpose of the programme was to maintain and develop the skills and knowledge of medical laboratory technologists and/or to keep up to date with developments in the medical laboratory science field.

The respondents who were actively participating in the MOLS programme were asked if their participation in medical laboratory related educational activities had changed since the introduction of the programme. Three (12%) of twenty-six had first registered after the MOLS programme had begun and therefore were not able to make the comparison. One (4%) individual had had a reduction in their participation in educational activities due to increase in work commitments. Sixteen (62%) had no change in their participation, while six (23%) had increased their participation in educational activities. The reasons for

the increased participation included changes in the work situation that resulted in increased opportunities to attend various activities. Two respondents mentioned greater awareness of the need for continuing education. Also the resurgence of a Special Interest Group had resulted in more suitable courses being available for one individual.

MOLS Credits

Twenty-six (31%) of the eighty-five individuals that responded to the postal questionnaire indicated that they were actively participating in the MOLS programme. These participants were asked to record the number of credits they obtained annually in the four years of the pilot programme and by activity during the same period. Twenty respondents gave the number of credits obtained each year. Eighteen of these had obtained the minimum requirement of 2500 points in the four years. The other two respondents had first registered as a medical laboratory technologist after the programme had begun and hence were not able to obtain credits in the first years of the pilot programme. Twenty-four respondents recorded the number of credits obtained by educational activity. Fifty-six percent of all credits were obtained by routine laboratory work; 29% by attendance at scientific meetings and workshops; 4% from a formal course of study; 5% by giving a lecture or other teaching; 2% by being an examiner or moderator and less than 1% by publications, workshop preparation or other activities. This is shown in Graph 1. Only four respondents stated that they had accumulated the same total number of credits when asked by year and also by activity. For all participants these two totals should have been identical. Fourteen individuals stated that they had obtained more credits for an educational activity than the maximum credits available for that activity.

Resources

Eight (31%) of the twenty-six participants spent up to five days engaged in activities to obtain MOLS credits, excluding those credits received by work practise. A further eight (31%) spent six to ten days, one person (4%) spent between eleven and fifteen days, three (12%) spent sixteen to twenty days and four (15%) spent more than twenty days on educational activities to obtain MOLS credits.

The financial resources used to obtain MOLS credits are illustrated in Figure 2. Twenty-two (85%) of the participants had personally spent up to $1000 on educational activities during the four year programme, with one person spending greater than $2000. On average the respondents' employers than had spent more money on educational activities than the individuals themselves. Twenty-one (81%) had had up to $1500 spent by their employer on educational activities resulting in MOLS programme credits and three (12%) had greater than $2000 spent on those activities.

Support

When asked how supportive their employers were towards their participation in the MOLS programme, all respondents said they had at least some support from their employer. Twenty (77%) recorded that their employer was moderately or very supportive. A similar response was given when asked about the supportiveness of their direct supervisors, with twenty-three (88%) responding that they were moderately or very supportive. One respondent reported that the supervisor was not at all supportive.

When asked about the type of support given, the majority of MOLS programme participants reported that financial assistance and paid leave to attend conferences and seminars had been given to them by their employers. Twenty-two (85%) had received leave with pay and twenty-one (82%) had been given financial assistance. Other support included paid study leave, financial assistance to sit a relevant examination and leave with pay to prepare papers, presentations or workshops. This is shown in Figure 3.

Practise Changes and Programme Benefits

Eleven (42%) of the twenty-six MOLS programme participants reported that their professional practise as a medical laboratory technologist had altered due to their participation in the programme, while fifteen (58%) said that they had not altered their practise as a technologist.

Eight (31%) of the respondents had increased their clinical knowledge and nine (35%) had increased their technical knowledge in issues relating to the discipline they mostly worked in. five (19%) and seven (27%) had increased their clinical and technical knowledge respectively in issues relating to disciplines other than those they mostly worked in. Five (19%) respondents had introduced a new diagnostic test into their laboratory as a result of their participation in the MOLS programme and seven (27%) had introduced a new analytical technique.

When asked if they found their participation in the MOLS programme beneficial, thirteen (50%) said they had; five (19%) said they had not and eight (31%) were unsure. For the thirteen participants that indicated that they received some benefit from the MOLS programme, three stated that the programme had improved their networking with other technologists. Six had increased their clinical and technical knowledge and three respondents had commented how the programme had increased their employers' awareness of the need for continuing education, which had resulted in increased funding and fairer allocation of those funds. Other benefits listed were increased motivation to participate in educational activities, a record of professional development and increased problem solving skills.

Figure 1.

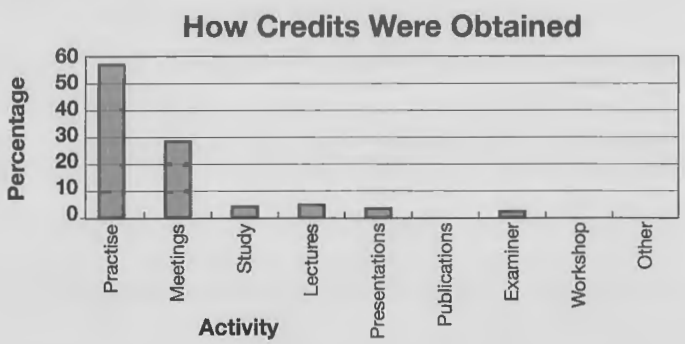


Figure 2.

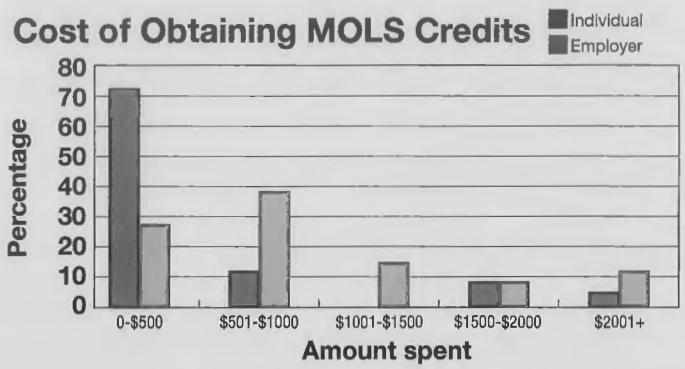
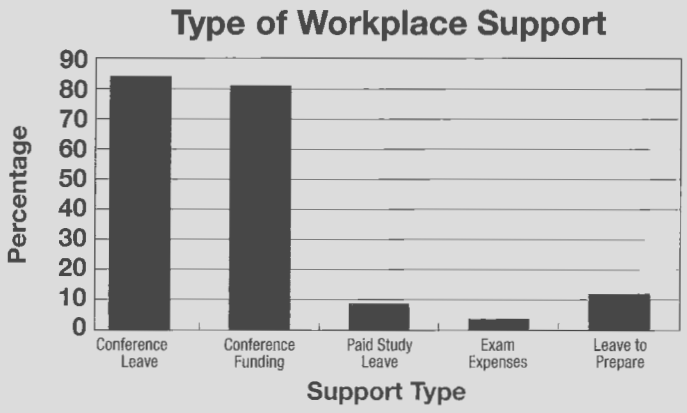


Figure 3.



Problems

The MOLS programme participants were asked to identify any problems they had encountered in their participation of the programme. Eight (31%) had not encountered any problems; ten (38%) were not able to find sufficient time during work hours to participate in activities; four (19%) were not able to find sufficient time out of work hours and three (12%) stated that they had a lack of access to suitable resources. A number of problems were identified by individual respondents, these include the practical difficulties in the credit record keeping of the MOLS programme; the geographical distance from many meetings and workshops and the difficulties in obtaining credits due to working part time.

Compulsory / Voluntary

Respondents were asked if they thought that a programme such as the MOLS programme should be a compulsory requirement of continuing registration as a medical laboratory technologist.

Twenty-one (50%) of the forty-two replies received to this question thought that the programme should be compulsory. Five of these twenty-one replies were from individuals not currently participating in the MOLS programme. Six (14%) thought that programme should not be compulsory, three of these respondents were participating and three were not currently participating in the programme. Fifteen (36%) of the forty-two respondents to this question were unsure, with seven of these being current participants, while eight were not.

The reasons why respondents thought a programme similar to the MOLS programme should be compulsory included:

- the assurance and preservation of high laboratory standards (3 responses)
- to keep up to date with new ideas and relevant knowledge (6 responses)
- the promotion of the medical laboratory profession (3 responses)
- to encourage participation in educational activities (7 responses)
- the ability to assert pressure on employers for financial support for educational activities (3 responses)
- to have a means of measuring the amount of continuing professional development activity engaged in (1 response).

The reasons given why a programme like the MOLS programme should not be compulsory included:

- the limited availability of resources (2 responses)
- the lack of employer support (1 response)
- that participation in educational activities is required by International Accreditation New Zealand (IANZ) as part of the laboratory accreditation process and therefore a separate compulsory programme not required (1 response)
- that technologists know the importance of continuing education and therefore do not need a compulsory programme (1 response)
- it may be difficult to return to the profession after a break (1 response)

Programme Changes

When asked if the MOLS programme should be continued in its present form either on a voluntary or a mandatory basis thirteen (31%) of forty-two respondents said it should. Fourteen (33%) said it should not and sixteen (36%) were unsure.

The respondents were also asked what changes they would like to see to the MOLS programme, nine (19%) of forty-seven respondents said none and thirty-eight (81%) said they would like to see some changes to the programme.

These changes included:

- changes to the way the MOLS credits were allocated (9 responses)
- the inclusion of a wider range of educational activities for which credits can be obtained (12 responses)
- less disadvantage to part time workers in the allocation of credits (8 responses)
- increased information and more feedback on the programme itself, especially with regard to what activities can be used to obtained credits (8 responses)
- less emphasis on laboratory practise, as this disadvantages technologists working in other types of institutions e.g. teaching (2 responses)
- more financial support to attend activities (3 responses)
- increased emphasis on professional development and advancement rather then the maintenance of standards (3 responses)
- a change in the name of the programme (2 responses)
- computerisation of credit recording (1 response)

Discussion

One of the potential problems with the use of a self-administered questionnaire is the issue of a return bias. Individuals may be more motivated to complete and return a questionnaire if the topic is of particular interest to them or they hold certain views regarding the topic. The degree of this return bias is difficult to determine because information regarding the individuals that choose not to participate is, difficult to obtain. In this study, being able to compare some of the demographic characteristics of the respondents to that of the total population of active medical laboratory technologists gives some degree of certainty. This showed that there was no significant return bias with regard to the gender of the respondent, the type of laboratory they worked in, or the discipline they mostly worked in. This data is also similar to the demographic information for Ontario medical laboratory technologists (17).

This information is however not available for other characteristics. The response to one question in particular indicates that there may be a return bias in this study. Forty-one percent (41%) of the total number of respondents had staff reporting directly to them. Despite the fact that technologists are more likely to be in senior positions in a laboratory, often having less qualified technicians reporting to them, this proportion would seem unusually high and may indicate a bias in the study. It is possible that technologists who have staff reporting to them may be more involved in education and development activities, for both themselves and their staff, as it is often a requirement of their senior roles. Therefore they may be more likely to return a questionnaire on this topic.

This study found that only 31% of medical laboratory technologists were actively participating in the MOLS programme. This is considerably less than the 80% participation rate reported in the Annual Report of the Medical Laboratory Technologists Board, 1st July 1998 to 30th

June 1999. This dramatic difference is most likely to be due to the difference in the way the data was collected. In this study the anonymity of the respondents was completely assured and the individuals were asked directly if they were participating in the MOLS programme. The data reported by the Board is obtained from an annual survey where selected individuals are asked to submit details to support MOLS claims. In this instance, anonymity is not seen to be preserved and participation in the programme is assumed by receipt of a completed MOLS return. It is possible that when requested to participate in the annual survey, those selected may retrospectively complete a logbook solely for the purpose of complying with this request and would not consider themselves to be active participants in the MOLS programme. Comparison of the participation rate of the New Zealand MOLS programme with similar programmes is difficult as there is little published data. This information is available for some countries and some health professions, however none these are voluntary programmes, making a direct comparison impossible.

To answer the research question regarding the characteristics of the technologists in the two subgroups of those participating and those not participating in the MOLS programme a number of demographic questions were asked of all respondents. Significant differences were seen in this study between those technologists that reported that they were actively participating in the MOLS programme and those that stated they were not. Technologists were significantly more likely to be participating in the MOLS programme if they had one or more of the following characteristics:

- worked more than twenty hours per week
- usually worked the day shift
- had staff reporting directly to them
- did not usually work in the disciplines of microbiology or virology

It is probable that staff are more likely to participate in the MOLS programme if they perceived that they are likely to be successful in obtaining the minimum credits required. This is supported by the fact that all MOLS programme participants who entered the programme at its inception had achieved the minimum number of credits required for the four-year period. This may explain why technologists working less than twenty hours per week are less likely to participate in the MOLS programme. Due to the structure of the credit allocation, technologists who work less than thirty-five hours per week must attend more educational activities than their full time colleagues in order to obtain the same number of credits. Also day shift staff have a greater opportunity to attend activities during work hours than staff working other shifts. This is because the activities are usually held during the day when more staff are available to cover the absences created by staff attending such activities. This is in contrast to the evening and night shifts, which usually have a smaller number of people working.

It is not clear why staff who work in the microbiology or virology disciplines are less likely to participate in the MOLS programme. There are active Special Interest Groups for these disciplines and recent annual conferences have had similar numbers of papers presented compared to other disciplines. This would imply that a lack of suitable conferences and courses for microbiology and virology technologists to attend is not a contributing factor. This non-participation may be due to a lack of peer support. Staff may be less likely to participate in the MOLS programme if their immediate work mates and supervisors are not participating.

This study found that one of the major reasons why non-MOLS programme participants were not actively involved in the programme was because they needed more information about the programme and how it functioned. This reason was stated by 45% of the non-programme participating questionnaire respondents. It is also clear that many of the participants in the MOLS programme require more information about the programme especially in the area of credit allocation and distribution. Fourteen (54%) participants listed that they had accumulated more credits for an educational activity than the maximum allowable for that activity. Also as only four of twenty-six participants listed the same total number of MOLS programme credits by activity as they did by year over the four year period, it would appear that the recording of the credits is also not clearly understood by most participants. This would imply that there is still much education needed in the area of the practical aspects of the programme. Other reasons given for non-participation included that the MOLS programme was not compulsory (27%) and that it was not relevant to their current work practise (23%).

The type of educational activities that the MOLS programme participants were attending to obtain their MOLS credits found in this research project was similar to that found in a previous survey carried out by the Medical Laboratory Technologists' Board. Fifty-six percent (56%) of credits were obtained by laboratory practise and 29% from conferences and scientific meetings.

Sixty-six percent of the MOLS programme participants had decreased or not changed their involvement in medical laboratory science educational related activities during the time of their participation in the programme. Of the six individuals that had increased their attendance of educational activities, only two stated that it was due to a greater awareness of the need to participate in such activities. This low rate of increase in attendance of educational activities may be due to the fact that the technologists who choose to participate in the MOLS programme were already participating in sufficient activities to maintain their clinical and technical knowledge. An interesting question that needs to be answered is the rate of participation in educational activities of the technologists who are not involved in the MOLS programme.

The MOLS programme participants appeared to have a reasonable level of support from their employers. All but one respondent stated that their employers and direct supervisors were supportive of their participation in the MOLS programme. All had received direct financial support, paid leave or other assistance to attend educational activities. Of the technologists that were not participating in the MOLS programme, only 6% stated that the lack of employer support was a reason for this non-participation. It is also probable that the level of employer support for the MOLS programme participants is adequate, as all that had been involved in the programme for the full four years of the pilot programme had obtained the minimum required credits.
Half of all MOLS programme participants stated that they had received some benefit from participating in the programme. These benefits included increased technical and clinical knowledge, increased motivation and problem solving skills. In addition to this, three respondents stated that their participation in the MOLS programme had increased their employer's awareness and support of such educational activities.

The most commonly encountered problem with participation in the MOLS programme was lack of time to attend activities. This reason was given by over half of the participants. Other problems included lack of access to suitable resources and the geographical distance from various activities.

Fifty percent of the technologists surveyed thought that a MOLS-like programme should be a compulsory requirement for all practicing medical laboratory technologists. This included 62% of the participants and 31% of the non-participants. Eighty-one percent (81%) of the respondents identified changes they would like to see to the MOLS programme. Many of these changes concerned the allocation and distribution of credits and the lack of information and feedback regarding the programme. Forty-five percent (45%) of the non-MOLS programme participants stated that they too needed more information regarding the programme.

In summary the MOLS programme was introduced to ensure medical laboratory technologists participate in ongoing educational activities to maintain professional standards after registration. For those technologists who have chosen to participate in the programme, it is achieving its stated aim. The majority of the participants have accumulated the required minimum number of MOLS credits. However it is possible that these same technologists would be actively involved in educational activities and be motivated to maintain their professional standards whether the MOLS programme existed or not. For the non-MOLS programme participants we can not be so certain. It is probable that many are participating in various educational activities, but without documenting their involvement this is impossible to quantify.

All respondents were able to identify the aims of the MOLS programme despite a reported lack of information regarding the programme. This may be due to the actual name of the programme, which spells out one of the aims, that is, maintenance of laboratory standards. The MOLS programme makes the assumption that participation in educational activities actually helps to maintain laboratory standards. Some measure of competency and laboratory standards needs to be developed so that a comparison can be made to ensure competency has been achieved.

There is a significant need to address some of the problems identified with the programme, particularly in the area of information and feedback to the participants, in order to encourage more active participation in the MOLS programme. In the future, the Medical Laboratory Technologists Board in conjunction with the Institute members will need to address the question of whether the programme should be a mandatory requirement of registration as it is in many other countries. The experience of these other countries and other health care professionals would suggest that this will become a necessity, forced on it by government and others outside the profession. It would be of great advantage to encourage voluntary participation and foster a positive attitude toward continuing education within the profession before such a step was taken.

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Obituary

Alan Forbes Harper 1928 - 2000
Born Invercargill 4/3/1928. Died suddenly Wellington 9/6/2000

Alan was a great servant of the Institute and the profession and will be remembered by many with fondness and the highest regard. To use a cliche: he was a gentleman and a gentle man. In all respects he was a professional.

Born and educated in Southland, we were told at his funeral that his grandparents had immigrated to the Deep South from the Shetland Islands. How great Southland must have seemed although their first endeavour was to grow strawberries on Stewart Island.

After leaving Southland Boys High School, Alan trained as a bacteriologist at Kew Hospital. Later he worked at both Wellington and Palmerston North Hospital Laboratories before being appointed Chief Bacteriologist at Wanganui Hospital. In Wellington and Palmerston North he would have worked with Dr. Joe Mercer and Dr. Thos Pullar, as they were the respective pathologists during his time there. In Wanganui his predecessor was Laurie Buxton, the Institute's first President. How fitting that Alan would follow him as President over thirty years later.

He was first elected to Council as the Wellington Regional Representative in 1971. So began a thirteen-year association with the National Executive: as Regional Representative, Vice president, President, and Immediate Past President. Very few have served the National Body for longer. In addition he was the Institute's nominee to the Medical Laboratory Technologist's Board for nine years, from 1977 to 1985. Alan was an examiner at all levels for many years and continued to moderate papers long after his active involvement with examining ended. He was made a Life Member of the Institute in 1985. Life membership recognised the commitment of this professional to the profession.

Many members will recall his astute and pertinent speeches at the Annual Conferences. Few who knew Alan well will forget his friendliness and sociability in the less formal portions of the Annual get together. This was especially so with his friend from Yorkshire and later Napier, Frank Smith. Those who were present will remember Frank in jest referring to Alan as Judas because Alan wasn't sharing a room with Frank when Alan became President. They had in fact shared rooms at Conference for many years. Of course Frank would agree that Alan would never betray anyone.

Alan was passionate in his desires to improve the educational status of medical technologists. He was tireless in his efforts to see a Batchelor's degree in Medical Laboratory Science. There were many meetings held between Massey University and members of the Institute during the seventies and eighties. He was involved with most of these discussions. Therefore it gave him tremendous pleasure to see the various degree courses come to fruition in the nineties. Without his efforts the profession may still not have gained these educational opportunities. Alan had strong views about the role of the Pathologist and Technologist in Laboratory Medicine. History has proven his view that teamwork and an emphasis on quality in all aspects of the laboratory were correct.
His Scottish heritage was reflected and demonstrated by those traits of honesty, integrity, charity, and humility. He had a great sense of humour. Alan enjoyed gardening, classical music, walking for pleasure, and loved the sounds of the New Zealand bush. He was a Rotarian for over thirty years and participated in many of the projects undertaken by the South Wanganui Rotary Club. Rotarians provided the Guard of Honour at his funeral.

We travelled together to many meetings for over thirty years. He was my mentor and my friend. He will be missed by many. Our sympathy is extended to his wife Catherine, and daughter Ann-Marie and her family in Luxembourg.

Farewell Alan.

Colvin Campbell, Palmerston North

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Commercially available CRP kits.were developed to measure elevated CRP levels well above the normal range: >6mg/l. However, new research has revealed important clinical applications, for CRP measurement at levels within the normal range, This has lead to the development of the new ultra sensitive CRP assay from RANDOX.

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Needle and Syringe Destructor can be used anywhere

A simple manually operated device developed by a British company to dispose of used hypodermic needles and syringes safely and economically can be used anywhere by anyone and overcomes the costs and dangers to health associated with traditional sharps boxes.

Balcan Engineering has redesigned its Hypodermic Needle and Syringe Destructor to meet recommendations of the World Health Organisation making it easier to clean. Other modifications have doubled the -number of needles it is expected to destroy from 100 000 to 206000 before requiring sharpening or any other maintenance.

Needles attached to their syringes are inserted up to the end of the syringe into the toploading hole of the device and the operating handle is pushed downwards. This rotates a cutting disc, which chops the needle into pieces while, with the same action, completely removing the nib from the syringe to render it unusable. The debris falls into a disposable lidded debris pot below that can hold the remains of 250 green hubbed needles.

There is no risk of contaminants or aerosols escaping into the atmosphere because the cutting chamber is automatically sealed during operation.

By removing both the needle and nib from syringes, it allows considerable economies in disposal costs to be achieved because, without the needle attached, a syringe is no longer considered to be a sharp and therefore does not have to be disposed of in expensive sharps boxes, which can be filled very quickly when needles remain attached to them. Instead, they can be placed in normal clinical waste sacks along with such waste, which is a very much cheaper method of sending them for incineration.

The main markets for the Destructor are obviously the medical and scientific markets, but there is considerable other interest from industry in general where needles are used for lubricating instruments and other purposes. While these are normally put into sharps boxes, there is no need for this because they are not contaminated with body fluids, so once they have been destroyed they can be disposed of as ordinary waste. Similarly, local authorities that have to reclaim premises previously occupied by drug users, find the Destructor of use because contaminated needles and syringes left behind can be destroyed as they are collected, overcoming the problems of keeping sharps boxes secure to prevent them being stolen and needles reused.

The Destructor has been selected by the United Kingdom Design Council as a Millennium Product, for which there were more than 5000 submissions and only 1012 products chosen. Balcan Engineering achieved the prestigious status of gaining three awards.

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Balcan Engineering Ltd, 41 Witham Road,
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Company contact: John Rinfret. Telephone: +44 1526 353075;
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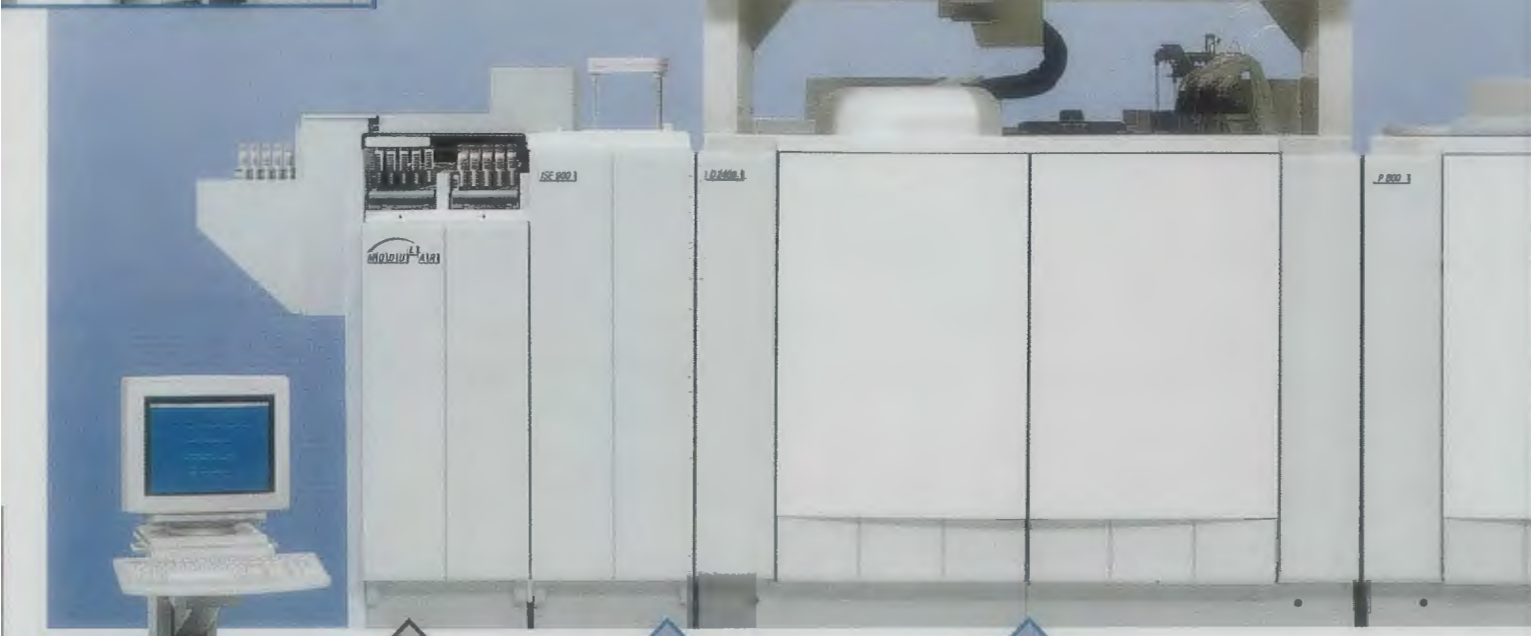

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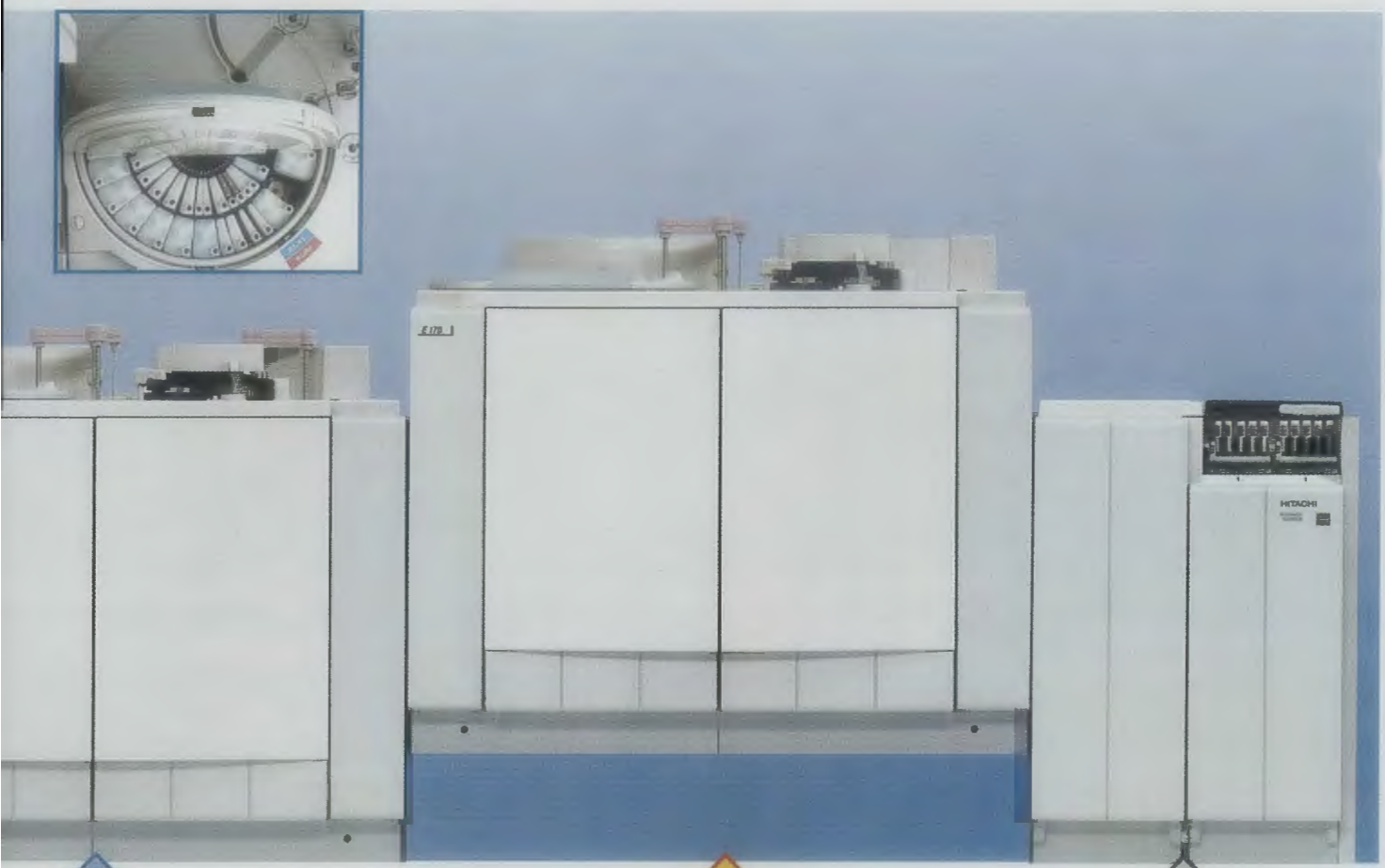

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Book Review

Selection of basic laboratory equipment for laboratories with limited resources.
Warren L. Johns and Mohamed AL EI-Nageh
WHO Regional Publications, Eastern Mediterranean -Series No. 17,2000
World Health Organisation Regional Office for the Eastern Mediterranean. ISBN 92-9021-245-4

This book is the culmination of several years' work by the co-authors Warren Johns and Mohamed El-Nageh in emergency and disaster areas in underdeveloped countries. These situations have been far removed from manufacturers and suppliers. Here is a consumer's guide to obtaining appropriate equipment suitable for the laboratory under all circumstances.

The book is divided into *three sections,*

- choosing and buying laboratory equipment
- energy requirements for laboratory equipment
- information annexes

With chapter headings in the *first section* such as:

1. Choosing and buying laboratory equipment,
2. The buying business,
3. Common consumer problems,
4. Equipment receipt and maintenance,
5. Buying secondhand laboratory equipment,
6. Choosing minor equipment and consumables, and
7. Buyer's guide to choosing major equipment for intermediate and peripheral laboratories.

There is a wealth of information and guidance for the laboratory technologist.

Clinical and hospital administration staff can be guided by these chapters in the purchase of equipment for clinics and at bedside testing.

In intermediate and peripheral laboratories the technologists are able to look at their own laboratory facilities and choose what they think may best suit their needs.

Chapter 7 the last in this section and the most important one in the book contains equipment information sheets which enables a dialogue to be set up between the technologist and supplier to ensure that the most appropriate and safest equipment is bought.

In conjunction with this chapter, use must be made of Annex I at the end of the book. Herein are equipment data specification sheets where the buyer can give companies or agents a clear idea of the environment in which the equipment is to be used as well as indicating what will possibly be the most suitable item.

On the return of quotations based on the above specifications the technologist is able to assess and compare the suitability and cost of the equipment available,

Chapter 3 on consumer problems contains information regarding consumer protection and,how to talk to suppliers about problems arising from purchase of faulty equipment.

Section 2 is devoted completely to energy requirements for laboratories and this contains it seems all that you need to know about energy supplies where there is no main power supply system.

Detailed information is given about the types of batteries available for use in battery powered equipment to be used either in remote areas or in emergencies and disasters.

In certain areas the use of solar energy, wind turbines, micro hydroelectric generators and petrol or diesel generators in combination with other sources is discussed.

Excellent information is given about solar energy systems from the advantages and disadvantages of such systems to the selection, running and maintenance of a solar energy supply. Obviously solar systems are particularly applicable in certain countries. Again it is stressed that the dialogue between user and supplier is most important so that the correct system is installed.

Section 3 is a mine of information and contains 10 annexes bringing together details on how to contact manufacturers and distributors of equipment and consurnables, reagents and chemicals. Sample order, quotation, shipping and equipment record forms are found in Annex 2. Contained in Annex 3 are particularly pertinent comments on Equipment donation guidelines.

The following quote is worth noting:-"The donor and the recipient must get together as equal partners to work out how the effort and goodwill involved in making a donation can be put to best use. Recipients should have a clear policy on their equipment requirements, which should be known to their staff as well as their donors. The right to give and receive a no, thankyou should be used, appreciated and accepted."

This quotation summarizes the unportance of ensuring that suitable and appropriate equipment is donated to areas in need,

Annex 6 headed Laboratory equipment supply and Annex 7 Information and materials both contain details about non-profit and low-profit organizations supplying secondhand, reconditioned or new scientific and laboratory equipment.

These organizations are to be found in Canada, Germany, New Zealand, The Netherlands, United Kingdom, and United States of America.

Overall this book deserves a place on the bookshelf of all technologists involved in the purchase of equipment for laboratories whether they be in developed or underdeveloped countries. Equally a place could be found for this book in the office of manufacturers and suppliers to enhance their customer service.

Perhaps the publishers should give consideration to the possibility of translation to other languages thus allowing a wider use by non-English speaking laboratory staff.

Reviewed by Gilbert Rose.

This book is available from the WHO sales agent, Medical Books, 8 Park Ave, Grafton, Auckland. Price $NZ 20.00.

Abstracts from articles in the *Australian Journal of Medical Science,* the official publication of the Australian Institute of Medical Scientists.

Adams MJ, Oostryck. **Tissue factor pathway inhibitor: regulator of the tissue factor pathway of coagulation and a future antithrombotic agent? (Review).** *Aust J Med Sci 2000* 21(1): 2-9.

Abstract: Tissue factor pathway inhibitor (TFPI) is a "rediscovered" inhibitor of tissue factor mediated coagulation that has a central role in the modern hypothesis of coagulation. The regulatory role of this inhibitor has redefined the classical extrinsic and intrinsic pathways of coagulation and helps to explain why haemophiliacs bleed. Comprehensive investigations have been performed during the last 15 years to elucidate the structure, distribution, function and physiological characteristics of TFPI. More recent work has focussed on the therapeutic potential of TFPI as an antithrombotic agent. Augmentation of TFPI levels may provide treatment for thrombotic disorders such as disseminated intravascular coagulation and deep vein thrombosis. Full length and truncated forms of TFPI molecules are also being considered as antithrombotic agents. These have been used in a number of animal models with initial results demonstrating the alleviation of thrombotic tendenciesl. Trials are currently ongoing.

Isouard G. **Improved emergency department specimen handling time using a continuous quality improvement approach.** *Aust J Med Sci 2000* (1): 10-5.

Abstract: A study was undertaken to reduce the patient specimen handling time involved in the period from the blood collection phase in the Emergency Department to the delivery of the specimen in the Pathology Department of the hospital. Through the use of continuous quality improvement (CQI), a team approach was introduced that involved the systematic analysis of the laboratory test ordering, blood collection, specimen pickup and transport mechanisms. The improvement initiatives focussed on developing strategies for improving current processes, and included the development of new policies for specimen handling and transport, the establishment of a policy for priority setting in the transport process, introduction of education programs, the recognition of the need to improve communication between the emergency department and pathology department staff, and the establishment of a system that seeks to satisfy pathology service user requirements. Following the introduction of the CQI approach, there was a statistically significant improvement to the specimen handling time achieved. The CQI specimen delivery times were all within the acceptable user requirement range of 30 minutes.

O,Brien J, George N, Faoagali J. **Detection of *Salmonella typhimurium* in a wound infection.** *Aust J Med Sci 2000* (2): 4-6.

Abstract: A strain of *Salmonella typhimurium* was isolated from a surgical wound following drainage of a haematoma on the knee. This organism was present in a mixed culture with another Gram negative organism, *Enterobacter cloacae.* Initially the wound culture was reported as "moderate growth of mixed coliforms consistent with colonisation". Due to ongoing wound discharge, full identification of the two Gram negative isolates was undertaken. Standard laboratory procedures for culture of wound swabs do not routinely include media that would allow the differentiation of *Salmonella* from the other *Enterobactericeae.* Substitution of the MacConkey Agar medium with Xylose Desoxycholate Agar would allow rapid presumptive identification of most *Salmonella* strains from extra-intestinal sites of infection.

Angel LA, Harden TJ, McKenzie GH, Moriarty HT. **Evolution of medical laboratory science in Australia: an educationalist perspective.** *Aust J Med Sci 2000* (2): 8-14.

Abstract: This paper reviews the changes which have occurred in medical laboratory science over the last 25 years. It examines the role of universities in the education of the profession. Using Charles Sturt University as a model it provides an historical overview of course offerings over that period. It describes the evolution of the course content and in particular this paper evaluates those academic changes and assesses the driving forces behind them. The changes can be classified as those which are reactive and made in response to industry requirements, and those which can be considered pro-active and made after academic judgment of relevant scientific advances. There are also circumstantial changes made in response to institutional pressures which have an impact on medical laboratory science courses. Such evolutionary changes in medical science programs flow into the pathology industry and hence prepare graduates for leadership in health science.

Siebers RW. **The accuracy of references in the Australian Journal of Medical Science.** *Aust J Med Sci 2000* (2): 16-8.

Abstract: Previous studies have shown high reference error rates in biomedical journals. This study determined the reference error rate in articles published during 1998 in the *Australian Journal of Medical Science.* References were checked with Medline, and errors recorded in the six main elements of a reference (authors, title, journal, year, volume, and page numbers). Four hundred and sixty-one out of 617 references that were Medline listed contained one or more errors, giving a reference error rate of 74.7%. The most frequent errors were author(s) name(s), followed by the journal and title (676, 154, and 90 errors respectively). Seventy-three errors were deemed as major, making it difficult to retreive the cited article. The reference error rate in articles published in the *Australian Journal of Medical Science* is very high, and is preventable. Greater emphasis and responsibility should be placed on authors, and perhaps on Editors and referees, to ensure accuracy of references in published articles.

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A Review of Current Concepts of the Rh Blood Group System

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Abstract
The Rh blood group system is clinically significant and serologically complex. Molecular analysis is finally bringing insights into the cellular and genetic basis of Rh.

Rh antigens are carried on two non-glycosylated, 416 amino-acid polypeptides, which loop through the red cell membrane. One carries the D epitopes and the other the CcEe antigens. These occur in a tetrameric complex of two Rh polypeptides with two 50kD glycoproteins, in association with Glycophorin B, CD47, LW and other proteins.

The polypeptides are encoded by two closely linked and highly homologous genes on chromosome 1. The *RHCE* gene has four common alleles, giving rise to the Ce, ce, cE and CE haplotypes. The *RHD* gene codes for all nine (or thirty) D epitopes, except in the rare D variant phenotypes arising from gene conversions or point mutations. The Caucasian D-negative phenotype arises from a deletion of the *RHD* gene (although this is not invariably so in non-Caucasians). The DNA sequence of Rh genes and the amino acid sequences of the resulting polypeptides have now been defined for most of the common and several of the rare phenotypes. Some of these, including several D variants, CcEe polymorphisms and deletion phenotypes, are detailed in the text.

Rare inheritance of a mutated *RH50* gene (which normally codes for the Rh glycoprotein), results in an absence or great reduction of the entire multi-subunit protein complex, and therefore of detectable Rh antigens. This is recognised as the modifier type of Rh deficiency syndrome. The amorphic type appears to arise from silent or deleted alleles at both *RHD* and *RHCE* loci.

Molecular insights into the Rh genes and their membrane protein products continue to clarify our concepts of the Rh blood group system. However, even such fundamental questions as the function of Rh proteins and the reason D is so immunogenic have not yet been answered.

Keywords
Rh blood group system, antigen, gene, molecular

Introduction
Blood group serologists have known of the existence and importance of the Rh blood group system for nearly sixty years. Because of the immunogenicity of its antigens, it is the second most clinically significant blood group system, after the ABO system. Almost from the beginning, the complexity of the Rh blood group system was apparent and provoked controversy.

In the half century following Levine and Stetson's 1939 discovery (1), a plethora of investigations and publications added to the collective knowledge of Rh antigens and speculated about their genetic origins. By the mid-1990s there were forty-eight identified Rh antigens (numbered RH1 to RH51 with six obsolete (2)); three systems of nomenclature in current use; and as much debate about the genetic basis of the Rh antigens as there had been in the days of the transatlantic debate by Wiener (in the United States of America) and Fisher & Race (in Britain).

It was not until Moore et al (3) utilised the new SDS-PAGE technique in 1982 and then the developing technology of polymerase chain reaction (PCR) was used to clone Rh genes in the early 1990s by independent groups in Paris (4) and Bristol (5), that definitive and logical answers to some fundamental questions about the basis of the observable serological reactions began to emerge.

The Rh protein complex
The Rh antigen is a protein embedded in the red cell membrane. It does not occur on other types of cells in the body. Proteins are chains of, or more complex structures involving, amino acids. In their simplest form they are known as polypeptides. Rh polypeptides are very unusual in that they have no carbohydrate in the molecule. (Glycosylation is a normal part of the processing of a membrane protein). However, the Rh polypeptide exists in the cell membrane closely associated with other molecules. The core is a tetrameric complex comprising two Rh polypeptides and two Rh glycoprotein molecules. There are likely to be multiple contact sites between the polypeptide and glycoprotein molecules involved in assembly of the multisubunit Rh protein structures, including both N-terminal (6) and C-terminal ends (7).

Glycophorin B (which carries the S, s and U antigens) appears to be closely associated with, or to interact with, the multi-subunit Rh protein complex, although it is genetically independent of Rh, being coded for at a locus on chromosome 4 (2). It is of note that equal numbers of Glycophorin B, Rh polypeptide and Rh glycoprotein molecules occur in normal red cell membranes. It seems likely that Glycophorin B accelerates the movement of newly synthesised Rh glycoprotein to the cell surface.

The LW glycoprotein also appears to be part of the Rh protein complex although it is also genetically independent of Rh, being coded for by a gene on chromosome 19 (2). LW exhibits a phenotypic relationship with Rh serologically, in that D-positive cells have a higher expression of LW than D-negative cells (8). However LW(a-b-) cells express normal Rh antigens, indicating that LW is not essential for assembly of the Rh complex, nor is Rh a precursor of LW (9).

The serologic activity of Rh proteins depends on the presence of phospholipid. The phospholipid bilayer of the cell membrane is abnormal in Rh null red cells and it appears that Rh polypeptides probably require specific flanking phospholipid in order to attain their proper conformation on the membrane surface. Fatty acylation of the Rh protein is probably related to cysteine residues on cytoplasmic loops of the protein. The Rh protein complex may be indirectly linked to the cytoskeleton (11).

The Rh protein multi-subunit complex has a complex three-dimensional shape with specific surfaces available for antibody binding. The immunological hot spot on the folded molecule where the antibody

binds is the epitope. The region of contact between the antibody and antigen may be four to five amino acids (12). This is significant, since the polymorphisms are often defined as a single amino acid substitution in the polypeptide chain, (which then alters the entire epitope and its binding ability). Because the shape and presentation of the Rh complex is influenced by folding of the molecule, the site of the epitope need not necessarily be the site of any polymorphism.

CD47 is a well-characterised protein which occurs on many tissues throughout the body. It is associated with integrin, and appears to have a function related to structural integrity of the cell. It is coded for by a gene on chromosome 3. Its function on red cells is unclear, but it occurs on red cells in numbers of about one molecule per tetramer of Rh protein and is also thought to be associated with the Rh protein complex as its expression is reduced on Rh null cells (regardless of the genetic background) (7). Since CD47 genes are carried on chromosome 3, this molecule is also genetically independent of Rh (2).

Other proteins lacking in Rh null cells such as those carrying the Fy5 and Duclos antigens may also be part of or associated with the Rh membrane complex (10) although their role is less clear.

Rh polypeptides

The Rh polypeptides comprise 417 amino acid residues in a long snake-like molecule which loops in and out of the red cell membrane (11). The N-terminal methionine residue, which is the messenger RNA translation initiation signal, is cleaved after translation, leaving 416 amino acids on the mature protein with serine at the N-terminus. It has a molecular weight of 45 kDa . There are six extracellular loops and twelve membrane-spanning domains. Both N-terminal and C-terminal ends are intracellular.

The Rh D polypeptide defines the D antigen. The Rh CE polypeptide occurs in four major allelic forms that specify the ce, cE, Ce or CE antigens. In spite of early evidence suggesting two non-identical polypeptides for C/c and E/e, it is now clear that both C/c and E/e antigen specificities arise from the one polypeptide (13).

The D and CE polypeptides are highly homologous; they have the same number of amino acids and the same structure. They differ by 36 amino acids but the N-terminal and C-terminal regions are well conserved. Only seven extracellular amino acids are different in D and CE polypeptides, but other intracellular differences may affect protein configuration and therefore epitope expression.

Rh glycoproteins

The glycoproteins which co-precipitate with the Rh polypeptides are genetically independent of Rh. They are 50 or more kDa in size, and known as the Rh50 glycoproteins.The Rh glycoproteins carry ABO determinants on their carbohydrate portions (2).

The Rh 50 glycoprotein has an amino acid sequence and membrane topology which has similarities to that of the Rh polypeptides (14). It has 409 amino acids, with twelve membrane spanning domains, and both N-terminal and C-terminal domains are intracellular (15). Like the Rh polypeptides, the Rh glycoprotein is only expressed on red cell lines (16).

The Rh glycoproteins are critical for the expression of Rh polypeptides as antigens. When the Rh glycoproteins are absent, in Rh null cells, the Rh antigen is not expressed. The C-terminal region is important in the protein-protein interactions involved in forming the Rh complex (17). The Rh glycoprotein may play a role in the assembly or transport of the Rh membrane complex to the red cell surface (18).

Genes

The Fisher-Race concept of three closely linked loci (19) was based on observable reactions of anti-C, anti-c, anti-D and anti-E. Although it is easy to understand and to use in the routine Immunohaematology laboratory, its validity had always been debated. Almost simultaneously, Wiener proposed an alternative theory of multiple alleles at a single locus (20), which would code for a single "agglutinogen" composed of several blood group "factors" or serological determinants. Some of the shortcomings of Fisher's theory soon became apparent. For example rare individuals were discovered with a haplotype that produced neither E nor e but apparently did produce ce and therefore could not accurately be described as *Dc-* . Wiener's theory coped more easily with the increasing complexity brought by new findings, including the concept of epitopes as part of an antigen. However, biochemical analysis of the Rh polypeptides in the early 1980s (3) which indicated that the D, c and E antigens are carried on different polypeptides seemed to confirm Fisher's theory of three separate genes.

In 1986, Tippett (21) proposed a new model comprising two Rh genes, one encoding D and the other encoding the CcEe antigens. This seems logical given such hints as the existence of compound antigens involving C/c and E/e antigens (such as anti-f and anti-Rh) but not involving D. A few years ago molecular analyses of the Rh genes (5) supported the two gene model, and apparently definitive proof has now been published (22).

The Rh locus is now considered to comprise two very similar genes, known as *RHD* gene and *RHCE* gene, which collectively may be known as the *RH30* genes. The *RHD* gene encodes for the D polypeptide and has no allele; while *RHCE* is the name given collectively to alleles at the locus which codes for the polypeptide which carries the C or c and E or e antigens. The *RHCE* gene has four main alleles - *Ce, CE, ce* and *cE*.

The *RH30* genes are found in tandem on the short arm of chromosome 1, between the positions 1p34.3 and 1p36.13. The *RHD* gene is located 3' to the *RHCE* gene. Each has ten exons, ranging in size from 72 to 247 bp, and nine introns of various sizes, spread over a genomic sequence of approximately 75kb (23).

There are only 29 nucleotide differences between *RHCE* and *RHD* over both exons and introns (i.e. 98% homology). Most of these differences occur in exons 4, 5 and 7. Exons 1 and 2 of the CE gene are involved in the determination of C or c; exon 5 encodes the determination of E or e. Because the *RHCE* and *RHD* genes are tightly linked they are best described as a two-gene locus.

Using exon-specific probes on a DNA sample (24), it is at last possible to distinguish *in vitro* a sample from a homozygous *DD* individual from a heterozygote.

The Rh 50 glycoproteins are genetically independent of the *RH30* genes, and are coded for by genes on chromosome 6 at between 6p11 to 21.1, probably at 6p12 (25). Despite their location on different chromosomes, the *RH50* genes (also referred to as *RHAG*) are very similar to the *RH30* genes, having ten exons whose size and exon/intron junctions are notably homologous compared to the *RH30* genes. In evolutionary terms, the *RH50* gene is considered to be the original gene (26). Following duplication and differentiation of the *RH30* from the *RH50* genes about 300 million years ago, *RH50* evolved about 2.6 times more slowly than *RH30*, a finding which is considered to indicate the functional significance of the Rh50 glycoproteins in widely varying species (27). The duplication event producing the RHD and RHCE genes occurred only about 5 million years ago.

D-positive / D-negative polymorphism

The D-negative phenotypes (rr, r'r, r"r, $r^{y}r$) are widespread in white and black populations but rare in other races. They arise from a complete lack of the entire D polypeptide. The total number of Rh protein molecules on each cell is relatively constant (28) but in D-negative individuals the Rh protein tetramers comprise only CE polypeptides with Rh

glycoprotein. This explains the serological observation that no "anti-d" has ever been found.

Early investigations, using primarily Caucasian samples, indicated that the lack of D polypeptide was due to a complete deletion of the *RHD* gene (5). This is the major cause of the D-negative phenotype in whites, but is not always the case (29). Some individuals with a D-negative phenotype carry portions of the *RHD* gene, and some carry an intact but dysfunctional gene (30). Notably in Japanese (31), in Chinese (32), and in Blacks (33), D-negative individuals may have at least some portion of a detectable *RHD* gene. In Japanese, some of this finding is correlated with the D_{ei} phenotype, in which cells are not agglutinated by anti-D, even by antiglobulin technique, but will adsorb and elute anti-D (34). Subtle changes in *RHD*, such as mutations which result in nonsense translations, splicing defects, the introduction of a stop codon or small deletions causing a frame-shift, may account for those D-negatives who carry an apparently intact *RHD* gene.

PCR typing assays applicable for use in the clinical management of haemolytic disease of the newborn commonly rely on the complete absence of the *RHD* gene in D-negative individuals. Although this is usually the case in Caucasians, the existence of rare individuals with rearranged *RHD* genes whose phenotypes do not match that predicted by PCR analysis warns of the necessity for using the amplification of at least two different regions of the *RHD* gene. The so-called "multiplex" PCR techniques use amplification of several regions simultaneously (35). The ethnic background of the individuals should also be considered when designing these test systems and interpreting the results.

D variants or partial D antigens

Using monoclonal antibodies, 30 epitopes of the D antigen have been defined (36) although for many purposes the less refined system of nine epitopes is commonly used. Red cells from D variant (more correctly called "partial D") individuals lack one or more of these epitopes. Individuals with partial D antigens may produce alloantibodies to the D epitopes which they lack. The alterations in Rh polypeptide which results in the partial D phenotype may also result in the expression of a distinctive low incidence antigen.

The partial D phenotypes were categorised using serological reactions into six major categories, named D^{II} to D^{VII} (D^{I} is obsolete). Today characterisation of partial D is performed using monoclonal antibodies or molecular analysis.

Partial D phenotypes may arise from two types of genetic backgrounds - either from gene conversion (resulting in a hybrid *RHD-RHCE-RHD* gene) or from point mutations (35). Although those with a hybrid background are more numerous, partial D phenotypes arising from point mutations in the *RHD* gene are particularly useful studying the involvement of various polypeptide domains in epitope expression. Examples of partial D phenotypes arising from point mutations are:

D^{VII}	a point mutation at codon 110 (Leu to Pro) (37)
DNU	Gly 353 Arg (37)
D^{II}	Ala 354 Asp (37)
DHR	Arg 229 Lys (38)

The exact amino acid abnormality has been determined for each of the categories, and in all cases it involves the extracellular loops of the Rh protein chain. Useful summaries of the genetic basis of partial D phenotypes have been published in 1997 (30) and 1998 (35). Further complexities continue to be added (39), which highlight the heterogeneity of the partial D phenotypes and their origin.

This correlation between observable serological reactions and information gained by molecular analysis of genetic material is providing valuable insight into the mapping of the D epitopes and the requirements for their presentation. It is clear that there is not room on the molecule for more than about eight discrete epitopes, so there must be considerable overlap.Displacing the idea of several separate epitopes is a model that is more topographic in nature, with the fit of the antibody to antigen being likened to a footprint (40) or basic framework of residues. It is the number and arrangement of contact residues on the D polypeptides which define the D epitopes. The epitopes are not spatially distinct entities, and their absolute number is merely the number of different cell types than can be differentiated serologically.

D category VI (D^{VI}) is the clinically most important partial D phenotype since D^{VI} individuals commonly produce alloanti-D antibodies. Severe cases of haemolytic disease of the newborn have occurred in D-positive babies born to D^{VI} mothers with alloanti-D. Known D^{VI} individuals should be transfused with D-negative blood (although this is not necessarily true for all individuals with partial or weak D antigens). D^{VI} is reported to comprise 6-10% of partial D phenotypes identified. D^{VI} is not a single entity, but has been shown by DNA sequencing to comprise at least three types, with distinct RHD alleles which arose independently (41).

Weak D

Some cells which carry the Rh D antigen, react more weakly than normal with anti-D reagents. This phenotype, originally called D^{u}, may arise from three genetic backgrounds. Occasional so-called "high grade D^{u}" samples may arise from the suppressive effects of the *Ce* haplotype in trans position acting on a normal *RHD* allele. Occasionally the weak reaction may be a reflection of the reactivity of a partial D phenotype with the antisera in use. Partial D phenotypes do not express all of the epitopes of the D antigen, and may exhibit a variety of reactivity when tested with different "anti-D" antisera.

Most of the weak D reactions appear to have a genetic background which defines a weaker expression of an apparently normal D antigen. Early molecular analysis of the genes of weak D phenotypes appeared to show a normal sequence but reduced expression of RhD mRNA (42). This suggested a defect or regulation of transcription of the gene or an unidentified suppressor gene, resulting in normal Rh D polypeptides but simply fewer copies per cell. However, extensive work from Germany (43) showed that weak D cells do in fact have abnormal Rh D polypeptides. The authors defined (on the basis of nucleotide changes in the DNA) and categorised 16 different molecular types of Weak D.

In contrast to the D variants, the amino acid substitutions which define the weak D polypeptides occur in the trans-membrane or intracellular sections of the protein. These substitutions are clustered in four regions of the polypeptide. By far the most common was a T-to-G transversion at nucleotide 809 resulting in the change from valine at the transmembrane amino acid position 270 to glycine (43). Thus gene sequencing is bringing the ability to accurately identify and classify samples which would react differently in serological tests depending on the affinity of the anti-D reagents used.

C/c and E/e polymorphisms

Gene analysis indicated that the basis of specificity for C or c results from four amino acid differences, at positions 16, 60, 68 and 103 (44). However, more recent work has shown that only the serine to proline substitution at position 103 (on the second extracellular loop) is strictly correlated with the C/c specificity (29). Nevertheless, the presence of cysteine at position 16 could modulate C antigen reactivity (45).

The E/e polymorphism is determined by a single amino acid substitution arising from exon 5 at position 226 , proline for E and alanine for e (44). This would be in the fourth extracellular loop of the CE polypep-

tide (13). Expression of the CcEe antigens must depend on conformation of the protein, since the RhD polypeptide carries serine at position 103 and alanine at position 226 but does not cross-react with anti-C or anti-E. (However, see the next section, on the G antigen).

The CE polypeptide does not appear to be as mosaic as the D antigen, but some variability occurs. The molecular basis for some of these variants (R^N, $R_O{}^{Har}$, and r^G) has been determined as the formation of a hybrid Rh gene (46). The V and VS antigens, which occur commonly in blacks but only rarely in whites, have been shown to result from genes derived from a hybrid of *RHCE* and *RHD* (47)(48). In contrast, point mutations appear to account for other unusual RhCE antigens: C^W is characterised by having arginine instead of glycine at position 41, and C^X has threonine instead of alanine at position 36 (49).

The G antigen

The G antigen was first described in 1958 as an antigen present on almost all cells that carry either D or C, but usually not present on cells that carry neither (50).

The Rh D and Rh CE polypeptides differ by only 36 amino acids. The difference between a polypeptide carrying the C antigen and that carrying the c antigen is only four amino acids. Three of the four amino acids that distinguish C from c (Ile-60, Ser-68 and Ser-103) are also found on the D polypeptide. Molecular analysis of samples from the rare ccDEe G- and ccEe G+ phenotypes (51) showed that the serine residue at position 103 defines the G antigen. The c polypeptide has proline at 103. Replacement of the serine at position 103 with proline by a gene which would otherwise code for the D antigen leads to G negativity, whereas the presence of serine replacing proline led to the G positivity in a ccEe G+ individual. The D variant category IIIb, which is G-, also has a change in the exon which codes for the amino acid at position 103 (52).

Rh null

Rh null is a related group of phenotypes in which none of the common Rh antigens are expressed. The entire Rh multi-subunit complex, including Rh polypeptides, Rh 50 glycoproteins, CD47, LW and Glycophorin B (which carries the S, s and U antigens), is absent or greatly reduced in Rh null red cells (11). Rh null individuals exhibit a clinical syndrome called the Rh-deficiency syndrome, characterised by a mild to moderate chronic haemolytic anaemia due to the shortened life span of the red cells. At the cellular level, Rh deficient red cells exhibit stomatocytosis, spherocytosis, increased osmotic fragility, altered cation transport and abnormal phospholipid organisation (53).

Family studies show that the Rh null phenotype may arise from two genetic backgrounds. The "regulator" or "modifier" type is inherited independently of the Rh genes and results from homozygous autosomal inheritance of an independent defective suppressor gene. This gene, called X^Or, is responsible for the phenotypic suppression of Rh antigen expression on the red cells in spite of the presence of normal genes which code for Rh polypeptides CE and/or D (25). The X^Or gene is a mutational allele of the *RH50* gene which codes for Rh glycoprotein (54). Analysis of the RH50 gene in unrelated Rh null individuals reveals a heterogeneous spectrum of mutations (46). At least six different mutant alleles of the *RH50* gene have been determined (54).

Family studies of most cases of Rh null show homozygosity of a given mutation due to consanguinity (55). However, this is not always the case and rare individuals may inherit different defective genes from each parent. One individual studied (54), carried one mutant *RH50* allele with a single nucleotide substitution (inherited maternally) plus a different transcriptionally silent *RH50* allele (inherited paternally). Another case (55) also revealed two different but defective *RH50* genes, one a splice donor mutation and one missense mutation, in an individual without any known consanguineous family background. In the regulator type of Rh null, in which the *RH50* gene is altered but the *RH30* genes are normal, both Rh polypeptides and Rh glycoproteins are lacking at the cell surface (53).

The "amorphic" type is inherited as a recessive trait as a result of a silent (or perhaps deleted) gene complex at the *RH30* locus, and is much rare than the regulator type. In the amorph type of Rh null, the genes for Rh 50 glycoproteins and CD47 are normal (53). Clearly both *RHD* and *RHCE* genes on the same chromosome must be inactivated for there to be no detectable Rh polypeptides. Partly because of the rarity of the amorph type of Rh null, few examples have been analysed to determine their molecular defects. The first published example of an amorph defect at *RH30* (7) revealed a deletion in exon 7 of the *RHCE* gene, in addition to complete deletion of the *RHD* gene. A recent molecular study (53) of samples from two unrelated Rh null individuals revealed a homozygosity for a silent allele at the *RH30* locus arising from two types of mutation affecting the *RHCE* gene. One was caused by a splice-site mutation in intron 4 of a dce gene; the other had a mutation in exon 7 which introduced a frameshift. Unlike the regulator type of Rh null, the amorph types, with normal RH50 genes but altered RH30 genes, have some detectable Rh glycoprotein in the cell membrane (but no detectable Rh polypeptide).

In a slightly different phenotypic condition, ^{Rh} mod, the Rh antigens are barely detectable. Given the variety of genetic defects which result in the Rh null phenotype, and the identification of two different single nucleotide changes in the RH50 gene of two different examples of Rh mod (54) (56), it seems likely that a range of substitutions along the RH50 gene may be responsible for a range of modulation of the Rh antigens.

The Function of Rh proteins

Over the years the Rh blood group system has become established as an attractive model to study owing to its clinical diversity and its biological relevance to the structure and function of cell membranes, but the exact function of the Rh proteins is not yet known.

The Rh protein complex is essential for red cell membrane architecture, as evidenced by the structural and survival defects of Rh null red cells. Although this was the first indication that a blood group antigen could play a role in the physiology of the red cell membrane, complete understanding of the interactions of the Rh proteins in the cell architecture is still unclear. LW(a-b-) cells and those lacking Glycophorin B have normal cell morphology and physiology (7), indicating that these proteins, although related to the Rh protein complex, do not have the same functional role.

The observation of proteins almost identical to Rh glycoproteins in animals as different to humans as a marine sponge (57) and the worm *Caenorhabditis elegans* (55) reinforces the hypothesis that the Rh complex has an essential (although as yet unidentified) function. This function is unrelated to antigen presentation, but is critical to the architecture and physiology of the red cell membrane. The acidic amino acid residues Glu21, Asp95, Glu146 and Glu340 which occur in the transmembrane sections of the CE polypeptide, and Glu13 and Glu146 in the Rh glycoprotein, may indicate that these proteins are involved in ion transport. Of interest is the close relationship of human Rh30 and Rh50 proteins to a large family of genes coding for ammonia transporters (58).

Remaining challenges.

Burgeoning knowledge about the genetic basis of the Rh groups is already finding clinical application. With some caution regarding test construction and interpretation, it is now possible to determine Rh blood type by applying PCR techniques to DNA (59). This technology is

of course being used in a research setting (60). The ability to apply this technique to small samples of fetal material from amniotic fluid (61) and more recently to fetal DNA isolated from maternal plasma (62) has the potential to bring increased safety to babies of Rh immunised mothers. For this technology to find widespread clinical application, the major requirement yet to be fulfilled is for it to become more cost efficient.

Despite the increasing amount of information about Rh at a molecular level, there remain unanswered questions about Rh antigen expression and the structure and function of the Rh proteins. Little is known about the exact interaction of the Rh 30 polypeptides, the Rh 50 glycoproteins and the other proteins involved in the multi-subunit protein complex, or the factors which dictate that interaction during their assembly in the red cell membrane. The detailed locus structure of the Rh genes, including the intergenic distance and transcriptional orientation of *RHCE* and *RHD* genes, is still unknown.

Since point mutations in the *RHD* gene which occur naturally (and give rise to partial D phenotypes) have been so useful in studying the genetic basis of D epitope expression, the next logical step was to produce artificial site-directed mutations in the *RHD* gene and study their phenotypic effects. Technology is now available to do this (63). Initial experiments have used retroviral gene transfer of Rh cDNA into a culture of K562 cells followed by flow cytometry with monoclonal antibodies (64).

Fine epitope mapping of the antigens remains a challenge, although evidence seems to be accumulating regarding the overlap of D epitopes, to such an extent that the whole concept of epitopes is undergoing radical change. It is also still unknown why the D antigen is much more immunogenic than the CcEe antigens.

For many years there was little more than speculation and deduction about the basis for the observable serological reactions of the Rh antigens. Molecular analysis of the genes and their protein products has unveiled the current concepts of the Rh blood group system, but our knowledge is still far from complete.

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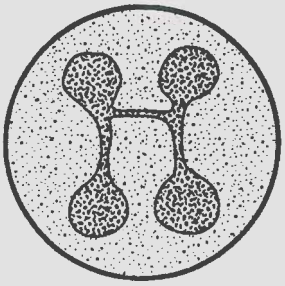

JOURNAL QUESTIONNAIRE

THE LANCET: Vol.355; p 1169-75; April 1st 2000. D.J Weatherall, A.B Provan.
Review; Red cells 1 : Inherited anaemias.

1. Name the 3 major components of the red cell.
2. What is Actin?
3. What is the function of the protein band 3?
4. What is a multipass protein? Name one.
5. Which blood group genes are located on the chromosome 9?
6. Where is 2, 3 DPG generated?
7. Name the embryonic α and B like genes.
8. What genes combine to form HbA2?
9. The oxygen dissociation curve is modified by pH, CO2 and what other conditions?
10. What is the effect of increased concentrations of 2, 3 DPG on the oxygen dissociation curve?
11. What does CFU stand for?
12. What is erythropoietin? Where is it mainly produced in the adult?
13. How is erythropoiesis regulated?
14. Why may anaemia of slow onset be associated with no symptoms?
15. Inherited anaemias involve what 3 aspects of the red cell?
16. What is the molecular change resulting from the sickle-cell mutation?
17. Name 2 other sickling disorders beside homozygous HbS.
18. What physically happens to cause red cells to "sickle"?
19. What is a common cause of an "aplastic crisis" in sickle-cell anaemia?
20. What is the inherited genotype of HbH disease?
21. What is the pathological cause of anaemia in homozygous beta thalassaemia?
22. How many people worldwide are affected with G6PD deficiency?
23. How many G6PD gene mutations are there?
24. What is the inheritance mode of pyruvate kinase deficiency?
25. What is the inheritance mode of the hereditary spherocytosis?
26. In "sickling" crises, often no precipitating factor can be found.
    TRUE/FALSE
27. Administration of hydroxyurea can aggravate "sickling crises".
    TRUE/FALSE
28. Thalassaemias occur sporadically in all racial groups.
    TRUE/FALSE
29. In beta thalassaemia, carrier parents have a 1 in 2 chance of having a homozygous child.
    TRUE/FALSE
30. The carrier state for α° thalassaemia and homozygous state for α"thalassaemia have normal concentrations of HbA2.
    TRUE/FALSE
31. Haemolytic crises in G6PD deficiency are largely extravascular.
    TRUE/FALSE
32. HS and HE result from several defects of membrane skeletal proteins.
    TRUE/FALSE

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HSIG Morphology Workshop - Evaluation

1. *Do you work full time?*
   (Yes) 23/33 (No) 10/33

2. *Do you work shifts alone? i.e. the only Staff Tech performing duties in Haematology.*
   (Yes) 18/23 (of which 6 of the 10 part time staff work alone, i.e. 60%)

3. *How many other Staff Tech's/Senior staff are in your Haematology Laboratory?*
16/31 work with 1-2 other technologist's
3/31 work with 3-4 other technologist's
12/31 work with 5 or more other technologist's
i.e. 52% attending the workshop work in laboratories with only 1-2 other staff technologist's on their duty.

4. *Are you more likely to attend a workshop/seminar on a:*
   (Sat-Sun) 2/33 (Weekday) 13/33 (Wouldn't matter) 20/33
   Part time staff: 4/10 prefers weekday
   6/10 doesn't matter
   Full time staff: 7/23 prefers weekday
   2/23 prefer Sat-Sun
   14/23 doesn't matter

5. *How would you rate this workshop of its overall value to you?*
Most rated the W/S overall as excellent value to them, with the exception of two participants. One said there was not enough information/theory given and the other said that it was too in depth especially in some of the abnormal blood films which would be referred to a Haematologist.

6. *Did you find having the workshop set over two days inadequate, adequate or too lengthy?*
It was found by most to be an adequate time frame. Although two participants thought that a three day W/S would be of more value. One other person thought the W/S was too lengthy and could be cut down leaving out more of the well known morphological examples, as some of the more interesting films on the first day were rushed through.

7. *Did you find the number of blood films to be reviewed inadequate, adequate or too lengthy? (92 in total)*
Majority found the number of films adequate. Although a couple of participants thought the first day was a little too lengthy.

8. *Would you prefer an additional in-depth workshop? If so how long and in which subjects?*
Suggestions for other workshops include:
- Leukemia's/MDS/MPS
- Lymophoproliferative disorders/Bone marrows
- Cell marker analysis and cytogenetic studies in reference to the Acute Leukemia's.

9. *Are you a member of the New Zealand Institute of Medical Laboratory Science?*
(Yes) 11/33 (No) 22/33
8/23 full time staff are members
3/10 part time staff are members
- A couple of those attending the workshop joined at the work shop.

10. *Do you participate in the HSIG journal based learning questionaire, printed in each edition of the NZIMLS journal?*
(Yes) 3/33 (No) 30/33
- Only one member of the NZIMLS currently does the questionnaire.
- Of the 11 members 5 intend to do the questionnaire from now on.
- Currently 2 non-members do the questionnaire.
- 1 part time who does the questionnaire is not a member of the NZIMLS.
- Of the 2 full time staff who do the questionnaire, one is a member and the other is not of the NZIMLS.

Thank you to everyone who responded.

Recently HSIG donated the 1999 Blood Film Morphology teaching material (set of 100 blood film slides) and workbooks used in last years workshop to the Pacific Paramedical Training Centre in Wellington. They were extremely grateful, so much so that we thought maybe other laboratories would like to consider donating any duplicate sets (with work books if they wish) to the PPTC. If so, please contact John Elliot, at Pacific Paramedical Training Centre, P.O. Box 7013, Wellington.

ANSWERS TO JOURNAL QUESTIONNAIRE

THE LANCET: Vol.355; p 1169-75; April 1st 2000. D.J Weatherall, A.B Provan.
Review; Red cells 1 : Inherited anaemias.

1. Membrane, haemoglobin and metabolic pathways.
2. An integral red cell membrane protein.
3. An anion exchanger.
4. Proteins which pass in and out of the membrane many times. (Kidd and Rhesus antigen carrying proteins)
5. Blood groups A and B.
6. A metabolic sliding in the Embden-Meyerhof pathway.
7. e (zeta) and 6 (epsilon).
8. a and B genes.
9. Chloride concentration and the amount of 2,3 DPG.
10. Shifts the curve to the right (causing a state of lower oxygen affinity).
11. Colony forming unit.
12. The specific growth factor involved in the regulation of erythropoiesis, mainly produced in the adult in the kidney.
13. The degree of tissue oxygenation sets the amount of erythroprotein production; the concentration of erythroprotein in turn drives the bone marrow to produce a level of red cells at which oxygen delivery is sufficient to lower erythroprotein production.
14. Because of the adaptive changes in a healthy heart being able to cope with the shift in the oxygen dissociation curve.
15. Haemoglobin, red cell metabolism and membrane.
16. A single amino acid substitution at position 6 of the beta globin chain (Valine for Glutamic acid).
17. Haemoglobin S/C disease and haemoglobin S/beta thalassaemia.
18. Haemoglobin S molecules form rod-like structures in the de-oxy configuration (lowered oxygen tension) deforming the shape of the red cell, causing increased rigidity and aggregation in the microcirculation.
19. Parvovirus infection.
20. Inheritance of α° thalassaemia and α^{+} thalassaemia.
21. Deficiency of beta chains resulting in excess of alpha chains which precipitate in the red cell precursors leading to their damage, in the bone marrow or in the blood.
22. 400 million people.
23. 400 different mutations.
24. Autosomal recessive.
25. Autosomal dominant.
26. True.
27. False.
28. True.
29. False.
30. True.
31. False.
32. True.

Transfusion Science

Special Interest Group

The annual National Immunohaematology Continuing Education weekend was held 28th - 30th April 2000 at THC Wairakei in Taupo. The weekend kicked off on Friday with a Quality Forum (coordinated by NZ Blood Service) and a Diamed Users Group (co-ordinated by Will Perry of Diamed NZ). I understand the Diamed Users Group had a very "hands on" approach this year!

The NICE weekend, co-ordinated by the TSSIG, was again very successful. It was good to see a more positive atmosphere this year after the uncertainties and changes of the last few years. Plenty of discussion and interesting topics were presented by 49 attending delegates with 17 NICE "virgins" this year. (Two of these were pregnant!) Once again the simplest of topics generated the most discussion and debate, These included:

- Specimen Labelling - Htar Kahlyar
- Antenatal Titrations (standardisation of national result reporting) - Diane Murton
- Specimen holding time - Jacqui Jones

One rather interesting topic promoted a bit of humorous banter throughout the weekend. Heather Henshaw reviewed a book called "EAT RIGHT FOR YOUR TYPE'. This outlined dieting by Blood Group and indicated certain predispositions of some blood types. (Apparently, not much of this book has any basis in fact but it did highlight the gullibility of some of our patients!)

The overall winner was **Darryn Knight (NZBS - Auckland)** who spoke about **"S-59 - The end of infectious screening".** This paper highlighted the use of psoralen S-59 (currently under trial) that may remove the need for infectious screening of donations for plasma product production. Thanks,to Abbott's generous sponsorship, Darryn will be presenting a more in depth talk on this subject at NZIMLS Conference 2000.

We would like to acknowledge our sponsors for their support and for helping make this a "NICE" weekend.

Special thanks to:

Abbott Diagnostics Division
Medtel NZ Ltd
CSL Bioplasma
Baxter Healthcare
Pharmaco (NZ) Ltd
Biolab Scientific
NZBS - Waikato & Lakeland Health

Once again, a very educational and inspirational weekend. Due to the cooler weather we did have a change from swimming to dancing this year (including a bit a Super 12 for some of the troops!)
We look forward to next year and even more new and controversial topics!

Raewyn Cameron & Andrew Mills. Co-convenors

ABSTRACTS

POSTER : REPEAT REACTIVE INFECTIOUS SEROLOGY STATISTICS

By Fiona Yuill, NZBS - Auckland
How many repeat reactives (RR) are there?
How many RR are reference laboratory (ref lab) reactive?
How many donors are consistently RR with a nonreactive ref lab?
How are these results spread over the donor population?
Are these figures what we would expect?
These questions answered in the poster "NZBSN (Auckland) Repeat Reactive Infectious Serology Statistics"

THE ROLE OF TRANSFUSION REVIEW NURSE

By Margaret Dewse, Middlemore Hospital
The role of Transfusion Review Nurse was established at Middlemore Hospital in 1997. This presentation describes the experience of working at the interface between laboratory and clinical staff. It also outlines the strategies developed to promote excellence in the delivery of Transfusion Medicine in this organisation.

ADD DRUGS TO OUR BLOOD - NO WAY!

By Iris Lee, NZBS - Wellington
Various drugs (especially analgesics) were added to samples of red cells, resuspended, to study their possible detrimental effects on the cells.

A REACTION OR NOT A REACTION

By Tareq Mustafa, Hawkes Bay Hospital
A summary of a bloodbankers time wasted investigating a transfusion reaction.

ECCCCCCC!

By Leisa Cournane, Southland Hospital
A patient was admitted to Kew Hospital with a gastric ulcer and anaemia. Whilst hospitalised she received two separate transfusions, four days apart and was then discharged.

Nine days later she was back in A & E with abdominal pain and jaundice. A specimen was sent to the laboratory for routine chemistry but due to its brown colour a repeat was requested. The second sample was also brown!

Upon further investigation the DAT was IgG positive and C3 negative and anti-c and anti-E were identified in the patient's serum. Anti-c was eluted off the red cells.
Ecccccccc, a delayed transfusion reaction!!!

A CASE HISTORY

By Gillian Morley, Hawkes Bay Hospital
A man's unfortunate health problems!

TRIVIAL PURSUIT - OR IS IT?

By Heather Henshaw, Timaru Hospital
People may be unaware of their blood type unless they have donated blood or needed a transfusion.

This presentation traces a query by a patient about her blood group.

NAT TESTING

By Stacey Waterson, NZBS - Auckland

NAT testing is a technology which is becoming more and more commonplace in today's rapidly developing world of infectious serology. It is poised to swoop on NZBS, and before it does, I would like to give an introduction. So for those of you who may, or may not, know what this technology is about, I present NAT- the what, why and how.

A CASE HISTORY — MALARIA

By Helen Muir, NZBS - Otago

A case of life threatening malaria caused by p. falciparum presented in our hospital last year. The successful treatment of this man was due largely to the resources of our bloodbank.

"NEW LAMPS FOR OLD" AND "WASTE NOT WANT NOT"

By Geoff Herd, Whangarei Hospital

This paper outlines the role of new products available for the control of bleeding and the management of sepsis. Conjugated oestrogen compounds are now being used to control bleeding in liver transplantation. Human Antithrombin III has recently been evaluated in large (2300 patients) multicentre trial in the management of sepsis in intensive care patients. Mannose binding lectin (MBL) fractionated from human plasma has been used in the management of recurrent infection in 2 deficient individuals. A brief review of the role of MBL in infectious disease and its potential as a screening marker and replacement therapy examined.

AUTOLOGOUS BONE MARROW TRANSPLANT - THE BASICS!

By Amanda Hayward, NZBS - Waikato

This topic will cover the basics of bone marrow and peripheral blood stem cell transplants as performed by NZBS and Health Waikato. The presentation will outline sources of marrow, diseases treated, harvest, storage and transport procedures, complications involved and relevant statistics from the service in Waikato since 1992.,

CONTINUING EDUCATION

By Janine Gundersen, NZBS - Manawatu

An overview of the new Masters in Medical Laboratory Science Degree. Covering all aspects of prerequisites, entry, course structure and contacts.

BONE BANKING - 12 YEARS ON

By Raewyn Cameron, Lakeland Health, Rotorua

A brief history of the bone banking service at Lakeland Health is presented. Some statistics and processes used are covered. Some gory pictures too!!

PRESERVING PATERNITY

By Sheryl Khull, NZBS - Manawatu

A brief overview of procedures and issues related to sperm banking.

In summary, potential sperm donors are identified by the oncology team, their sperm quality is assessed microscopically, and a blood sample is tested for infectious viruses, before acceptance for banking. Semen samples are mixed with cryoprotectant then sealed into glass straws for freezing at a controlled rate followed by storage in liquid nitrogen.

Sperm banking has many similarities with (especially autologous) haemopoietic progenitor cell banking, and falls easily into the repertoire of the transfusion laboratory which serves an Oncology department.

HOW FAR CAN YOU GO?!

By Robert Eagling, NZBS - Southern

An extensive study was required to validate transport systems to satisfy minimum standards and to meet the demands of centralisation. The aim is to validate a specific packing procedure and develop a suitable ongoing QC process.

Initially controlled experiments under extreme temperature challenges were used to identify suitable containers and determine the limits of the system. Once an SOP is written, transport will be validated using blood and components undergoing actual trips. Recommendations for further research will be made and a QC system developed to monitor the system.

OVER THERE, OVER THERE!

By Christine van Tilburg, NZBS - Auckland

NZBS supplies the New Zealand Defence Force with blood support for the peacekeeping force in Timor. I will give a brief overview of procedure, protocol and problems.

DOUBLE SPIN

By Andrew Mills, NZBS - Waikato

In February 1997 Waikato Regional Blood Centre introduced a double spin technique for Platelet production. A review of data 3 years on.

CLOTS IN BLOOD UNITS

By Charlotte Sankey, Taranaki Base Hospital

Brief report on the incidence of clot formation in resuspended red cells during their 35 day shelf life with results from a student project carried out at the Auckland Regional Blood Services in 1998. Details of type of clots and the speed at which they are formed will also be presented.

UNIVERSAL LEUCODEPLETION

By Ray Scott, NZBS - Northern

A Ministerial directive requires that as part of a package of measures to further enhance the safety of the blood supply in New Zealand, Universal Leucodepletion is to be implemented nationally by 31 December 2000.

This presentation will briefly outline the scope of the implementation, options available, current implementation plans and the implications of this project on the Blood Service and blood supply.

SIR RATIA LIQUEFACIANS

BY Bevan Lockwood, NZBS - Waikato

If it's in the fridge, it's ready to be transfused! Isn't it?

What do we as bloodbankers take for granted, or think subconsciously, when we go to issue blood products for transfusion. Especially in emergency situations. What are the checks we should all be aware of at all times when going to issue blood products?

THE SECOND TIME AROUND

By Carole Watson, Middlemore Hospital

Returning to a Blood Bank laboratory as a bench technologist, at a trauma hospital, after more than thirty years absence, was exciting, interesting and just a bit scary. I would like, through this short presentation, to share the experience with you. How I found the new technology, different ways of crossmatching and issuing blood compared to the old, and adjusting to bench work after many years in supervisory positions. Also how knowledge stored and not used can be restored with effort and determination. Realising that you are never too old to learn new skills and acquire new knowledge.

THE LOW DOWN ON LIFE IN A LONDON LAB

By Jandhe Carter, Medlab Tauranga

A general look at the ups and downs, ins and outs and goings on, in a small Transfusion lab in North London.

DIC - A BLOODBANKER'S PERSPECTIVE OF DRUNKEN IN CHARGE!

By Nick Page, Lakeland Health, Rotorua

Now that I have surpassed the milestone of 30 golden years, I have noticed small dark holes of emptiness invading the grey matter. This is a chance for me to plug up one of those small dark holes with a refresher on what is really happening in DIC and why we treat it the way we do.

USE OF BLOOD PRODUCTS IN A CASE OF PRE-ECLAMPSIA

By Dyan Farr, Middlemore Hospital

A primagravida woman collapses in Delivery Suite and an emergency LSCS is performed.

This paper outlines the Blood Product management of her DIC over the next three days.

THE POTENTIAL BLEEDER - A COMMON PROBLEM IN THE ACUTE SURGICAL WARD

By Luke Soo, Middlemore Hospital

A haematological opinion is requested by the acute surgical service. Their 28 year old female patient has abdominal pain and is due for surgery in two hours. Her mother has a known history of von Willebrand's disease. This case illustrates the practical diagnosis and management issues in a surgical patient with a bleeding tendency and shows that transfusion of blood products can be avoided.

USE OF ANTI-D INSTEAD OF INTRAGAM

By Jude Willis, NZBS - Wellington

No abstract available.

THINK....AND THINK AGAIN!

By Susan Duncan, NZBS - Wellington

The case of a baby with a strongly positive DAT for no apparent reason.

ANTENATAL TITRATIONS

By Diane Murton, NZBS - Southern

Correlation between the -maternal antibody titre and the severity of Haemolytic Disease of the Newborn is often inaccurate. However titration does identify women who are candidates for amniocentesis. A change in titre of more than 2 tubes or a score change of 10 or more is significant.

How are laboratories around NZ reporting titres and their endpoints? Is a score interpreted from an endpoint of a 3 grade or from a 5 grade reaction? Are we being consistent in our reporting techniques?

HOLD ON A MINUTE!

By Jacqui Jones, Middlemore Hospital

How long is it safe to hold samples on patients who have not been transfused in the last three months?

A discussion on the logistics of having a suitable sample for cross-match transfusion purposes on elective surgery patients.

DU TESTING - IS IT OBSOLETE?

By Julie Clark, NZBS - Waikato

With improved Anti-D reagents, most weak D(Du) cells will give a positive reaction without indirect antiglobulin technique however there remains a few donors who do not react. Are they significant?

POSITIVES OF HAVING SO MANY NEGATIVES

By Rachelle Quin, Taranaki Base Hospital

An amazing phenomenon that is happening at Inglewood. A small country community is outdoing the rest of the country by donating above average numbers of 0 Rh Negative blood in one donor bleed.

SPECIMEN LABELLING - IS IT A TRIVIAL MATTER?

By Htar Kahlyar, NZBS Waikato

Accuracy and safety of blood transfusion work depends greatly on patient identification and sample collection. Most haemolytic transfusion reactions are the result of clerical errors. Surveys on specimen labelling errors are conducted twice due to continued problems associated with labelling and identification.

ADHERENCE TO THE CODE OF GOOD MANUFACTURING PRACTICE

By Suzanne Williams, NZBS - Southern

Some of you will have read this document, others may not. What is GMP all about? Accountability. Transparency. Providing a safe product.

CRYPTANTIGENS

By Lorna Wall, NZBS - Auckland

Polyagglutination or cryptantigen exposure is not detected as often in the routine blood banks as it was in the past. Grouping anomalies are less common as monoclonal ABO typing sera do not contain anti-T antibodies. The mechanism by which red cells become T-activated in vivo is that bacteria or viruses infecting the individual produce neuraminidase. This enzyme activity removes carbohydrate residues, exposing T antigen receptors. These are then accessible to the naturally occurring anti-T, which is not present in neonatal plasma but are present in adult (donor) plasma. Lectin panels are used to identify the specific cryptantigen and this may provide clues as to the causative agents involved.

ANTI-T TESTING. IS THERE A FUTURE IN NZ BLOODBANKS?

By Colleen Behr, NZBS - Auckland

It is known from literature that severe haemolytic transfusion reactions may occur in premature infants or young children with an activated T antigen when they are transfused with blood or plasma-containing blood components from donors with strong anti-T, fact or fiction? An infant presented at Starship Hospital with pneumococcal meningitis and associated haemolytic uraemic syndrome. During his illness he was transfused with 3 washed red cells, 3 platelets and 1050ml of 4% Albumex resulting in sub-optimal rises in his haemoglobin and associated evidence of haemolysis.

CRYPTANTIGEN TEST - POLYAGGLUTINATION DETECTION

By Sobna Lal, NZBS - Waikato

Polyagglutination is a state in which red cells are agglutinated by all or most normal sera from adults. Most of the time this involves in vivo or in vitro - exposure of receptor sites on the red cells that are not normally available to agglutinins in the sera. NZBS Waikato had a very strange positive Crypt antigen test late last year. This is a very rare occurrence. Blood Bank and Microbiology results will be discussed.

WHEN IS AN ANTIBODY NOT AN ANTIBODY?

By Linda Giddy, Taranaki Base Hospital

When you get a positive antibody screen it usually follows that the person has an atypical antibody - doesn't it? Follow the investigation we performed that proved to be as frustrating as it was interesting to try and identify an antibody in a patient's serum.

COLD, WARM OR HOT?

By Tony Morgan, Hawkes Bay Hospital

In January 1999 Mr S was admitted with a ?retroperitoneal bleed. 3 units of resuspended red cells were requested. Investigations resulted in us reporting "These results are consistent with those found in patients with warm type auto immune haemolytic anemia". But how close were we to finding the hidden treasures - cold, warm or hot?

A CHANGE TO THE CORE

By Brydon Bradley, NZBS - Wellington

This is a presentation that covers the past 12 months of operation at the Hutt Hospital Blood Bank and looks at some of the issues (e.g. Blood Products/Transportation expenditure) that have arisen since we joined the NZBS that affect our management of a small New Zealand Blood Bank.

THE NEW WORKPLACE

By Lorraine Rimmer, NZBS - Auckland

With the establishment of the NZ Blood Service and the need to restructure, the workplace has changed. The new workplace demands people to have the "can do" attitude, to be flexible and to standardise our practice. The big question is - How does one keep up to date? This brief talk offers you a few tips on how to survive.

PROGRESSING WITH PROGESA

By Mark Bevan, NZBS Manawatu

A brief overview of Phase Two of the PROGESA system, with time to hopefully be answering any questions anyone may have about the system.

IS PROGESA FUN?

BY Les Milligan NZBS - Southern

What we call the beginning is often the end and to make an end is to make a beginning. The end is where we start from.... So, here we are, almost one year down the trail of Progesa. Congratulations, we have made it so far and there is a glimmer of hope for us all. It has been like being on a roller coaster ride and some of us did not really have a choice about jumping aboard this ride. It has been scary - many different characters have shared this ride and has it been fun?

MATERIALS MANAGEMENT - NUISANCE OR NECESSITY?

By Karen Webber, NZBS Auckland

A brief overview of inwards goods inspection as done at Northern Region.

INCIDENT POT POURRI

By Anne Burnand, NZBS - Waikato

What can go wrong and what can we learn from it?

2020 REVISITED

By Roger Austin, NZBS - Auckland

At the first NICE weekend in 1990, a paper was presented outlining one person's tongue in cheek view of how New Zealand' s blood banks would be operating in the year 2020. We are now one third of the way to that date and already a number of these predictions are either part of our everyday operation or on the near horizon. This presentation will highlight these.

100 YEARS OF ABO.... IN 5 MINUTES.

By Jenni Webb, NZBS - Manawatu

A short story of discovery, compatibility and guilt by association.

HUMAN PARVOVIRUS B19

By Diane Whitehead, NZBS - Southern

An outline of a "PCP," method (Clewey, Cohen et al) will be given for the detection of human parvovirus B19 DNA in serum.

Human parvovirus B19 is one of the most resistant viruses that can be transmitted parenterally, so a PCR technique suitable for screening blood donor pools could be regarded as a quality benchmark model for the exclusion by NAT of other "unknown" pathogenic viruses that may contaminate blood products and the donor plasma pool.

S-59, THE END OF INFECTIOUS SCREENING

By Darren Knight, NZBS - Auckland

The uses of psoralen S-59 within the blood transfusion service.

A photochemical treatment process has been developed for the inactivation of high titres of viruses and bacteria in blood components. It involves a psoralen, S-59, which once activated, binds with pyrimidine bases preventing DNA replication.

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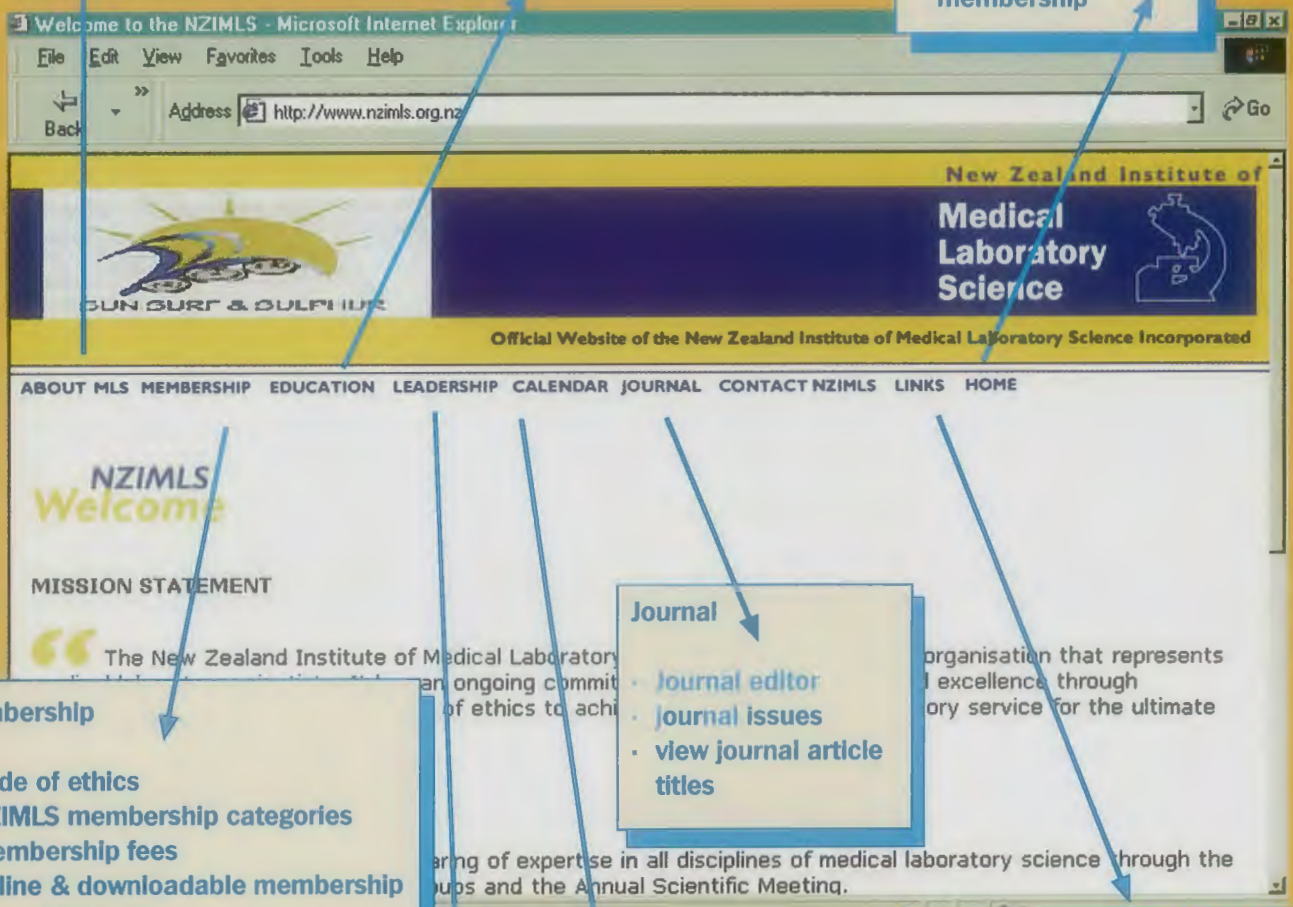

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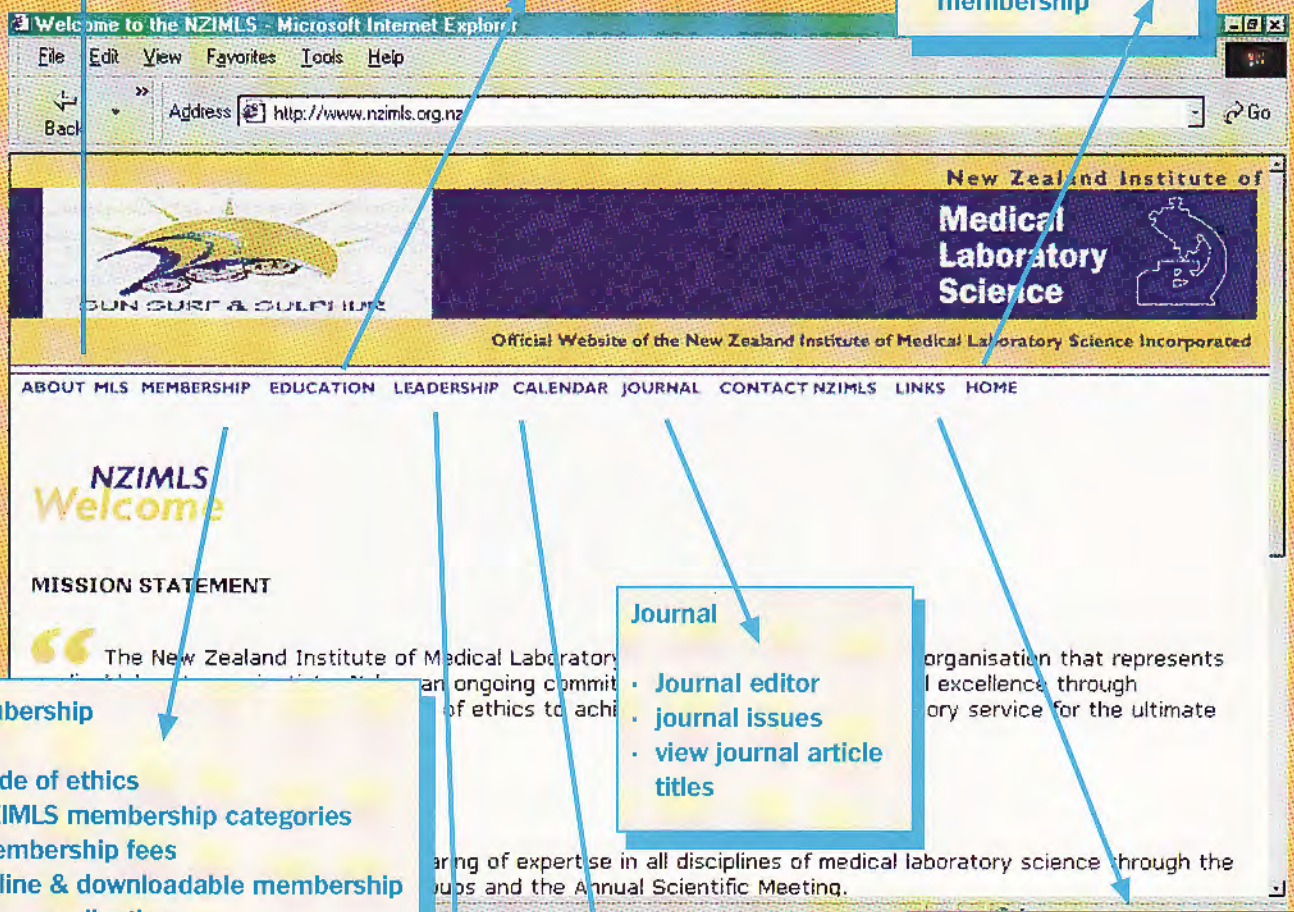

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