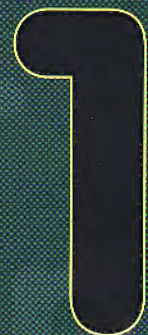
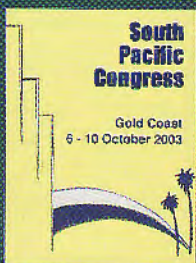


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Classical enteropathogenic *Escherichia coli* or atypical strains? Examination of shigatoxin negative, eaeA positive isolates received in the Enteric Reference Laboratory in 2000

Jenny Bennett, FNZIMLS
Enteric Reference Laboratory, ESR Kenepuru Science Centre, Porirua.

Abstract

Enteropathogenic *E coli* (EPEC) were first recognised in the 1940s as an important cause of diarrhoea in young children, responsible for serious outbreaks of disease and some deaths. The enteropathogenic phenotype was associated with certain serotypes, and this was the only way of differentiating EPEC from commensal *E coli*. The mechanism for causing diarrhoea was not known, and to some extent remains so. Modern molecular methods have enabled the detection of the genes responsible for some of the pathogenic effects of EPEC strains and retrospective testing of historical isolates has demonstrated the presence of these markers.

In the mid-eighties, EPEC strains became less important as a cause of diarrhoea in children of developed countries, although they remain an important cause of morbidity and mortality in the Third World. The importance of shigatoxin-producing *E coli* has overshadowed EPEC and most laboratories in industrialised countries no longer carry out serological screening for EPEC in young children with diarrhoea. There is some evidence that EPEC strains may still be a cause of diarrhoea in both adults and young children in industrialised countries however, causing both outbreaks and sporadic disease.

The multiplex PCR used in the Enteric Reference Laboratory at ESR to identify enterohaemorrhagic *E coli* (EHEC) detects the eaeA gene as well as the shigatoxin-producing genes stx1 and stx2 and the EHEChlyA gene. The primer pair used in this PCR amplifies a conserved area of the eaeA gene common to both EPEC and EHEC. When this PCR became part of the ERL protocol for investigating EHEC, approximately ten percent of the isolates tested were eaeA positive but stx negative.

The significance of these isolates was unclear. A second PCR was developed that amplifies the bfpA gene, a gene found on the EAF plasmid. This plasmid is a virulence factor found in classical EPEC strains. Retrospective analysis of strains referred to ERL in 2000 for shigatoxin testing was carried out on eaeA positive, stx negative isolates to determine whether these strains were classical or atypical EPEC, and the isolates were also serotyped.

No isolate was positive for bfpA. Six of the isolates belonged to serotypes described in the literature as frequently isolated atypical EPEC serotypes; five were serotype O125:H6 and one was serotype O119:H2. Three isolates were O145:H34, which has been reported in the literature as a possible new atypical EPEC serotype.

The pathogenicity of eaeA positive, stx negative strains remains unclear.

Key words: *Escherichia coli*, EPEC, enteropathogenic, molecular markers, eaeA, bfpA diarrhoea, outbreak

Abbreviations: A/E -attaching/effacing, bfpA -bundle forming pili gene, eaeA - *E coli* attaching and effacing gene, EAF - *E coli* adherence factor, EHEC - enterohaemorrhagic *E coli*, EHEChlyA - enterohaemorrhagic *E coli* enterohaemolysin, EPEC - enteropathogenic *E coli*, ERL - Enteric Reference Laboratory, HRP - horse radish peroxidase, STEC - shigatoxigenic *E coli*, nt -nucleotide

Introduction

There are currently six categories of *E coli* associated with diarrhoea: enteropathogenic (EPEC), enterotoxigenic (ETEC), enteroinvasive (EIEC), enteroaggregative (EAEC), diffusely adherent (DAEC) and shigatoxigenic (STEC). STEC are found in animals as well as humans, and are not necessarily pathogenic to people. A subset of shigatoxin-producing strains, known as enterohaemorrhagic *E coli* (EHEC), have the eaeA gene, produce enterohaemolysin, and are capable of causing serious human disease. The latter have become increasingly important since the association was made between infection with a rare serotype (O157) and development of haemolytic uraemic syndrome (1).

The first association of *E coli* with diarrhoea was made in the 1940s when severe outbreaks of infantile diarrhoea in nurseries and paediatric wards were found by epidemiological means to be the result of infection with certain serogroups of *E coli* (2). These serogroups, O26, O44, O55, O86, O111, O114, O119, O125-O128, O142, and O158 are known as EPEC serogroups. Within these groups are specific serotypes (O and H types) which are regarded as classic EPEC serotypes. Examples of classic EPEC serotypes are O55:H6, O86:H34, O111:H2, O114:H2, O119:H6, O127:H6, O142:H6 and O142:H34 and O127:H6. These serotypes are frequently isolated in countries where EPEC strains are common.

Nosocomial infection with EPEC was a serious problem throughout the 1940s and 1950s (3). Outbreaks of diarrhoea due to EPEC were often widespread throughout a community and affected mainly children under the age of two. As an example, a community outbreak was investigated in a study of paediatric diarrhoea necessitating hospital admission in the Chicago-Northwestern Indiana metropolitan area of the United States during August 1960 to May 1961 (4). Seven hundred and nine of 1,313 study cases had a stool culture taken (54%). Despite the fact that less than 50% of hospitals at that time were serologically screening *E coli* isolates, 43% of the cultured population had EPEC isolated from their stool on at least one occasion, and 89% of these organisms were EPEC O111:B4. There were 77 deaths due to gastroenteritis recorded during the study period with an overall mortality rate of 5.9%.

In 1995, the Second International Symposium on EPEC reached a consensus on the basic characteristics of EPEC. The most important of these were the attaching/effacing histopathology and the absence of shiga toxin. Possession of specific O and H antigens is no longer deemed an essential characteristic since serotypes other than the classic EPEC serotypes have been associated with diarrhoeal disease. Some members of the classic EPEC serogroups, for example O111, are known to produce shigatoxin, and O55:H7 strains are generally accepted to be the precursors of the best-known shigatoxin-producing serotype O157:H7. However, part of the definition of EPEC is that they are not shigatoxin producers.

The EAF plasmid (see below) is found in classical EPEC strains. EPEC that are eaeA and EAF positive are also known as class I, or typical EPEC, whereas EPEC that are eaeA positive but EAF negative are known as class II or atypical EPEC (5).

Classical EPEC remain an important cause of infantile morbidity and mortality among children in many developing countries, but in developed

countries classical EPEC strains are no longer as important as they once were, for reasons that are unclear⁵. Nevertheless, reports of outbreaks and sporadic cases of EPEC in industrialised countries continue to be reported in the literature (6-8).

A study of EPEC and EAEC isolated from children under the age of three in Britain found that EAF negative EPEC were probably of greater importance than EAF positive strains (6). Researchers in Brazil, where infection with typical strains is common, suggest that atypical strains may be less virulent although not less pathogenic (9). Frequently isolated strains of atypical EPEC include the following serotypes: O26:H11, O55:H7, O55:H34, O86:H8, O111ac:H8, O111:H9, O111:H25, O119:H2, O126ac:H6 and O128:H2.

A one-year prospective study of stool specimens submitted for culture to a Seattle paediatric hospital was undertaken between 1991 and 1992 (7). Researchers found that EPEC were relatively common, being present in 3.6% of specimens submitted to the laboratory. This frequency exceeded the recovery rate of *E coli* O157, *Yersinia*, *Campylobacter*, *Salmonella* and *Shigella*. The authors contend that the clinical significance of *eaeA* positive, *bfpA* negative isolates cannot be determined from this study because no control cultures were carried out and detailed questionnaires of symptomatic patients were not taken.

In a study of community-acquired diarrhoea requiring hospitalisation in Swiss children, pathogens such as *C parvum*, *Aeromonas spp* and diarrhoeagenic *E coli* were isolated from 18% of inpatients with acute diarrhoeal illness⁸. Of the diarrhoeagenic *E coli*, EPEC strains were the most common type detected.

The exact mechanism by which EPEC strains cause diarrhoea remains unclear. The characteristic lesion caused by EPEC is the attaching-effacing lesion, which results in intimate attachment of the organisms to enterocytes and effacement of the brush border. There are three steps involved in this process, although the order in which they occur is uncertain, and they may in fact occur simultaneously (5).

- i) Localized adherence: this effect can be demonstrated by tissue culture using Hep-2 cells. The factor mediating attachment is found on a 60-Mda plasmid designated the EPEC adherence factor (EAF) plasmid. A 1-kb fragment of this plasmid has been developed as a diagnostic probe. This probe is from a part of the plasmid with no known function, and although it has proved useful in identifying EPEC strains, a PCR using primers that amplify part of the *bfpA* gene cluster, also located on the EAF plasmid, is more sensitive (11). The *bfpA* locus consists of 13 genes that code for bundle-forming pili (BFP) which mediate bacterium-to-bacterium adherence in the localised adherence pattern. The EAF plasmid also encodes Per, a global regulator of EPEC pathogenesis, which is required for the expression and assembly of BFP and also plays a part in signal transduction.
- ii) Signal transduction: adherence of EPEC to epithelial cells induces a variety of signal transduction pathways in the eukaryotic cell (5). The genes coding for this activity are found on a 35-kb pathogenicity island located on the bacterial chromosome. This pathogenicity island is termed the locus of enterocyte effacement (LEE), and is inserted in different positions on the chromosome in EPEC and EHEC. LEE genes code for a type III secretion system, multiple secreted proteins, and a bacterial adhesin called intimin. The net effects of these proteins are: an increase in intracellular calcium ions, which can inhibit sodium and chloride ion absorption and lead to stimulation of chloride secretion and diarrhoea; cytoskeletal changes induced by receptor binding activity leading to the accumulation of actin and activation of several kinases which induce rapid changes in intestinal water and electrolyte secretion; and migration of polymorphonuclear leukocytes.

- iii) Intimate adherence: this is mediated by the action of intimin, which is encoded by the *eaeA* gene. This gene is present in all EPEC, EHEC, *Citrobacter rodentium*, and some strains of *Hafnia alvei*. It is absent in commensal *E coli*, ETEC and other bacteria that do not produce the A/E lesion (5). The *eaeA* gene is essential for full virulence of EPEC but is not the only virulence factor required to cause disease. In EPEC one of the signal transduction events is the tyrosine phosphorylation of a 78-kDa bacterial protein that is injected into the enterocyte. Once phosphorylated, which increases its molecular weight to 90-kDa, this protein becomes the translocated intimin receptor or Tir, enabling intimate attachment (13,14). This is the first known example of a bacterium encoding its own attachment receptor.

The traditional test for determining the intimate attachment of EPEC and EHEC to cells is the fluorescent actin-staining (FAS) test using the mushroom toxin phalloidin (15). This test detects actin accumulation, which occurs during bacterial adherence in tissue culture, and is the in vitro counterpart of the attaching-effacing lesion. Phalloidin is very expensive and is one of the most toxic substances known. A cheaper and safer alternative is to replace the test with a PCR to detect the *eaeA* gene. Correlation between FAS and *eaeA* positivity is close to 100% (16).

As discussed above, the Second International Symposium on EPEC in 1995 defined *E coli* that are *eaeA* positive and *bfpA* negative as class II or atypical EPEC. Opinion is divided as to the clinical significance of these organisms. In a 1993 study of historical strains of EPEC isolated in Britain between 1947 and 1960, using modern molecular techniques, five of nine strains were class I EPEC, two were class II EPEC, one was EAEC and one had no detectable virulence factors (17). All isolates were from cases of diarrhoea in infants, and all were amongst the first isolates of that particular serotype reported in infantile diarrhoea. All of the class I EPEC were from diarrhoea epidemics, whereas the two class II EPECs were from cases of sporadic diarrhoea. The isolate with no detectable virulence factors was isolated from an epidemic in a nursery, which was unusual in that the infants had been colonised for eight weeks before cases of diarrhoea had occurred. In this particular case, the authors concluded that the isolate was probably not the cause of the patients' symptoms. The results of this study showed that the majority of these historical EPEC isolates would have been identified as either class I or class II EPEC using modern methods and that class I EPEC are associated with epidemic diarrhoea, whereas class II EPEC are more likely to be found in sporadic disease. A similar study, testing historical isolates sent to CDC, Atlanta between 1934 and 1987 also used molecular methods (18). All strains had been isolated from outbreaks of diarrhoeal disease in children under two years old. Classical EPEC serotypes or strains demonstrating localised adherence were found in 60% of outbreaks, but for the remainder, no *E coli* virulence factors were detected. The authors concluded that this could imply virulence factors as yet unidentified (at that time) or the loss of virulence markers during storage. This study was undertaken in 1989, before the *eaeA* gene had been discovered.

A study of isolates of *E coli* from sporadic cases of diarrhoea in Britain found that EAEC and atypical EPEC were more frequently isolated and probably more important than class I EPEC (6). A Brazilian study of the virulence properties of atypical EPEC strains found that most classical and atypical EPEC strains have similar virulence properties, with the exception of those coded by the EAF plasmid (19). In a study currently underway and yet to be published, Pelayo and colleagues found that most atypical EPEC strains have the *astA* gene encoding EAST-1 toxin, also produced by some EAEC and EHEC, while the typical ones do not.

The role of EAST-1 toxin in diarrhoea is not clear. A comprehensive review of the diarrhoeagenic *E coli* published in 1998 states that in every case control study of *eaeA* positive EPEC strains, only the EAF positive and not EAF negative strains were significantly associated with diarrhoea (5). In an extensive genotypic and phenotypic analysis of atypical EPEC recently published (20), the authors conclude that serology and the presence of *eaeA* are not sufficient to distinguish truly pathogenic strains found in the class II EPEC studied.

There are two other aspects to consider in deciding whether an apparent atypical strain of EPEC is causing diarrhoea in a particular patient. It is possible that the isolated strain has lost virulence factors in vitro. One example of this is the loss of the *stx* genes, which are phage encoded and very easily lost on subculture, with the result that a strain producing shiga-toxin in vivo may be misidentified as an atypical EPEC. In New Zealand, most STEC, and by definition all EHEC, carry the *EHEC_{hlyA}* gene coding for enterohaemolysin. An *eaeA* positive, *hlyA* positive, *bfpA* negative organism would suggest an STEC/EHEC with missing *stx* genes. Another possibility is a class I EPEC which has lost the EAF plasmid and thus the *bfpA* gene, being misidentified as a class II EPEC. The loss of the EAF plasmid also occurs quite readily. Levine et al found that the EAF plasmid was lost in two thirds of volunteers fed with *E coli* strain E2348/69 (serotype O127:H6) on recovery of the organism from faecal specimens (21). In this case, serotyping would indicate a typical EPEC serotype. In either of the above situations, a further test to identify the type of intimin encoded by the *eaeA* gene may differentiate between EPEC and EHEC strains, since intimin type *alpha* seems to be specifically expressed by human EPEC strains belonging to classical serotypes (22). Other intimin types include *gamma*, which is found in several EHEC serogroups highly pathogenic for humans, including O157. It is interesting that serotype O55:H7, the likely EPEC progenitor of O157:H7, also produces type *gamma* intimin. Type *beta* is found in both human and animal strains of EPEC and EHEC.

The reason for undertaking the present study was that few New Zealand community and hospital laboratories examine faecal specimens from children under the age of five for EPEC. The *E coli* isolates referred to the Enteric Reference Laboratory are usually for toxin testing. The current protocol includes a multiplex PCR used to detect the shigatoxin genes of shigatoxigenic (STEC) and enterohaemorrhagic *E coli* (EHEC), and the EHEC enterohaemolysin gene (*EHEC_{hlyA}*). This PCR also detects the *eaeA* gene, which codes for intimin, a protein involved in the attaching-effacing phenotype of EPEC and STEC/EHEC (10). The primers used for detecting the *eaeA* gene were chosen to amplify a region of the gene conserved between EPEC and STEC/EHEC. Some isolates from both adults and children are *eaeA* positive but *stx* negative, suggesting that they may be EPEC strains. For this investigation, 26 *eaeA* positive, *stx* negative strains identified by the Enteric Reference Laboratory during 2000 were further characterised to see if they represented classical or atypical EPEC. A modification of the method described by Gunzburg and colleagues was used (11) to detect the *bfpA* gene.

Materials and methods

Bacterial strains

Human strains of *E coli* from cases of diarrhoea referred by hospital and community laboratories in 2000 for toxin testing were stored on dorset egg medium slopes at room temperature in the dark until tested. Isolates selected for testing with the *bfpA* PCR were previously identified as *eaeA* positive, *stx* negative by multiplex PCR (10). Twenty six isolates were tested. Subcultures were made to trypticase soy agar and brain heart infusion (BHI) broth and incubated at 37°C for approximately 18 hours. The broth was incubated on an orbital shaker.

Control strains were obtained from the New Zealand Reference Culture Collection. The strains selected were those used by Robins-Browne and colleagues (17) to examine archetypal strains of EPEC for properties associated with virulence. Positive control was ACC1662, strain number E990, serotype O86:K61(B7):H- *eaeA* positive, EAF positive; originally isolated in 1950 in England from an epidemic of diarrhoea. Negative control was ACC1426, strain number E611, serotype O126:K71(B16):H2 *eaeA* positive, EAF negative; originally isolated in 1949 in England from a case of sporadic diarrhoea.

PCR

The primers used were designed by James Paton (personal communication) from the published *bfpA* sequence (23) and amplify the complete *bfpA* open reading frame, giving a 584bp amplicon. These sequence data appear in the EMBL/GenBank/DBJ Nucleotide Sequence Data Libraries under the accession number LO7028.

bfpA F 5' - ATGGTTTCTAAAATCATGAATAAG -3' (nt121-nt145) and
bfpA R 3' - GATTACTTCATTAATAATATGTAAC - 5' (nt682-nt705).

A 1ml aliquot of the BHI broth was boiled for 10 minutes to release plasmid DNA. This was used as template DNA. A master mix was made containing 25µl Qiagen (Biolab Scientific), 16µl distilled water, 2µl 50mmol MgCl₂ (Gibco BRL, optimum concentration determined by titration), and 1µl of each primer per reaction. Qiagen master mix contains Taq DNA polymerase, PCR buffer, 1.5(M MgCl and 200(M each dNTP. The addition of 5µl template DNA gave a final reaction volume of 50µl. The PCR conditions were 29 cycles of 30s at 94°C, 1 min at 56°C, 2 min at 72°C followed by indefinite hold at 4°C, using a Perkin Elmer 2400 thermocycler. The PCR product was electrophoresed in a 2% agarose gel run in 0.5 TBE at 115V for approximately 1 hour and stained in ethidium bromide 1mg/ml. The results were recorded by photographing with a Polaroid land camera (Figure 1).

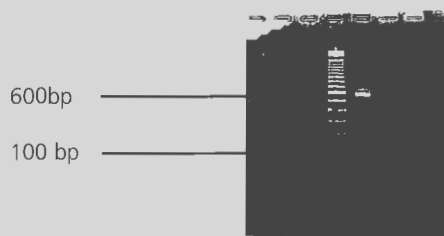


Figure 1

Product confirmation

The identity of the 584bp amplicon was confirmed by hybridisation with a Biotin labelled 21nt probe internal to the amplified fragment. This probe corresponded to nt435- nt455 of the published sequence for the bundle-forming pilin gene of EPEC (23), and was obtained from Life Technologies.

Two microlitres of the PCR product were spotted onto a nylon membrane (Hybond) and denatured. The product was fixed by exposing to UV light and kept at room temperature in the dark until tested.

Probe sequence: Biotin – TAGGTCCAGCAACAATAACA.

Hybridisation was carried out using the following conditions:

Prehybridisation at 55°C for 30mins in 5x sodium chloride, sodium orthophosphate, EDTA buffer (SSPE) +1% sodium dodecyl sulphate (SDS). Hybridisation for 4 hours at 55°C in 5x SSPE +1% SDS. Washed for 10 min at room temperature 2x SSPE + 1% SDS. Washed for 10 min at 55° in 2x SSPE +1% SDS (twice). Detection was with Streptavidin/HRP conjugate (Dako) at a final concentration of 30ng/mL for 15 mins at room temperature. ECL detector reagents (Amersham)

were applied for 1 minute, followed by overnight exposure to Hyperfilm photographic film in a cassette at room temperature.

Serotyping

All isolates were typed using in-house antisera raised in rabbits. The Enteric Reference Laboratory carries antisera to the 173 known O antigens of *E. coli*, including all of the classic EPEC serogroups, and the 59 H antigens. Serotyping was carried out using overnight nutrient broth cultures as antigens for the O-typing, these were boiled for one hour before using to destroy K capsular antigens. Screening tests were carried out in microtitre plates using 1:50 dilutions of each antiserum in saline followed by titration against control strains for each positive agglutination reaction. Isolates were passaged at least twice through semisolid medium at 30°C to obtain fully motile cultures for H typing, and then incubated in tryptose phosphate broth at 30°C for 6 hours. After checking microscopically for full motility, the broths were killed using formalin to a final concentration of 0.5%. H antigen identification was carried out by screening with 1:50 dilutions of each antiserum, and titrating positive agglutination reactions against control strains.

Results

The *bfpA* PCR amplified a fragment of the expected size with the positive control strain E990 (EAF positive), but not with the negative control E611 (EAF negative) (Figure 1). The identity of the PCR product was confirmed by hybridization with a probe internal to the amplified fragment, under stringent conditions. A positive signal, denoting the presence in the product of a sequence complementary to the probe, was obtained (data not shown). Twenty-six *eaeA* positive, *stx* negative human isolates from the year 2000 were tested with the *bfpA* PCR. No *bfpA* positive isolates were identified. All of the isolates were serotyped. Eleven (42%) of them were untypable. Of the serogroups identified, one was O13:H not identified, one was O49:H10, one was O119:H2, one was O123:H11/21, five were O125:H6, one was O125:HNM, one was O132:H not identified, three were O145:H34, one was O145:HNM and one was rough (Table 1).

ER no.	Date	Sex/Age	Clinical details	<i>eaeA</i>	<i>bfpA</i>	Sorbitol fermentation	Serogroup
000753	Feb	M/2	No details	+	-	+	ONT:HNM
001136	Mar	M/1	No details	+	-	-	O13*
001184	Mar	M/78	No details	+	-	-	O145:HNM
001266	Mar	M/67	No details	+	-	-	O125:H6
001394	Apr	M/39	No details	+	-	-	ONT:H33
001534	Apr	F/1	Diarrhoea	+	-	+	ONT:H45
001780	May	M/22	Gastroenteritis, bloodstained stool	+	-	-	O145:H34
001796	May	M/26	PR bleed, change in bowel habit	+	-	-	ONT:H6
001835	May	F/18	No details	+	-	-	ONT:H34
001836	May	F/9m	No details	+	-	-	ONT:H6
001838	May	M/16m	No details	+	-	-	ONT
002271	May	M/3	? EHEC	+	-	Weak +	O125:H6
002338	Jun	M/87	? EHEC, contact of 002271	+	-	Weak +	O125:H6
002415	Jun	M/2	Diarrhoea	+	-	-	ONT:H45
002456	Jun	M/4m	Malaise, change in motions	+	-	-	ORough:H49
002583	Jun	M/2	Diarrhoea	+	-	Delayed +	O123:H11/21
002589	Jun	M/68	Bloody diarrhoea	+	-	-	O132*
002775	Jun	M/15m	No details	+	-	-	O119:H2
003102	Aug	M/2	No details	+	-	Weak +	ONT:HNM
004028	Sep		No details	+	-	-	ONT:H6
004141	Sep	M/1	No details	+	-	Delayed +	O125:HNM
005080	Nov		No details	+	-	-	O145:H34
005197	Nov	F/2	Generally off colour	+	-	-	O125:H6
005568	Dec	F/28	? O157	+	-	+	O49:H10
005569	Dec	M/36	Diarrhoea 2 weeks	+	-	-	ONT:HNM
005808	Dec	F/11m	No details	+	-	-	O145:H34

Table 1. *bfpA* PCR result and serogroup of *eaeA* positive, *stx* negative isolates received in 2000.

ONT = *O* not typable; ORough = autoagglutinable; * Isolate became non-viable before H typing completed

Discussion

Three hundred and thirty six pure cultures or mixed sweeps of organisms were tested by multiplex PCR for *E coli* shigatoxin genes and accessory virulence factors from human cases of diarrhoea by ERL in the year 2000. Of these, 41 (12%) were positive for *eaeA* only. Pure cultures of *E coli* were stored on dorset egg slopes, and all viable, pure cultures ($n=26$) were selected for *bfpA* testing. The remainder of the isolates were either non-viable following storage, or were mixed sweeps of organisms, which were not stored. Further examination of stored isolates for the presence of the *bfpA* gene did not yield any positive results, but retrospective examination of isolates received to date in 2001 has revealed one positive (data not presented). The EAF plasmid is known to be unstable and easily lost, and it is possible that cultures stored for more than a year may have lost the plasmid.

The large proportion of untypable atypical EPEC isolates is in agreement with the recent study of *eaeA* positive isolates from children in Sao Paulo, Brazil, in which 57% of isolates were untypable (17). The O-untypable strains identified in the Brazilian study also had different Tir subtypes and LEE insertion sites, suggesting that they represented different serogroups.

No classical EPEC serotypes were identified in this study, but five isolates were O125:H6 and one was O119:H2. Both of these serotypes have been described as frequently isolated atypical EPEC strains (9). Three isolates were O145:H34, which has been described as a new atypical EPEC (Dr Flemming Scheutz, WHO *Escherichia coli* and *Klebsiella* Reference Laboratory, Denmark, personal communication).

Nearly all of the study organisms were isolated from children under the age of five. The one exception was an O125:H6 isolated from an 87 year-old man who was a contact of a young child with the same serotype. Unlike classical strains of EPEC, atypical strains are not solely associated with diarrhoea in very young children.

It is possible that some of these isolates represent shigatoxin-producing strains that have lost the *stx* genes. O13, O49, O123, O132, and O145 are all serogroups that have been associated with the production of shigatoxin. None of the isolates in this study had the *EHEC/hlyA* gene however, which is often present in shigatoxin-producing strains. As described above, intimin typing could be useful to differentiate between EPEC and STEC that have lost the *stx* genes.

The importance of classical strains of EPEC as a cause of infantile diarrhoea in developed countries declined in the mid-1980s, as STEC became emerging pathogens. Tissue culture for heat-labile toxin and verocytotoxin was available in ERL from the early 1980s. Prior to this, strains sent to ERL were serotyped and their potential pathogenicity inferred from the serotype. H typing was discontinued in ERL in the late 1970s (with the exception of H7 typing of *E coli* O157:H7) and recommenced in 1999, following overseas training of a staff member. Between 1988 and 1993 the following O types were identified in New Zealand isolates: O1, O2, O4, O6, O8, O15, O18ab, O25, O26, O50, O55, O68, O73, O75, O86, O111, O126, O127, O128 and O133. Interestingly, the O type most frequently identified in this study, O125, is not represented. During 1993, the first isolate of *E coli* O157:H7 was identified in New Zealand, and this pathogen rapidly became the focus of attention in faecal testing by diagnostic laboratories around the country. Sorbitol negative strains of *E coli* were referred to ERL as suspected O157s. Eighteen of the isolates (69%) tested in this study were sorbitol non-fermenters, and of the remainder, 5 (19%) were weakly positive or delayed positive. Only 3 (11%) were strongly positive at 24 hours.

This indicates a selection bias in the strains tested as well as a possible selectable characteristic, at least for serotypes O125:H6 and O145:H34.

The isolates tested in this study were not classical (class I) or typical EPEC as defined by the Second International Symposium on EPEC in 1995. They do, however, fit the definition of atypical or class II EPEC. All strains were isolated from symptomatic individuals. It is not known whether any other faecal pathogen was isolated. They may represent emerging pathogens, in the same manner that STEC became emerging pathogens during the 1980s. Given that there is a possibility that these strains represent true faecal pathogens, their presence and a brief explanation of their possible clinical significance should be reported to the referring laboratories. The use of the *bfpA* PCR in addition to the multiplex PCR for STEC already used in ERL would enable surveillance of the presence of classical and atypical EPEC in New Zealand. A prospective trial is required to elucidate the significance of these isolates.

Conclusions

This study has shown that atypical EPEC strains are isolated in New Zealand from cases of diarrhoea. Some of the serotypes identified in this study are described as "frequently isolated" by overseas authors. The proportion of *E coli* isolates sent to ERL for toxin testing that are found to be *eaeA* positive but *stx* negative (approximately 10%), suggests that these organisms are found relatively frequently, although their clinical significance remains unclear. International studies of atypical EPEC generally conclude that more research is needed on the significance of these organisms in developed countries. A prospective study of the incidence of atypical EPEC in New Zealand including case controls is required to elucidate their importance here. In the meantime, all *E coli* isolates received by ERL and found to be *eaeA* positive and *stx* negative by multiplex PCR will be further characterised by *bfpA* PCR and serotyped. These results will be reported as "clinically significant" EPEC in the case of classical serogroups that are *bfpA* positive, and as atypical EPEC, "clinical significance undetermined", in the case of *bfpA* negative strains.

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References

1. Karmali MA, Petric M, Lim C, Fleming PC, Steele BT. *Escherichia coli* cytotoxin, haemolytic-uraemic syndrome, and haemorrhagic colitis. *Lancet* 1983; ii: 1299-1300.
2. Taylor J, Wright J. Infantile diarrhoea and vomiting: a clinical and bacteriological investigation. *Br Med J* 1949; 2: 117-25.
3. Robins-Browne RM. Traditional enteropathogenic *Escherichia coli* of infantile diarrhoea. *Rev Infect Dis* 1987; 9: 28-53.
4. Kessener D, Shaughnessy H, Googins J. An extensive community outbreak of diarrhoea due to enteropathogenic *Escherichia coli* O111: B4. *Am J Hyg* 1962; 76:2 7-43.
5. Nataro JP, Kaper JB. Diarrheagenic *Escherichia coli*. *Clin Microbiol Rev* 1998; 11: 142-201.
6. Scotland SM, Smith HR, Said B, Willshaw GA, Cheasty T, Rowe B. Identification of enteropathogenic *Escherichia coli* isolated in Britain as enteroaggregative or as members of a subclass of attaching-and-effacing *E coli* not hybridising with the EPEC adherence-factor probe. *J Med Microbiol* 1991; 35: 278-83.

7. Bokete TN, Whittam TS, Wilson RA, Claussen CR, O'Callahan CM, Moseley S, et al. Genetic and phenotypic analysis of Escherichia coli with enteropathogenic characteristics isolated from Seattle children. *J Infect Dis* 1997;175: 1382-9.
8. Essers B, Burnens AP, Lanfranchini FM, Somaruga SGE, von Vigier RO, Schaad UB, et al. Acute community-acquired diarrhoea requiring hospital admission in Swiss children. *Clin Infect Dis* 2000; 31: 192-6.
9. Trabulsi LR, Keller R, and Gomes TAT. Typical and atypical enteropathogenic Escherichia coli. *Emerg Infect Dis* 2002; 8: 508-13.
10. Paton AW, Paton JC. Detection and characterisation of Shiga toxinogenic Escherichia coli by using multiplex PCR assays for stx1, stx2, eaeA, enterohemorrhagic E coli hlyA, rfbO111 and rfbO157. *J Clin Microbiol* 1998; 36: 598-602.
11. Gunzburg ST, Tornieporth NG, Riley LW. Identification of enteropathogenic Escherichia coli by PCR-based detection of the bundle-forming pilus gene. *J Clin Microbiol* 1995; 33: 1375-7.
12. Donnenberg MS, Giron JA, Nataro JP, Kaper JB. A plasmid-encoded type IV fimbrial gene of enteropathogenic Escherichia coli associated with localised adherence. *Mol Microbiol* 1992; 6: 3427-37.
13. Kenny B, DeVinney R, Stein M, Reinscheid DJ, Frey EA, Finlay BB. Enteropathogenic E coli (EPEC) transfers its receptor for intimate adherence into mammalian cells. *Cell* 1997; 91: 511-20.
14. McCarthy M. Escherichia coli makes its own receptor. *Lancet* 1997; 350: 1605.
15. Knutton S, Baldwin T, Williams PH, McNeish AS. Actin accumulation at sites of bacterial adhesion to tissue culture cells: basis of a new diagnostic test for enteropathogenic and enterohemorrhagic Escherichia coli. *Infect Immun* 1989; 57: 1290-8.
16. Schmidt H, Plaschke B, Franke S, Russmann H, Schwarzkopf A, Heeseman J, Karch H. Differentiation in virulence patterns of Escherichia coli possessing eae genes. *Med Microbiol Immunol* 1994; 183: 23-31.
17. Robins-Browne RM, Yam WC, O'Gorman LE, Bettelheim KA. Examination of archetypal strains of enteropathogenic Escherichia coli for properties associated with bacterial virulence. *J Med Microbiol* 1993; 38: 222-6.
18. Moyenuddin M, Waschsmuth IK, Mosely SL, Bopp CA, Blake PA. Serotype, antimicrobial resistance, and adherence properties of Escherichia coli strains associated with outbreaks of diarrheal illness in children in the United States. *J Clin Microbiol* 1989;27: 2234-9.
19. Pelayo JS, Scaletsky ICA, Pedroso MZ, Sperandio V, Giron JA, Frankel G, Trabulis LR. Virulence properties of atypical EPEC strains. *J Med Microbiol* 1999;48: 41-49.
20. Viera M, Andrade JRC, Trabulsi LR, Rosa ACP, Dias AMG, Ramos SRTS, Frankel et al. Phenotypic and genotypic characteristics of Escherichia coli strains of non-enteropathogenic E coli (EPEC) serogroups that carry EAE and lack the EPEC adherence factor and Shiga toxin probe sequences. *J Infect Dis* 2001; 183: 762-72.
21. Levine MM, Nataro JP, Karch H, Baldini MM, Kaper JB, Black RE, et al. The diarrheal response of humans to some classic serotypes of enteropathogenic Escherichia coli is dependent on a plasmid encoding an enteroadhesiveness factor. *J Infect Dis* 1985; 152: 550-9.
22. Oswald E, Schmidt H, Morabito S, Karch H, Marches O, Caprioli A. Typing of intimin genes in human and animal enterohemorrhagic and enteropathogenic Escherichia coli: characterization of a new intimin variant. *Infect Immun* 2000; 68: 64-71.
23. Sohel I, Puente JL, Murray WJ, Vuopio-Varkila J, Schoolnik GK. Cloning and characterization of the bundle-forming pilin gene of enteropathogenic Escherichia coli and its distribution in Salmonella serotypes. *Mol Microbiol* 1993; 7: 563-75.
24. E coli isolates annual tables. *ESR Lablink* 1999; 7 (1).
25. Wilson JB, Clarke RC, Renwick SA, Rahn K, Johnson RP, Karmali et al. Verocytotoxinogenic Escherichia coli infection in dairy farm families. *J Infect Dis* 1996; 174: 1021-7.
26. Pradel N, Livrelli V, De Champs C, Palcoux JB, Reynaud A, Scheutz F, et al. Prevalence and characterization of Shiga toxin producing Escherichia coli isolated from cattle, food, and children during a one year prospective study in France. *J Clin Microbiol* 2000; 38: 1023-31.
27. Bennett J, Bettelheim K. Serotypes of non-O157 verocytotoxinogenic Escherichia coli isolated from meat in New Zealand. *Comp Immunol Microbiol Infect. Dis* 2002; 25: 77-84.

Address for correspondence:

Jenny Bennett
 Enteric Reference Laboratory
 ESR Kenepuru Science Centre
 PO Box 50 348
 Porirua, New Zealand

Neuroblastoma: biology of a tumour model

Richard J Mackay, FRACP, Registrar

Department of Clinical Biochemistry, Canterbury Health Laboratories, Christchurch.

Abstract

Neuroblastoma, a childhood tumour of high malignant potential, nevertheless may regress spontaneously in some individuals. Research into the molecular biology and biochemistry of this tumour may therefore provide useful insights into the mechanisms of tumour behaviour and ultimately improve treatment outcomes. Genetic aspects of neuroblastoma, including ploidy changes, deletions of chromosome arms 1p, 11q and 14q, gain of chromosome arm 17q, amplification of the oncogene MYCN, alterations in apoptosis and neurotrophin signalling pathways have all been identified and great progress has been made in relating these abnormalities to tumour behaviour. Knowledge of the catecholamine metabolic pathways has enabled improved detection and screening methods. Application of this information in the clinical field has encouraged the development of a range of new laboratory tests.

Keywords: neuroblastoma, neuroblastoma genetics, MYCN oncogene, catecholamines, neurotrophin signalling pathway, apoptosis.

Introduction

The clinical study of malignancy has gained major impetus over the last decade from new insights into the molecular biology of tumours, and many such insights have resulted in laboratory analyses that are becoming routine. Neuroblastoma, a malignant tumour unique to childhood, was one of the earliest malignancies to be studied and understood in this manner and progress is being made in relating tumour biology with malignant behaviour.

Neuroblastoma has a very serious prognosis, particularly as it is already metastatic at diagnosis in 50% of infants and 75% of older children, yet at the same time spontaneous regression of even disseminated tumour (in those under one year) is sufficiently common that most general paediatricians would have witnessed this. The median age at presentation is 2 years but the tumour may even be present at birth. Neuroblastoma is the cause of about half of the malignancies of infancy and is the commonest extracranial tumour of childhood (1,2). New Zealand has about 6 - 8 cases per year and all are now managed initially in one of three specialist Paediatric Oncology centres in the country.

Origin and presentation

Neuroblastoma arises from sympathoblasts which differentiate from the stem cells of the neural crest. This structure is a broad plate of tissue extending from cephalad to caudad on the dorsal surface of the developing embryo, and which rolls up transversely to form the neural tube. This will eventually develop into the brain and spinal cord. During this process two thin rods of neural tissue parallel to the neural tube remain behind and eventually form the sympathetic chain of neural tissue containing the sympathoblasts, found on either side of the spinal cord. The adrenal medulla is also formed from this tissue (2).

The embryological origin of sympathoblasts explains the anatomical localisation of neuroblastomas. Over 50% arise from the adrenal, and the remainder from ganglia along the sympathetic chain. Whilst the majority are abdominal, some are found in the thorax, pelvis and even the neck.

Not surprisingly, the initial symptoms and signs reflect this distribution. Many present as an abdominal, pelvic or cervical mass, which may have been noticed by a parent, or might have been discovered fortuitously, for example by visualising an adrenal mass on a renal ultrasound done for other reasons. Many will also have an enlarged liver, reflecting metastatic liver disease, and sometimes the finding of an enlarged liver will provoke a search for the primary mass. A cervical mass in the stellate ganglion may cause a drooping eye (ptosis), absent ipsilateral facial sweating and even different coloured irides, a combination of signs called Horner's Syndrome. Thoracic masses are usually noticed incidentally on chest X-ray, or may cause symptoms of mediastinal origin. Metastatic bone disease can cause bone pain or pathological fractures. Bone metastases have a special predilection for occurring around the orbital region, causing bruising and proptosis. Even more bizarre presentations can occur. A few children will present with fever, misery and failure to grow. Because many tumours occur in the sympathetic chain, they may penetrate the spinal foramina into the spinal canal causing spinal compression with a slowly evolving paraplegia. Rarely a baby will be born with multiple subcutaneous blue masses, from neuroblastoma which has metastasised to the skin. Extraordinarily, rare children will present with the "dancing eyes - dancing feet syndrome" (myoclonus - opsoclonus) of jerking movements of the eyes and legs, caused by secretory products of the tumour.

Secretory diarrhoea from tumour vaso-intestinal peptide production has been recorded, as has a syndrome of tachycardia and flushing, reminiscent of a pheochromocytoma, another neurogenic tumour (1).

Staging

Diagnosis of the disease is confirmed by direct tissue biopsy and histology with histochemistry, supported by biochemical and genetic tests described later. It is extremely important however to establish the extent of spread of the tumour as well as the malignant potential, in order to plan the appropriate treatment and offer a reasonable prognosis to the family. This process is called "staging" and an abbreviated outline of the stages is shown in Table 1 (3). Each stage has been somewhat arbitrarily chosen, but has been shown by wide clinical experience to give an approximate hierarchy of severity and thus the need for increasingly aggressive treatment.

Stage 1	local, complete gross excision.
Stage 2A	local, incomplete excision
Stage 2B	same, but lymph nodes positive
Stage 3	unresectable unilateral tumour
Stage 4	distant metastasis - distant lymphatic, bone, bonemarrow, liver, skin etc.
Stage 4S	local tumour with skin, liver and bone marrow spread only, < 1 year age.

Table 1. Stages of spread in neuroblastoma (abbreviated from reference 3)

The stage 4S deserves separate mention. It applies specifically to those infants under one year with disease restricted to the primary tumour, bone marrow, skin and liver only, and which has about a 50% or better spontaneous remission rate, presumably by apoptosis, even if it is untreated. It is also well known that some primary tumours "mature" from malignant undifferentiated primary tumours to more or

less well differentiated ganglioneuroblastomas or benign ganglioneuromas. Such behaviour is more common in neuroblastoma than any other human malignancy although the frequency of such remarkable behaviour is uncertain (1). Some conjectures about this behaviour are remarked upon later.

Biochemical tumour products

The unregulated production by neuroblastoma cells of the normal sympathetic cell products catecholamines - has been documented for nearly 30 years. The major metabolic pathway of production and metabolism of catecholamines is shown in Figure 1 (1,2). Essentially, the precursor dopamine is produced from tyrosine and then converted to noradrenaline by a hydroxylase. Neuroblastoma cells lack the methyltransferase required to convert noradrenaline to adrenaline, which is however present in phaeochromocytoma cells, another neurogenic tumour. Dopamine and noradrenaline are catabolised by the enzymes catechol-O-methyl transferase and monoamine oxidase to homovanillic acid (HVA) and vallinylmandelic acid (VMA)/ methoxyhydroxyphenylglycol (MHPG) respectively. It has been traditional to measure at least VMA excretion as a marker for neuroblastoma and often HVA as well, at least to confirm that it is present with VMA in order to help reduce false positive tests. Some units have also measured MHPG as well, but this metabolite is present only in very small quantities. VMA can be measured, after anion exchange, and washing to remove dietary and drug cross reactants, by elution with acetate and oxidation to vanillin followed by spectrophotometry, a simple method available to all laboratories. A relatively simple method for measuring VMA and HVA by high performance liquid chromatography (HPLC) with electrochemical detection has been described, but for establishing the presence of HVA a simple thin layer chromatography technique is available and more convenient. Capillary gas chromatography (GC) with either flame ionisation detection or mass spectrometry (MS) both require extraction and derivitisation, with the latter used in some mass screening programmes. Monoclonal antibodies to VMA and HVA have been used in immunoassays and incorporated into Japanese mass screening programmes (4).

becoming popular and GC-MS has been described. A small number of tumours will only be detected if dopamine is measured as well. A recent publication concluded that adrenaline and noradrenaline were not elevated in isolation in neuroblastoma, and therefore not useful in diagnosis. However surprisingly little work appears to have been done on normetadrenaline. Recently a new marker in diagnosis, N-acetyl-dopamine, measured by HPLC, was found to be considerably higher in patients than normals (4,5).

The role of measuring catecholamine excretion is to assist in the separation of patients with tumours which can look very similar histologically, known as small blue round cell tumours and includes rhabdomyosarcoma, lymphoma and Ewings tumours. Also they may be useful in following response to treatment in established cases, and in tumour screening programmes (1).

It has been shown that blood levels of ferritin, lactate dehydrogenase, membrane ganglioside GD2 and of neurone specific enolase are higher in patients with disseminated neuroblastoma, but the findings are too non specific to have found much use in clinical diagnosis (1,2). Chromagranin A and Neuropeptide Y are developmentally regulated components of neurosecretory granules and serum levels may prove useful in the future for characterisation of tumour differentiation stage, or for patient monitoring (1).

Neurotrophin signalling pathway

More recently, three cell membrane receptors for the nerve cell differentiation, maturation and maintenance factors, nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF) and neurotrophin-3 (NT-3), have been identified. These receptors are known as TrkA, TrkB and TrkC respectively and appear to be tyrosine kinase type receptors. All may be expressed in full-length form in patients with neuroblastoma, but TrkB and TrkC may also be found in truncated form. Further, the level of expression of these receptors is quite variable but nevertheless tends to relate to the malignancy of the tumour and to other genetic factors. In this way, high levels of TrkA and TrkC and truncated TrkB seem to correlate with rather better prognosis, low TrkA, TrkB and TrkC with an intermediate prognosis and full length TrkB with a poor prognosis.

Neurotrophic signals may therefore exert some modulating effect on the malignancy of the tumour, for example by facilitating spontaneous maturation to a more innocent ganglioneuroblastoma or even ganglioneuroma, but the precise biochemistry is far from clear (2, 6-9).

Genetics

In 1983 an expansion of a region at chromosome 2p24 was shown to occur in 25% of neuroblastomas and subsequently proved to be associated with advanced stages of disease, rapid progression and a poor outcome (10). It turned out that the expansion was due to an amplification of the *MYCN* gene, the protein product of which, *myc*, is a transcription factor which controls the production of some mRNAs. The precise function of the proteins affected by the amplification is not clear, although they are considered to have a role in cell maturation or cell cycle control. Under normal circumstances there is one copy of the *MYCN* gene per chromosome but expansions in neuroblastoma may result from over 200 copies. They may be quantified in the laboratory by Southern blot, fluorescence in-situ hybridization or quantitative PCR, and these are routinely performed by most western oncology centres (2, 11-13).

The details of *myc* control of transcription are rather more complex than this. In fact transcription is modulated by both *myc* and a second protein *max*, the product of the *MAX* gene. When the two combine in a heterodimer, transcription is stimulated, but if two *max* proteins combine in a homodimer, transcription is inhibited. Thus transcription responds to the balance of *myc* and *max* protein in the cell nucleus. Where there

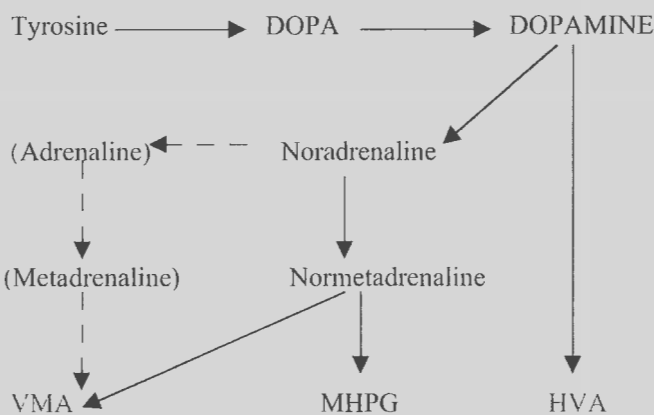


Figure 1. Neuroblastoma pathways of catecholamine metabolism (abbreviated). The additional pathway found in the normal adrenal but not neuroblastoma cells is shown in parentheses and dotted lines. DOPA = dihydroxyphenylalanine; DOPAMINE = dihydroxyphenylalanine amine; VMA = vallinylmandelic acid; MHPG = methoxyhydroxyphenylglycol, HVA=homovanillic acid. (2,4).

Measurement of urinary free catecholamines is commonly done by purification with cation exchange chromatography, oxidation in the presence of ethylenediamine to a fluorescent compound detected by fluorimetry after HPLC separation. Electrochemical detection is also

has been an expansion of *MYCN*, this balance is greatly shifted in favour of the *myc-max* heterodimers, so that transcription is greatly enhanced. This process is shown in Figure 2 (11).

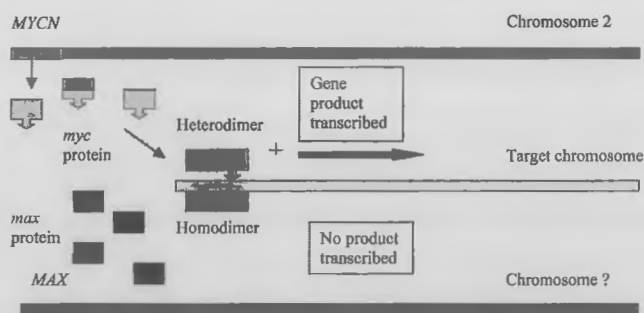


Figure 2a: MYCN transcription in normal cell nucleus

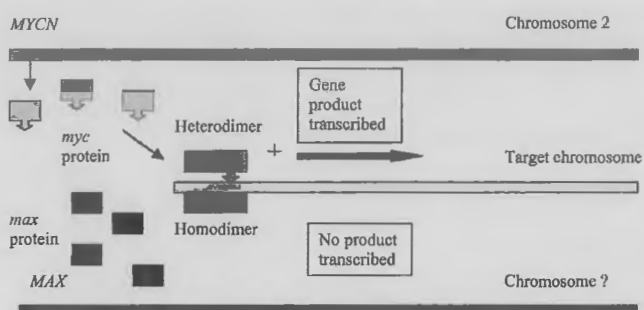


Figure 2b. Transcription in NMYC amplified cell nucleus

Other genetic risk factors

A number of other genetic abnormalities in tumour cell lines are known to increase malignant behaviour of the tumour. Tumour cytogenetic studies have shown that the diploid or tetraploid state (conveniently assessed by flow cytometry), and trisomy of the long arm of chromosome 17 (11,13) increase severity, presumably by increasing genome "dosage" of genes that favour malignancy ie. oncogenes. In some patients, loss of chromosome material from chromosomes 1p (10-14), 11q (13,15), and 14q (11,16), (loss-of-heterozygosity, LOH), and some studies have shown a variable relationship to risk. It is widely anticipated that the material lost from these chromosomes will contain tumour suppressor genes and some progress has been made in identifying these. Southern blot detection for these is giving way to faster and simpler metaphase two colour FISH, genomic PCR and other techniques (13).

Oncogenes and tumour suppressor genes identified in other tumours, including *HRAS*, *TP53*, *CDKN2A* and related genes, have also been investigated, but with controversial evidence of involvement in neuroblastoma (17,18,19).

The multidrug resistance gene *MDR1* and the gene that codes for the multidrug resistance-related protein *MRP* have been studied and the latter appears to correlate strongly with advanced disease, chemotherapy resistance and poor prognosis. *MRP* may therefore turn out to be a worthwhile additional marker to *MYCN* and Trk A, B, and C (11,12,20).

Telomerase expression

Telomerase is a nuclear enzyme which synthesises the telomeric termination of chromosomes, and telomeric shortening has been implicated in cell senescence and apoptosis. One group has studied the activity of telomerase on the grounds that high levels of expression may facilitate malignant behaviour, and identified that in neuroblastoma

cells a high level of activity does indeed correlate with higher clinical risk (21).

Apoptosis

Because neuroblastomas have the highest rate of spontaneous regression of any human tumour, the apoptotic pathway of programmed cell death has been extensively studied. Apoptosis could be caused by a variety of stimuli, including withdrawal of growth factors, down regulation of growth factor receptors, DNA damage, and expression of apoptotic effector molecules among others. While results are as yet tentative, it does appear that some caspases, intracellular enzymes responsible for execution of the apoptotic signal, are expressed in much higher levels in those neuroblastomas with a favourable outcome (22). Other apoptotic variations have been documented but the relationship to outcome is unclear (23).

Cell surface adhesion molecules.

The expression of CD44, a cell surface glycoprotein, has been identified as a very significant independent factor in survival probability in a multivariate analysis (24). As a cell adhesion molecule, any abnormality may play a role in development of metastasis.

Proposed groups

Gathering this information together has enabled the identification of groups of patients of a similar nature that differ in their clinical presentation and, most importantly, in their prognosis. This has allowed the clinician to be able to inform families of the outlook of the tumour, and recommend treatment according to the perceived tumour risk. Whilst arguments about the precise details will no doubt persist, one such risk stratification is shown in Table 2 (12).

Type I	MYCN not amplified, hyperdiploid, TrkA and TrkC high, TrkB truncated. Age <1 year at presentation, early disease and >95% 5 year Survival
Type II	MYCN not amplified, diploid or tetraploid, 17q trisomy, 11q & 14q LOH, Trka, Trkb, and TrkC all low. Age >1 year at presentation, late disease and 20 - 50% 5 year survival.
Type 111	MYCN amplified, diploid or tetraploid, 17q trisomy, 1p LOH, TrkB full length. Age 1-5 years at presentation, late disease and 0 - 20% 5 year survival.

Table 2. Proposed prognostic groups of neuroblastoma patients

Screening

In an attempt to improve prognosis by early detection, several studies have tried to detect the tumour in the first few months of life by mass screening of infant urine VMA. A mass population-screening programme in Japan has been running for more than 20 years (25), and other studies have been conducted in Canada and Europe (26). Whilst it has been possible to detect the tumour early by this means, the majority so detected have been tumours with an excellent prognosis, for example stage 4S tumours and tumours which mature spontaneously to a ganglioneuroma. In contrast, some patients from the previously screened group have presented clinically somewhat later with unfavourable disease. It remains doubtful whether screening has contributed much to reducing occurrence.

Treatment.

Treatment graded according to the spread (stage) of the tumour, and malignancy (risk groups) is now a reality, and includes surgery aimed at

removing, or at least debulking the tumour. Radiotherapy to the tumour may be used where there is bulky unresectable tumour or incomplete removal. In addition most children will receive intensive cyclic chemotherapy. Because chemotherapy may be limited by bone marrow toxicity, much higher doses may be used if followed by bone marrow transplantation. Treatment with monoclonal antibodies has already been studied in phase II trials and could hold promise (27).

Use of such intensive treatment has allowed major gains in outlook (1). In intermediate risk stage 3 patients, using moderately intensive chemotherapy and avoidance of radical surgery and external beam radiation where possible, a non-*NMYC* amplified group younger than one year achieved a 4 year event free survival of nearly 100%. This compares to an older and *NMYC* amplified group 4 year event free survival of 65%. In another group of high risk patients over one year age, in treatment which often included bone marrow transplant, survival at 5 years from diagnosis was nearly 30%, compared with 10% in the previous decade.

Conclusions

The unusual biology of neuroblastoma has rendered it a useful research model for improving the understanding of some of the basic molecular biological processes of cancer, in areas as diverse as oncological genetics, intercellular signalling and programmed cell death. Genetic alterations causing gain of material which stimulates the cell cycle, loss of material with possible tumour suppressor genes, changes in apoptosis, increased drug resistance, changes in cell maturation receptor proteins and loss of intercellular "adhesive" properties are some of the changes which have been identified in the neuroblastoma malignant process.

Future studies of neuroblastoma will refine further important prognostic and treatment variables such as additional disease markers for screening and early detection, characterisation of malignant potential, follow up of treated patients and identification of genetic predisposition. Already there has been a major improvement in prognosis in even advanced disease and further substantial gains are possible. Some research techniques stemming from this work are being applied routinely in clinical laboratories, in both genetic and biochemical areas.

References

1. Brodeur GM, Maris JM. Neuroblastoma. In: Pizzo PA, Poplack DG (eds). Principles and Practice of Pediatric Oncology. Lippincott Williams and Wilkin, Philadelphia, 2002: 895-937.
2. Brodeur GM. Clinical and biological aspects of neuroblastoma. In: Scriver CR, Beaudet AL, Sly WS, Valle D (eds). The Metabolic and Molecular Basis of Inherited Disease. McGraw Hill, New York, 2001: 1167-88.
3. Brodeur GM, Pritchard J, Berthold F, Carlsen NL, Castel V, Castleberry RP, et al. Revisions of the international criteria for neuroblastoma diagnosis, staging, and response to treatment. *J Clin Oncol* 1993; 11: 1466-77.
4. Fitzgibbon MC, Tormey WP. Paediatric reference ranges for urinary catecholamines/metabolites and their relevance in neuroblastoma diagnosis. *Ann Clin Biochem* 1994; 31(pt. 1): 1-11.
5. Graham-Pole J, Salmi T, Anton AH, Abramowsky C, Gross S. Tumour and urine catecholamines (CATS) in neurogenic tumours. Correlations with the other prognostic factors and survival. *Cancer* 1983; 51: 834-9.
6. Kaplan DR, Hempstead BL, Martin-Zanca D, Chao MV, Parada LF. The *trk* proto-oncogene product: a signal transducing receptor for nerve growth factor. *Science* 1991; 252: 554-8.
7. Borrello MG, Bongarzone I, Pierotti MA, Luksch R, Gasparini M, Collini P, et al. *trk* and *ret* proto-oncogene expression in human neuroblastoma specimens: high frequency of *trk* expression in non-advanced stages. *Int J Cancer* 1993; 54: 540-5.
8. Nakagawara A, Azar CG, Scavarda NJ, Brodeur GM. Expression and function of *TRK-B* and *BDNF* in human neuroblastomas. *Mol Cell Biol* 1994; 14: 759-67.
9. Yamashiro DJ, Nakagawara A, Ikegaki N, Liu XG, Brodeur GM. Expression of *TrkC* in favourable human neuroblastomas. *Oncogene* 1996; 12: 37-41.
10. Seeger RC, Brodeur GM, Sather H, Dalton A, Seigel SE, Wong KY, et al. Association of multiple copies of the *N-myc* oncogene with rapid progression of neuroblastomas. *N Engl J Med* 1985; 313: 1111-6.
11. Maris JM, Matthay KK. Molecular biology of neuroblastoma. *J Clin Oncol* 1999; 17: 2264-79.
12. Brodeur GM, Maris JM, Yamashiro DJ, Hogarty MD, White PS. Biology and genetics of human neuroblastomas. *J Pediatr Hematol Oncol* 1997; 19: 93-101.
13. Bown N. Neuroblastoma tumour genetics: clinical and biological aspects. *J Clin Pathol* 2001; 54: 897-910.
14. Caron H, van Sluis P, de Kraker J, Bokkerink J, Egeler M, Laureys G, et al. Allelic loss of chromosome 1p as a predictor of unfavourable outcome in patients with neuroblastoma. *N Engl J Med* 1996; 334: 225-30.
15. Maris J, Guo C, White PS, Hogarty MD, Thompson PM, Stram DO, et al. Allelic deletion of chromosome bands 11q14-23 is common in neuroblastomas. *Med Pediatr Oncol* 2001; 36: 24-7.
16. Thompson PM, Seifried BA, Kyemba SK, Jensen SJ, Guo C, Maris JM, et al. Loss of heterozygosity for chromosome 14q in neuroblastoma. *Med Pediatr Oncol* 2001; 36: 28-31.
17. Ballas K, Lyons J, Janssen JW, Bartram CR. Incidence of *ras* gene mutations in neuroblastoma. *Eur J Pediatr* 1988; 147: 313-4.
18. Hosoi G, Hara J, Okamura T, Osugi Y, Ishihara S, Fukuzawa M, et al. Low frequency of the *p53* gene mutations in neuroblastoma. *Cancer* 1994; 73: 3087-93.
19. Beltinger CP, White PS, Sulman EP, Maris JM, Brodeur GM. No *CDKN2* mutations in neuroblastomas. *Cancer Res* 1995; 55: 2053-5.
20. Goldstein LJ, Fojo AT, Ueda K, Crist W, Green A, Brodeur G, et al. Expression of the multidrug resistance, *MDR1*, gene in neuroblastomas. *J Clin Oncol* 1990; 8: 128-36.
21. Hiyama E, Hiyama K, Yokoyama T, Matsuura Y, Piatyszek MA, Shay JW. Correlating telomerase activity levels with human neuroblastoma outcomes. *Nat Med* 1995; 1: 249-55.
22. Nakagawara A, Nakamura Y, Ikeda H, Hisawa T, Kuida K, Su MS et al. High levels of expression and nuclear localization of interleukin-1 beta converting enzyme (*ICE*) and *CPP32* in favorable human neuroblastomas. *Cancer Res* 1997; 57: 4578-84.
23. Ramani P, Lu QL. Expression of *bcl-2* gene product in neuroblastoma. *J Pathol* 1994; 172: 273-8.
24. Combaret V, Gross N, Lasset C, Frappaz D, Beretta-Brogna C, Philip T, et al. Clinical relevance of *CD44* cell surface expression and *MYCN* gene amplification in neuroblastoma. *Eur J Cancer* 1997; 33: 2101-5.
25. Takeda T, Hatae Y, Nakadate H, Nishi M, Hanai J, Sato Y, et al. Japanese experience of screening. *Med Pediatr Oncol* 1989; 17: 368-72.
26. Schilling FH, Erttmann R, Ambros PF, Strehl S, Christiansen H, Kovar H, et al. Screening for neuroblastoma. *Lancet* 1994; 344: 1157-8.
27. Kushner BH, Kramer K, Cheung NK. Phase II trial of the anti-G(D2) monoclonal antibody 3F8 and granulocyte-macrophage colony-stimulating factor for neuroblastoma. *J Clin Oncol* 2001; 19: 4189-94.

Address for correspondence: Dr R. Mackay, Department of Clinical Biochemistry, Canterbury Health Laboratories, PO Box 151, Christchurch. Email: richard.mackay@cdhb.govt.nz

Validation of a von Willebrand Factor - Factor VIII binding assay to characterise atypical phenotypes of apparent Haemophilia A

Karen L Allan BMLSc, David M Patterson Dip MLT, Mark P Smith FRCPA, FRACP
Haemostasis Laboratory, Canterbury Health Laboratories, Christchurch

Abstract

A forty year old female was referred for investigation of menorrhagia. A detailed clinical history of the patient and her family revealed a significant bleeding history. Extensive laboratory tests including routine haemostasis testing, von Willebrand testing, PFA-100, platelet aggregations and Factor XIII screen discovered the only abnormality as a mildly reduced Factor VIII (FVIII) level in the presenting patient and some of her family members.

A diagnosis of mild Haemophilia A with female lyonisation was considered. However the inheritance pattern in the family was also consistent with an autosomal bleeding disorder, and the Normandy variant of von Willebrand Disease (vWD type 2N) could not be excluded. This disorder is characterised by markedly decreased affinity for FVIII, and may be assessed by a FVIII binding assay.

We have developed, standardised and validated an enzyme linked immunosorbent assay (ELISA) assay that measures the ability of von Willebrand Factor (vWF) to bind exogenous recombinant FVIII (rFVIII). Diluted plasma containing vWF is incubated on anti-vWF coated microtitre plates. Endogenous FVIII is removed followed by incubation with rFVIII and a peroxidase labelled anti-FVIII antibody. The assay gave FVIII Binding levels proportional to the level of functional von Willebrand Factor Antigen (vWF:Ag). Results are expressed as a FVIII Binding to vWF:Ag ratio. This assay allows accurate characterisation of vWD 2N subtypes.

Key Words: Type 2N von Willebrand disease, Factor VIII, Factor VIII binding assay, ELISA

Introduction

von Willebrand factor (vWF) is a multimeric glycoprotein that has two major roles. It is involved in platelet adhesion to subendothelial matrix at sites of vascular injury and serves as a carrier for FVIII and protects FVIII from proteolytic degradation.

vWD is the most common inherited bleeding disorder (1), and comprises two main categories. A quantitative defect (Type 1 and 3) and a qualitative defect (Type 2) (2). Type 2 vWD is subclassified into 4 subtypes, including type 2N characterised by defective binding of vWF to FVIII, and normal platelet adhesion (3,4). Phenotypically type 2N is characterised by levels of FVIII:c that are significantly lower than vWF activity. Routine laboratory tests in type 2N vWD show normal values for bleeding time, ex-vivo platelet function screen (PFA-100), vWF antigen, Ristocetin co-factor activity and Collagen Binding Assay. The only abnormality found is reduced FVIII:c, a pattern of results that is also found in mild Haemophilia A. To differentiate these disorders a Factor VIII Binding Assay must be performed (5).

Case History

The presenting patient was a forty year old female with a history of menorrhagia. There was no history of post partum haemorrhage or bleeding following surgery. A sister also had a history of menorrhagia and excessive bruising with a history requiring re-admission for bleeding following a tonsillectomy. A third sister also had a long history of menorrhagia.

The mother of the three sisters and five maternal aunts had all undergone hysterectomy for menorrhagia and each had a history of abnormal bruising and prolonged bleeding following trauma. Three maternal uncles had excessive bleeding following tooth extraction.

Haemostasis testing was performed on the three sisters initially with the only abnormality found being a consistent mildly reduced FVIII level of 34 - 45 IU/dL (Normal Range 50 - 200IU/dL) in two of the sisters. Both of the sisters with the reduced FVIII level were blood group A.

Later, some of the children of the sisters were also tested, two females had low FVIII levels of 25 and 32IU/dL, menorrhagia was already noted. Two young male offspring who have had no laboratory testing performed as yet were reported to have excessive bruising and increased bleeding following circumcision.

In summary there is a documented extensive bleeding history in three generations of this family involving males and females with the only consistent abnormality being a mildly reduced FVIII level in some symptomatic individuals. Although the phenotype in this family may be explained by Haemophilia A with lyonisation in females, it was critical to exclude type 2N vWD. We therefore set up and validated a Factor VIII binding assay, not previously available in our region.

Materials and methods

Samples

Blood was collected into 0.105M sodium citrate at a ratio of one part citrate to nine parts blood. The blood was centrifuged at 2000g for ten min to obtain platelet poor plasma. Plasma samples were separated and stored at -80°C until testing.

Thirty-six samples (15 male, 21 female) from healthy volunteers were used to establish a reference range.

Known vWD patient samples, one Type 3, 12 Type 1 and one known Type 2N were tested along with ten samples from patients in whom Type 2N was suspected.

vWF:Ag assay

vWF:Ag was measured using an in-house ELISA technique. Microtitre plates (Nunc Immunoplate Maxisorb) were coated with 100µL of anti-vWF polyclonal antibody (Dako) diluted in 0.05mol/L sodium carbonate-bicarbonate buffer pH 9.6. Plates are then left overnight at 4°C.

After washing plates with high salt buffer pH 7.2, 100µL of test plasma diluted in phosphate buffered saline (PBS) is added and incubated at room temperature for three hours. Following another wash step 100µL of horseradish peroxidase labelled anti-vWF antibody (Dako) diluted in PBS is added and incubated for a further three hours at room temperature.

After a final wash step colour is developed using o-phenylenediamine dihydrochloride (OPD), the reaction is stopped by the addition of 1.5M H₂SO₄ and absorbance is read at 490nm.

FVIII binding assay

Before starting the assay a literature review was performed to determine what assay methods were available for determining FVIII binding. Published methods vary, and include the use of a chromogenic FVIII assay (3), specific monoclonal antibodies for vWF (3), and capture of vWF by Sepharose beads (8). Some of these techniques or reagents were not readily available in our laboratory at the time so it was decided to work-up the method described by Casonato and colleagues (9).

Microtitre plates (Nunc Immunoplate Maxisorb) were coated with 200µL of anti-vWF polyclonal antibody (Dako) diluted in 0.05mol/L sodium carbonate- bicarbonate buffer, pH 9.6. Plates were then left overnight at 4°C.

After washing with high salt buffer pH 7.2, the plates were blocked for 1hr at room temperature with 200µL of phosphate buffered saline (PBS) containing 2% bovine serum albumin (BSA). All following steps were performed at room temperature. Plates were again washed with high salt buffer then 200µL of test plasma dilutions, prepared in PBS containing 0.05% polysorbate (Tween) and 2% BSA, were added and incubated for 1hr. Endogenous FVIII was removed from captured plasma vWF via incubation with 0.04mol/L CaCl₂ for 30min. After washing, 200µL of 1.0U/mL rFVIII (Baxter) was added and incubated for 1hr. After washing, the bound rFVIII was detected by adding 200µL of horseradish peroxidase labelled polyclonal anti-FVIII (Affinity Biologicals) antibody diluted in PBS-Tween BSA buffer for 1hr. Colour was developed by the addition of OPD, the reaction was stopped using 1.5M H₂SO₄ then absorbance read at 490nm.

Results

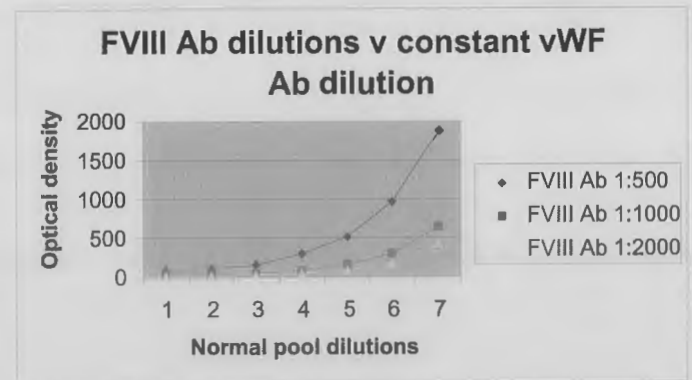
Antibody dilutions

Optimal dilutions of both the primary (anti-vWF) and secondary (anti-FVIII) antibody needed to be established. A microtitre plate was coated with varying dilutions of primary and secondary antibody with normal pooled plasma (NP) used to establish a standard curve.

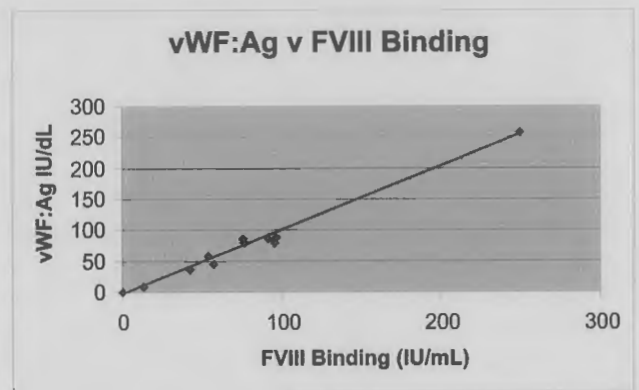
Three primary antibody dilutions (1:500, 1:1000, 1:2000) were coated onto a 12 row, 8 column flat bottomed microtitre plate. Three rows each were coated with either a 1:500, 1:1000 or 1:2000. Serial dilutions of NP plasma (1:25 to 1:1600) plus a blank were added to each row. The secondary antibody was applied using dilutions of 1:500, 1:1000 or 1:2000. The plate was then processed using the method previously described.

No difference was seen in the varying dilutions of the anti-vWF antibody. Therefore the highest dilution using the least amount of antibody was selected for use (Figure 1).

The anti-FVIII antibody gave poor optical density results at high dilutions (1:1000 and 1:2000) so the 1:500 dilution was used (Figure 2).



Patient samples with a range of vWF:Ag of 13 - 249IU/dL were then tested to establish the relationship between vWF:Ag (IU/dL) and FVIII Binding (IU/mL). A sample from a patient known to have Type 3 vWD was also tested to check for non-specific binding. (Figure 3)



Reference range

Thirty six normal samples were tested to establish an interim reference range for the ratio of FVIII Binding to vWF:Ag. Analysis determined a reference range of 0.7 - 1.3 (mean ± 2 SD, Table 1 [next page]). These results compare favourably with the original published method which demonstrated a reference range of 0.6 - 1.3.

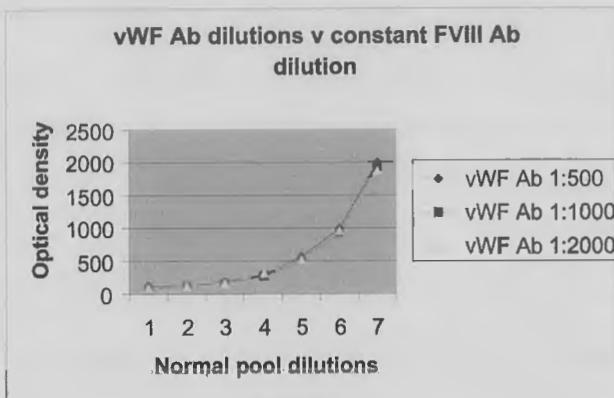


Table 1. Reference range for FVIII Binding/vWF:Ag

FVIII Binding (U/L)	vWF:Ag (IU/dL)	FVIII Binding/vWF:Ag
132	103	1.3
111	100	1.1
63	57	1.1
265	232	1.1
174	140	1.2
132	140	0.9
234	241	1.0
302	250	1.2
196	155	1.3
91	98	0.9
67	64	1.0
112	95	1.2
132	128	1.0
205	190	1.1
121	137	0.9
125	101	1.2
87	74	1.2
135	120	1.1
88	80	1.1
130	120	1.1
53	88	0.6
120	124	1.0
95	85	1.1
80	76	1.1
113	83	1.4
58	54	1.1
85	69	1.2
85	75	1.1
86	91	1.0
87	96	0.9
65	84	0.8
258	249	1.0
80	95	0.8
36	42	0.9
44	57	0.8
100	100	1.0

Mean = 1.0

Standard Deviation = 0.15

95% confidence interval = 0.995-1.105

Patient samples

Ten patient samples, three from our presenting family and seven referred from other centres throughout New Zealand were tested along with a known type 3 vWD and a known type 2N vWD, kindly provided by the Institute of Medical and Veterinary Science, Adelaide, Australia. (Table 2).

Table 2. Patient results

Patients	FVIII Binding (U/L)	vWF:Ag (IU/dL)	FVIII Binding/vWF:Ag
A	142	120	1.2
B	79	88	0.9
C	117	116	1.0
D	67	57	1.2
E	111	112	1.0
F	92	83	1.1
G	192	191	1.0
H	72	112	0.6
I	183	274	0.7
J	218	189	1.2
Type 2N vWD	2	118	0.02
Type 3 vWD	1	1	1.0

One patient gave a result slightly below the normal range but it was felt the result was not significant especially when compared to the known Type 2N vWD.

Discussion

We describe an ELISA method for FVIII Binding activity that appears sensitive to vWF variants affecting the Factor VIII binding site. Previous methods described (3,8) are cumbersome, time consuming and require reagents and techniques beyond the scope of many laboratories.

This method provides a quantitative evaluation of FVIII Binding capacity and appears to be sensitive, although we acknowledge that only one known type 2N vWD has been tested. The assay also appears to be specific as the plasma from a patient with type 3 vWD gave an absorbance similar to that of the buffer blank, indicating the absence of any non-specific binding of other proteins to the primary vWF antibody.

By comparing FVIII Binding to vWF:Ag and expressing the results as a ratio this assay has the ability to assess and report FVIII binding capacity even when the vWF:Ag is reduced in moderate and severe type 1 vWD.

While the family under investigation gave normal values for FVIII binding and therefore do not have type 2N vWD, the assay is now available for any similar patients presenting in the future. The assay is indicated for assessment of patients thought to have Haemophilia A with atypical bleeding symptoms or apparent autosomal inheritance, or in patients with type 1 vWD where the FVIII level is disproportionately low.

It appears that the FVIII binding assay is not performed by many laboratories, possibly due to the previous cumbersome methods employed. An international survey by the Scientific and Standardisation Committee of the International Society on Thrombosis and Haemostasis found only 16 laboratories performing a test for FVIII binding activity (10). Of those laboratories that perform the test, most have found patients with type 2N vWD, so it may be that the incidence of type 2N vWD is higher than is presently thought as some patients may be incorrectly classified as mild Haemophilia A. The recommendation from this survey was that all patients with a FVIII deficiency not demonstrating X-linked inheritance should be tested for FVIII binding activity.

In another study, 177 unrelated patients previously diagnosed as Haemophilia A and 199 unrelated patients with Type 1 vWD were tested for FVIII binding capacity (11). In this study 13 patients from 8 unrelated families were found to have type 2N vWD.

Distinction between type 2N vWD and mild Haemophilia A is important because the genetic counselling differs from that of Haemophilia A as type 2N vWD is autosomal recessive. Moreover the kinetic response to treatment of the two conditions is different, with substantially shorter Factor VIII elimination half-life, yet normal Factor VIII synthetic capacity in type 2N vWD.

In conclusion, we present the implementation and validation of an assay measuring FVIII Binding capacity that will be useful for the assessment of patients with reduced FVIII levels where inheritance is not clearly X-linked.

References

1. Rodeghiero F, Castaman G, Dini E. Epidemiological investigation of the prevalence of von Willebrand disease. *Blood* 1987; 69: 454-9.
2. Sadler JE. A revised classification of von Willebrand disease. *Thromb Haemost* 1994; 71: 520-5.
3. Nishino M, Girma JP, Rotschild C, Fressinaud E, Meyer D. A new variant of von Willebrand disease with defective binding to factor VIII. *Blood* 1989; 74: 1591-9.
4. Mazurier C, Dieval J, Jorieux S, Delobel J, Goudemand M. A new von Willebrand factor (vWF) defect in a patient with factor VIII deficiency but with normal levels and multimeric patterns of both plasma and platelet vWF. Characterization of abnormal vWF/FVIII interaction. *Blood* 1990; 75: 20-6.
5. Mazurier C, Gaucher C, Jorieux S, Parquet-Gernez A, Goudemand M. Evidence for a von Willebrand defect in factor VIII binding in three members of a family previously misdiagnosed mild haemophilia A and haemophilia A carriers: consequences for therapy and genetic counselling. *Br J Haematol* 1990; 76: 372-9.
6. Short PE, Williams CE, Picken AM, Hill FG. Factor VIII related antigen: an improved enzyme immunoassay. *Med Lab Sci* 1982; 39: 351-5.
7. Favalaro EJ, Smith J, Petinos P, Collecutt M, Street A, Hertzberg M. Laboratory testing, diagnosis, and management of von Willebrand's disease. Current practice in Australasia. *Am J Clin Pathol* 1999; 112: 712-9.
8. Miller C, Kelley L, Green D. Diagnosis of von Willebrand disease type 2N: a simplified method for measurement of factor VIII binding to von Willebrand factor. *Am J Hematol* 1998; 58: 311-8.
9. Casonato A, Pontara E, Zerbinati P, Zucchetto A, Girolami A. The evaluation of factor VIII binding activity of von Willebrand factor by means of an ELISA method: significance and practical implications. *Am J Clin Pathol* 1998; 109: 347-52.
10. Mazurier C, Meyer D. Factor VIII binding assay of von Willebrand factor and the diagnosis of Type 2N von Willebrand disease - results of an international survey. *Thromb Haemost* 1996; 76: 270-4.
11. Schneppenheim R, Buddle U, Krey S, Drewke E, Bergmann F, Lechler E, et al. Results of a screening for von Willebrand disease type 2N in patients with suspected Haemophilia A or von Willebrand disease Type 1. *Thromb Haemost* 1996; 76: 598-602

Correspondence: David Patterson, Haemostasis Laboratory, Canterbury Health Laboratories, PO Box 151, Christchurch. Email: david.patterson@cdhb.govt.nz

2003 EXAMINATION INFORMATION

The NZIMLS invites those wishing to sit the Fellowship Part One examination, the Qualified Technical Assistant or the new Qualified Phlebotomy Technician examinations this year to either:

- ◆ Go on-line to www.nzimls.org.nz to download the examination application form(s)

OR

- ❖ Contact the NZIMLS office at: nzimls@eenz.com, or write to PO Box 505, Rangiora or ring the NZIMLS Office (03) 313 4761 to request the examination information. This will be sent to you.

Important Dates in 2003:

30 April 2003 – closing date for Fellowship Part One Examinations
23 May 2003 – closing date for QTA / QPT Examinations

5 November 2003 – QTA / QPT Examinations
12 & 13 November 2003 – Fellowship Examinations

NB: The QTA examination discipline range is being extended this year to include Phlebotomy. Successful candidates undertaking this examination will receive certification as a:

Qualified Phlebotomy Technician

Obituary

Alexander Don Kirkland (1944 - 2003)

Don Kirkland began his long career in clinical chemistry in 1969, when, as a recent Otago graduate with a BSc, he was appointed to the Dunedin Hospital Chemical Pathology Laboratory as a graduate technologist. He was to continue working in the laboratory until his untimely recent death, following a protracted battle with cancer.

In his early days, Don worked with Jim Dunckley and Audrey Munro, in particular, and quickly developed expertise in the (then) time-consuming, hands-on methods required for various urine steroid measurements. By 1973 he was in charge of this area of testing, and for many years oversaw the weekly plasma cortisol run, and the regular struggles to produce timely urinary oestriol results for the clients of the obstetric services.

Don's employment status shifted to the Hospital Scientific Officer's group when that was developed. HSO's were put in place to provide some extra research and development skills; Don's forte was establishing and developing new techniques, rather than

original research, and he was very good at removing unnecessary steps and refining methods to produce good results with the minimum of fuss.

He continued to take a very active role in the day-to-day activities of the Chemical Pathology laboratory as they changed in response to the many pressures of the 1980's and '90's. He maintained a practically oriented and quizzical scrutiny over the shifts in management style, technique and focus, and his advice was always directed to the point of providing good quality test results for patients.

Outside of work, Don was a nationally ranked pistol marksman, and developed an intense love of the outdoors, and for hunting and shooting in the high country. He was an enthusiastic driver of large and powerful cars, and he enjoyed socialising with his friends in different clubs that reflected his mix of interests. He will be remembered by many people for his friendship, and by numerous past and present laboratory staff, as a committed and hardworking laboratory scientist, as well as a valued colleague and friend.

IFBLS Newsletter - November 2002

Dear Colleagues,

I send you greetings from my fellow Council Members and myself.

This is my first Newsletter following my election as President at the GAD in Orlando in August. Those of you who were present will already be familiar with some of what follows, for others it will all be news. It is my intention to make this Newsletter a regular feature and I would encourage you to reproduce it, all or in part, in your own national newsletters/journals/gazettes.

We on Council sometimes feel, in some instances, that IFBLS information sent to our member associations never travels beyond the national office and as a consequence the ordinary members of the national associations are unaware of what IFBLS is or what it does. We would like this to change and we seek your assistance in ensuring that all our members and colleagues worldwide are aware of the role of IFBLS.

I have listed below information that is of interest to our members.

Name change

Among the many decisions made by the General Assembly of Delegates at the World Congress of Biomedical Laboratory Science in Orlando, Florida, USA was the momentous one of changing our name from the International Association of Medical Laboratory Technologists to the International Federation of Biomedical Laboratory Science (IFBLS). As some of you may remember, and most of you will know, IAMLT was founded in Switzerland in 1954, so it retained its name for 48 years. When we meet again in 2004 to celebrate the 50th anniversary of the founding of IAMLT it will be the first GAD under the new name of IFBLS. I think most people present at the GAD had a real sense of the importance of the occasion and there was palpable excitement when the vote was carried by more than the required two-thirds of the delegates present.

The change in name has brought some associated difficulties and tasks. We have to register our new name and also make appropriate changes to our website and e-mail addresses. We require a new logo, albeit it is the same image of the globe and microscope with the new lettering underneath. We have to prepare new letterheads and envelopes and, last but not least, we have to estimate the cost of having the presidential silver regalia changed to reflect our new title.

World Congress 2004

Stockholm, Sweden and Lucerne, Switzerland both bid for the World Congress 2004. Prior to the World Congress visits were made by the President and President Elect to both venues. Both countries made presentations to the GAD Open Forum. It was the decision of Council that the 2004 World Congress should be awarded to Sweden. The Congress will take place at the Stockholm International Fairs Convention Centre from June 14th - 18th 2004. The theme of the Congress will be Public Health and Biomedical Laboratory Science. Considerable planning has already been done for the Congress and the President and Past President teamed up with the President Elect, who dwells in Stockholm, in October for a further meeting with the Congress organisers.

Those of you who have already visited Stockholm will be familiar with the charms of this ancient city. Those who will be visiting for the first time in June 2004 are in for a most pleasant surprise. Stockholm is built on a fresh water archipelago that connects with the Baltic Sea. Consequently, water plays a significant role in the way in which the city is laid out and also in its architecture. It is a truly beautiful place. There is a railway station in the convention centre and it is a very short ride

by rail from the city centre to the centre, making access for Congress delegates a simple matter.

The basic structures of both the scientific and social programmes are already in place and they look exciting. It is planned to have a limited number of presentations in Spanish, German and French in addition to the English language presentations. This will broaden the appeal of the Congress.

World Congress 2006

As we know, our colleagues in South Korea have been planning to host the World Congress in Seoul in 2006. During the Orlando Congress a letter of agreement between KAMT and IAMLT (IFBLS) was signed.

World Congress 2008

Council of IFBLS is now formally seeking bids from countries interested in hosting the World Congress in 2008. Those wishing to do so should express their interest by writing to me at the IFBLS office, either by e-mail or via the postal service. Experience shows that a lengthy planning period offers the best chance for a well-organised congress and six years would not be seen as excessively lengthy.

Biomedical Laboratory Science Day

The decision of the GAD 2002 was that the theme for Biomedical Laboratory Science Day (15th April) for both 2003 and 2004 should be "Biomedical Laboratory Science in Public Health". This is in keeping with the theme for the 2004 World Congress.

General Assembly of Delegates 2004

This year the GAD was divided into two parts, the GAD Open Forum, held early in the week and the GAD held on the final day of the Congress.

GAD Open Forum

During the GAD Open Forum on July 30th the delegates broke into three blocks to discuss various aspects of the role and function of the organization.

Group 1:

Mission and strategy on IAMLT finances and membership. Spokesperson was appointed: Ruth Pierce, Canada.

Group 2:

Mission and strategy on IAMLT work related to biomedical science and its presentation Spokesperson was appointed: Helene Breitschopf, Austria.

Group 3:

Mission and strategy on IAMLT work related to education in biomedical science (basic, further, continuing). Spokesperson was appointed: Marie Culliton, Ireland

Each block made a preliminary presentation of its deliberations and more formal and structured presentations were then made at the GAD. The findings and recommendations of the three groups became in turn the backbone of the Action Plan for Council for the next two years. Presentations for hosting the World Congress in 2004 were made by Sweden and Switzerland.

GAD

The President opened the meeting held on August 3rd and welcomed the delegates. Phyllis McColl was warmly welcomed as the new Office

Manager of the organization. The President addressed the meeting. She discussed the benefit of membership in IAML she had observed during her work with IAML, first as a President of her National Organization, then as a Council Member and a President. She weighted the pros and cons of participation she noted for her National Association and as well for other countries she had visited. The full text of the President's address is appended to this document.

Vote counters were appointed from the associations in Canada, Iceland, Ireland, Norway, and Switzerland. An observer from the association in Uruguay was welcomed to the meeting. The host association USA welcomed the delegation. The agenda was approved.

The Minutes from the GAD 2000, Vancouver Canada, were received and approved as correct.

The agenda was agreed as presented and distributed prior to the GAD.

An application for membership had been received from the Institute of Medical Laboratory Science and Technology in Nigeria. The Membership Committee proposed that the application be not approved and gave the following explanations:

According to the IAML Statutes, Article 3.1, the Council of National Associations must be elected by the free vote of their members. In the light of this the application from the Institute of Medical Laboratory Science and Technology in Nigeria cannot be accepted because:

- The Institute is a governmental statutory body established by government decree with Council appointed by government to regulate and control the practice of medical laboratory science and technology in Nigeria.
- It registers all medical laboratory scientists/technologists trained and worked in Nigeria.
- There is in Nigeria an association of medical laboratory science, which is the representative body for the profession. This body is not currently in membership of IAML.

It was stated the Membership Committee would encourage the National Association to seek membership of IAML. The proposal of the Membership Committee not to accept the application from Nigeria was approved.

The delegates had already received the Biennial Report. An addendum was presented and thus received by the GAD. It outlined an agreement with CSMLS Canada that the designated office of IAML will, as of September 1st 2002, transfer to the head office of CSMLS in Hamilton, Ontario, Canada. The CSMLS - IAML Service Agreement will include the following:

- The key staff resource person (Office Manager) will be contracted by and will be accountable to the IAML.
- CSMLS will provide basic office resources.
- CSMLS will provide basic bookkeeping services.
- Additional services requested of CSMLS will be available.

The GAD joined Council as its gratitude was expressed to CSMLS for the provision of the office facilities and its assistance in the recruitment of the new IAML Office Manager.

The Past President, William Younger presented the annual accounts for the years 2000 and 2001 on behalf of the Management Committee. It was noted that the Office cost was less than expected due to the illness of the Executive Director. In response to a query regarding high computer cost in 2000 it was explained that this arose from the anticipated move of the Executive Office to Singapore. As this did not materialise this was lost investment.

The President presented the proposals of the Regulation Committee of amendments of the Statutes and referred specifically to the final section

of the document explaining the reasons for the proposals. The proposals of the Regulation Committee with amendments were agreed. (The full text is to be found in the GAD minutes, which will be circulated.)

The recommendations and proposals of the GAD Open-Forum, along with additions from the Council for the Action Plan 2002 -2004, presented by Noel White President Elect, were accepted as the Action Plan for 2002 - 2004. (The full text is to be found in the GAD minutes.)

The Past President William Younger presented the Budget proposals of Council for the years 2003 and 2004. It was noted that the future arrangements made by the Management Committee regarding the IAML office, will result in considerably less expenditure in that field, making it possible for IFBLS to spend more on the work related to the biomedical science and the profession. It was explained that the books would be maintained and audited in Iceland for the year 2002 and in Canada thereafter.

As the Statutes had been amended requiring the ratification of Council's appointment of auditors the following proposal was made:

- 2002 Borghildur Sigurdardottir, Bakland, Iceland
- 2003 Stevenson & Lehocki, Canada.

These were accepted.

As the number of candidates equalled the number of vacant positions on Council no voting was required. The GAD ratified the following nominations:

- President Elect, Lena Morgan, Sweden
- President, Noel White, Ireland
- Past President, Martha A. Hjalmsdottir, Iceland
- Council Member, James Sakwa, Kenya
- Council Member, Jeanne Isabel, USA
- Council Member, Ruth Pierce, Canada
- Council Member, Stanley Chiek, Cameroon
- Council Member, Sun Chul Whang, Korea

Retiring Council Members, William Younger, Jeanne Irwin and Manabu Nobuoka were thanked for their contribution. They were presented with a certificate for their work on Council. With due respect to the other Council Members, William Younger was thanked for the enormous contribution he had made during his eight years on Council. He expressed his thanks to all those who had supported him and said it had been a truly rewarding time and a personal growth experience. Martha A. Hjalmsdottir then handed over the presidency to Noel White with all her best wishes for success knowing well his abilities to be successful and trustworthy.

Noel White, President addressed the delegates and thanked them for their support. He expressed his intention to work well as the IFBLS President. He spoke of the huge contribution that Martha had made to IFBLS during her term as President, in which she had to take on the role of the Executive Director in addition to the role of President.

There being no further business, Martha A. Hjalmsdottir brought the GAD to a close thanked the delegates for their contribution to the meeting and wished them all a safe journey on their return home.

New Council

It was agreed at its post-Congress meeting that the new Council would adopt the same structure for the IFBLS committees as heretofore.

Address of the IAML President, Martha Á. Hjalmsdottir to the General Assembly of Delegates 2002

Dear Colleagues I welcome you to the General Assembly of Delegates of the International Association of Medical Laboratory Technologists, and declare it open.

Often I have heard people say, what do we as individuals or associations gain from being members of the IAML? Some also state that they cannot see much benefit of membership, but I have not heard anyone state

that they do not benefit by its existence. The opinion that there is a need for an international association seems to be shared by the member associations and also by the national associations that are not in membership of IAMLTL, and that IAMLTL holds that role.

This is a food for thought. Why not participate if IAMLTL is needed? Surely, what IAMLTL needs most of all in order to become stronger, and to be able to do what we think is needed, are more members. I urge the national associations that are not in membership of IAMLTL and who read or hear this to consider membership. If it so happens that their opinion is that IAMLTL does not work as they would chose for their international association, please give feedback. What would you like to see different? I think that some of the things that may be an obstacle are also seen as a weakness within the organization, but a weakness that could be lessened or removed by increased membership.

I started with the question what do we gain from being members of IAMLTL. Before I give you my answer to that question, I would like to state that in my mind it is very necessary for any association and its members to ask this question. In fact I think this should be a part of self-evaluation, which every association should regularly make. Membership of IAMLTL is a part of the services that the association provide for their members and a tool that they use in their own work.

The members of National Associations should, in the same manner, ask themselves; is my association the tool that I want it to be for the best interest of myself and my profession, and preferably consider how they can self secure that it is. By this you can see that this is a question that I have asked myself, as a member of the Icelandic association, President of that association, and as member of Council and President of IAMLTL. I have also asked myself the same questions on a national and regional level.

To answer the question, I would like to mention a few events that I think of as steppingstones in the development of my National Association, and have thus identified as major gains of membership for the profession. I hope that you excuse that I take the examples from my nearest surroundings, and from what I have personally experienced and noticed over the years that I have been involved with IAMLTL, both as a President of a National Association and as a member of the IAMLTL Council.

In Iceland we are very few who belong to the profession of biomedical scientists. This reflects that Icelanders are few, 300.000 inhabitants. The members of the Icelandic Association is around 350, thus the rate is a bit more than 1 biomedical scientist per 1,000 inhabitants. It can also be mentioned that all biomedical scientists working in the health care sector are members of the association. It is often good to see how things develop generally by looking at small societies, where it is easier to have an overview, than in larger and more complex societies, but still the same things need to be implemented to provide good health services, which I believe my country has the reputation of doing.

Based on how few we are we have a strong feeling of the need to see how the associations of biomedical scientists are structured in other countries and what their main activities are. Through this we have developed our organization and provide wider services to the members than we would have done otherwise. I do not think that it is only based on the numbers that we need to see what others are doing. I think that all need to look outside of their own area to gain knowledge and increase their wisdom. This belief is firmly based in my mother tongue, as the word that we use for stupid or ignorant in Icelandic, means in fact, to stay at home.

The founders of the Icelandic association had at the very beginning the wisdom to join the global organization of the profession, namely IAMLTL, believing that it was important for the development of the association and the biomedical science in the country. For this I have ever been grateful, as I think it is one of the main things that has made it as good an association as it is.

I also saw this same opinion in the actions of one of the IAMLTL youngest members, Chile, when I had the opportunity last year to attend the First Latin American Meeting of Scientific Societies of Laboratory and Blood Bank that they organized, and witness the establishment of a Latin American Society. It impressed me to see how clear their vision is of belonging to the profession on a global level, and how they can learn from it and also provide their knowledge and experience regionally and globally.

In the eighties, when I was the President of the Icelandic association, we were very occupied with our identity and our image. The origin of this discussion was our need to define our profession and its responsibilities, both for internal and external purposes. A major help in these discussions came in the form of the IAMLTL Code of Ethics, where the view of the profession worldwide is defined very clearly, namely - what do we as biomedical scientists want to stand for, and how do we want to reflect our profession and be reflected. My association agreed with the IAMLTL Code of Ethics, but agreed to spend one wither in discussing how it fit the Icelandic situation and our way of thinking. The result was that we created our own Code of Ethics based on the IAMLTL one, and in fact very similar. Since then it has been the custom of the association to greet new colleagues, at their graduation as biomedical scientists, with a rose and the Code of Ethics and bid them welcome into our profession and association. When the discussions about the ideology and methodology in quality started in earnest and became the issue everywhere, we could see that other associations within IAMLTL were occupied with this and we could join this work and make use of the documents produced by IAMLTL.

The Nordic Group of Biomedical Science, NML, the forum for associations from the Nordic Countries, worked together on quality issues at that time. The discussions and ideas gained through IAMLTL were used as a basis for our work related to definitions of quality assurance and in creating the NML guidelines for developing quality standards for laboratories. This work we have in return given back to IAMLTL, in the form of active participation of members from the Nordic Countries in the IAMLTL Council in the work related to quality through the years. The main driver of that work, Marja-Kaarina Koskinen, is in fact still involved as the IAMLTL Liaison Officer with NCCLS, and the coordinator for the IAMLTL Expert Group that is being established in Quality.

The latest stepping-stone in this development for my National Association was put in its place during the celebration of its 35th anniversary in May. Then the association's policy and proposed methods, aimed at securing the quality of Near Patient testing, was introduced to the health authorities and health care providers in the country. The expertise of biomedical science in this field and the importance of using the knowledge of the profession were clearly pointed out. This work is based directly on the IAMLTL ideology and its documentation related to this matter.

The International Directory of Education in Biomedical Science, edited by Britta Karlsson et al. at the North-Eastern University in Boston, and issued by IAMLTL has been a treasure-trove of information on how the education in biomedical science is designed in different countries. It served me well indeed as the President of the Icelandic Association. In that capacity I was responsible for consultation for the Ministry of Health, who questioned the professional capacity of biomedical scientists from other countries who sought for licence to work in the country. By the Icelandic legislation the quality of the education is the prime factor related to get the licence to work as biomedical scientist, and my main tool in this was the Directory and it is still the main tool available for the present President. The Directory has also been very useful for me in my role as a member of the board of biomedical science education in my country, the main body of development of the education.

I am also pretty sure that I have seen the effect of the Directory and other work of IAMLTL related to education, in the work of the Danish

association in the past. For years it struggled with the education authorities with the purpose to raise the level of education in biomedical science in Denmark. It was at that time on a lower level than in the other Nordic Countries and also many other IAMLTL countries. I believe it has been one of the strongest arguments of the Danish association, to be able to indicate this difference by comparing the education in different countries within IAMLTL, and to have that cooperation available in this document issued by IAMLTL. Now this work has met gradual success, as those who have graduated the last few years have an education pretty close to the BSc degree, and after the next year all will graduate with that degree.

The IAMLTL Congresses have been very well attended by Icelandic biomedical scientists. They have learned a lot of things at the Congresses, but the knowledge that I value the most is that they come back knowing that the work they provide at the laboratories at home is quality work and that they stand at the front with their equals. This has been one of the best methods to raise their level and their belief in themselves - their self identity as individuals belonging to a profession that is global, and sets high quality standards.

I could continue for considerable time to refer to items that I think are of high importance to National Associations and are based on the output from IAMLTL to the associations. I think though that I have mentioned enough issues to get you started on making an evaluation for yourselves. Instead I will use our time to discuss the input my National Association has given in return to IAMLTL, in other words what the Icelandic Association has done to strengthen IAMLTL. For this purpose I will provide a list of the issues that I think are obvious and should in fact been recognised as minimal input of any National Association in membership of IAMLTL.

The Icelandic Association has during the time I have followed its development done the following things:

- Paid the membership fee on time.
- Appointed Chief Delegate and other official delegates to the General Assembly of Delegates. Given them the opportunity to prepare well for the meetings and provided them with authority to participate actively in discussions and decision-making.
- Answered questionnaires and given information that IAMLTL asked for.
- Provided its members with information on the policy and activities of IAMLTL, and encouraged them to make use of it.
- Encouraged members to participate in IAMLTL Congresses and assisted them to do so in many ways.
- Nominated a candidate for the IAMLTL Council and been supportive for this individual.
- Nominated a President for the IAMLTL, and stood as solid rock behind me, who happen to have been chosen for that responsibility.
- All those issues are in fact simple and easy to do, and in my meaning a fair price for the gains that the association gets from being a member of IAMLTL.

In this evaluation of the gain of being members of IAMLTL, I think it is also fair that I show you my evaluation on the gains and costs for me as a person of being involved in the work of IAMLTL for some time. If I start with the gains I would like to list them in the following manner:

- Through the work within IAMLTL, but not the least as the IAMLTL Liaison Officer with the World Health Organization, I have gained some understanding of laboratory services on a global level and its role in the health services and health sciences.
- I have gained some insight in how a huge UN organization, like the World Health Organization, is constructed and works. I have been introduced to health issues on a global level, and learned to understand somewhat how they are reflected on a regional and national level, and vice versa.

- I am not stating that I am now an expert in this field, but my knowledge is much improved.
- Through participation in the management of IAMLTL, I have been able to use the knowledge I have in that field, learn from others and develop my skills. Although it was not by choice, I have also had the experience of serving as the IAMLTL Executive Director and thus gained the knowledge of the organization from a different point of view than is normally possible for its Presidents. Thus I got the opportunity to clarify in my mind the difference of participating in the management of the organization as an employee and as elected on the Council. I also learned more about what actually has been done and needs to be done at the IAMLTL office.
- I can confess that I learned more than I really wanted in book keeping, accounts, rates of currency, and bank transactions. Who knows how I will gain from this in the future, but I have the feeling that I have become a bit more patient - a virtue that I can well use.
- I have visited many different countries and seen places that I would definitely not have seen otherwise, and what is even more important to me, been shown those places by my colleagues, who explained to my what I was seeing and sensing. I have thus experienced hospitality that I will never forget. So now I know more about different cultures, different ways of thinking, and the generosity of my colleagues worldwide. I sincerely hope that this has made me more understanding person.
- Last but not the least, I have made friends that I believe will remain so here after. It is in fact such a fun to work on the IAMLTL Council. We discuss indeed professional issues, but also the personal issues, how it is at home. It has been giving to learn how the other ones cope with their work and the IAMLTL responsibilities, and battle to find time for the family duties and to participate in the family pleasures. I can tell you that all Council Members have relatively high responsibilities in their jobs, plus this voluntary and time-consuming work for IAMLTL.

If I list the cost for these personal input in the same manner as I did for the input of my National Association I would mention following items:

- Time that I could have used for other purposes, but it is difficult to calculate if that time would have been spent on more valuable items to me.
- Effort to fulfil my responsibilities, again this is also difficult to consider only as cost, as it may have had effect on my personal development for the better.

Why do I take this on that personal level? The one and only reason is that I sincerely think that IAMLTL needs you to be interested in being nominated for Council. It needs you to understand what opportunities it can bring you as persons, and how the feeling is to be able to participate in making this organization work as you think it should work. I think one of the main weaknesses of IAMLTL is that we do not have enough Candidates to choose from when we are electing our Council. I say this with all respect to us who have been nominated and elected without voting, but I think that all can see that it serves the organization better to have healthy competition for the votes to become a Council Member. I challenge you, who are here, do consider if you would like your National Association to nominate you for Council. If you are not interested or otherwise bound, do consider whom you would like to see on the Council in the future from your association.

I believe that the future of IAMLTL is bright. I would like to think that now the path is clear to increase the professional work of the organization.

The Council that is now finishing its term has spent most of their effort in restructuring the organization, defining the mission and setting the strategy. This was based on the decision of the last GAD, but

became, because of the circumstances that are known to us all, a much more hectic and detailed work than we bargained for.

It is not a comfortable situation for any Council to start their work without having any host for the next Congress, and then to lose its Executive Director due to long-term illness. However that was not a problem in itself, but a task to solve, a person to say goodbye to as a co-worker, but to keep as a friend, a task to use to learn from through working on it. The proposal for the amendment of the Statutes is the Council's last project in this work, a work that we finished with the realisation that we could and should go all the way and make a proposal for a new name and thus state how we would like to look at ourselves as an organization and how we would like to be reflected in that name. I sincerely hope that the General Assembly of Delegates agrees with

the IAML Council in this.

My vision for IAML is that it is a truly an International Federation of Biomedical Science, representing biomedical science and biomedical scientists globally. I see it in the future as a respected organization that gives input to the health services globally, regionally, and nationally. Its strength will be the strength of the regions within IAML, as well as the National Associations, and vice versa.

Thus, on all levels will work at strengthening the individual biomedical scientists in performing their work at the laboratories and in other places in the health systems, for the benefit of those who use and need their services.

It is a responsibility to belong to a profession within the health sciences, but it is also a great opportunity to matter.

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CPD program - a report on the review

In December 2002 the NZIMLS undertook a review of its Continuing Professional Development (CPD) program. The review team comprised of practicing scientists, laboratory management and NZIMLS Council representatives and considered submissions received from interested parties and members of the NZIMLS. The following is a report outlining the recommended changes to the program submitted to Council for ratification. Many of the modifications recommended by the group have been made in anticipation of the expected changes to the regulations governing the annual licensing of Medical Laboratory Scientists in New Zealand. Once ratified by Council the modified program is to be introduced into use on the 1st April 2003.

The review group recommended retention of the administrative aspects of the old program to include continuation of the three-year term, collation of yearly claims, and retention of the auditing steps. Allocation of the points for various activities in the program received the closest scrutiny. Out of this has come the recommendation to reallocate points for many existing categories and the introduction of a several new categories. One of the most significant steps affects category one on the current CPD program list. In the old program 50 points were allocated for work in a laboratory, irrespective of hours. This has been modified into a "compulsory" category and has been renamed "Annual Training Document Review". Sixty points are available for the assessment of laboratory competencies within an individual's scope of practice. This provides the revised program with a measure of "in laboratory" competency together with the established sections focusing on professional development. The review group recommended a change to the name of the program to incorporate the term "competence". This has led to the adoption of the name of the program to read "Competence and Professional Development".

CPD Points Categories

1. Annual training document review (Compulsory)	60 / yr.
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New section: Compulsory - laboratory competence within the designated scope of practice. Peer review assessment conducted as part of the "in laboratory" requirements of IANZ accreditation. Points allocated in this category recognise, competence to practise within an individuals designated scope of practise and recognises also the less formal professional development that accompanies both part-time and full-time laboratory employment. Other "non-scientific" activities included within this group are laboratory and section management, the practise of occupational safety, and the application of the principles of quality assurance in routine laboratory testing. Please supply a copy of your updated annual training documentation and details of employment e.g. hours of work etc. if requested to do so as part of the audit process.

2. Laboratory technique - retraining, refresher courses	16 / day.
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Visits to laboratories (or elsewhere) for the purpose of updating, learning new scientific technique, or for training in the use of instrumentation (e.g. training visit to a regional, specialist, or reference laboratory). Sixteen points per day or pro rata for part day. If requested, please provide relevant details to include places, dates, equipment etc.

3. Laboratory method development & review	10/method
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New section: Development or assessment of new laboratory methodologies to be used as part of the laboratory's testing menu. Includes scientific evaluation of new technologies or the re-evaluation of current methods conducted prior to the introduction of new laboratory test procedures. If requested, please provide relevant details to include techniques, dates, equipment etc.

4. IANZ laboratory audit	internal 8 / day external 8 / day
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Divided into two areas. Internal audit - formalised in-house evaluation of laboratory quality as applied to equipment, supplies, documentation, quality control, staff performance and procedures. External auditor - technical expert member of the review team acting on behalf of IANZ or other agency(s). Eight points per day or *pro rata* for a part day claim. If requested, please provide relevant details of evaluation to include dates, times etc.

5. Student training supervision	5 / semester
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New section: Laboratory staff involved in "at the bench" student teaching as part of the 4th year of the New Zealand Bachelor of Medical Laboratory Science programs. (NB: **Only** designated laboratory training supervisors/personnel are eligible). If requested, please provide relevant details of students / institutions / semesters etc.

6. Scientific meeting, NZIMLS special interest group, user group meetings etc. (meeting attendance)	16 / day
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Sixteen points per day or *pro rata* for part day claims. A list of scientific meetings considered suitable for CPD points is provided on page 12 of this booklet. These include NZIMLS and AIMS Special Interest Group meetings and annual scientific meetings and others. Not included on this list are several User Group Meetings (UGM) that have become annual events. These are usually hosted by the laboratory supply companies and are valuable sources of CE. Most of these meetings have been evaluated and CPD points assigned for attendance. The provision of Certificates of Attendance on which the CPD point value is recorded is common. The list of pre-accredited meetings is not extensive. This does not mean that there are other meetings that are not suitable. If you attend a meeting that has not been evaluated for CPD points and you consider the meeting to have been sufficiently beneficial then submit a claim together with details of the meeting and a contact for a member of the organisation that hosted the meeting. If selected as part of the audit process please provide evidence of attendance to include registration details, certificates, programs etc.

7. Post graduate study (appropriate)	20 / paper.
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Enrolment and successful completion of an appropriate post-graduate tertiary qualification and/or NZIMLS Fellowship. Claims under this category are acceptable following receipt of notification of success by the Institution offering the qualification. If requested please provide programme details, receipts for enrolment, notification of results etc.

"Appropriate" = medical science, management, technology, quality, occupational safety and health etc.

8. Scientific paper publication (peer reviewed & non-peer reviewed)	20 / 10 per article primary author 10 / 5 per article - co-author
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Publication of a scientific or profession related article either as primary or co-author in refereed or non-refereed journals. Primary author in peer reviewed journal = 20, non-peer reviewed = 10. Co-author peer reviewed = 10, non-peer reviewed = 5. If requested please provide a copy of the publication, and any other relevant information.

9. Presentation (primary presenter at Scientific meeting)	20 / oral presentation 5 / poster presentation
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Oral or poster presentation at a scientific meeting (primary presenter only). If requested please provide meeting details and a copy of the abstract from the meeting's program.

10. Structured reading	20 / submission
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New section: Submission of a review article on a set topic. Reviews must be prepared and submitted according to the "Instructions for Authors" in the NZIMLS Journal. All reviews will be graded and returned with those receiving a "pass" grade eligible as a claim for CPD points in this category. If requested please provide a graded copy of the submitted review article.

11. Self assessment programs	5 / program
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Hard copy and web-based programmes are eligible under this category. If requested please provide copies of the program(s) and/or web address(es).

12. Journal articles, web based learning.	2 / article
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New section: Reading of the scientific literature in both hard copy and using web-based access, are eligible under this category. If requested as part of the audit process please provide a 150 word synopsis for each of articles claimed under this section together with a photocopy of the first page of the original article. If claims for web-based articles have been included please (in addition to the above) provide URL, dates and times etc.

13. Book review (published)	10 / review
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Publication of a book review on MLS related subjects. Unpublished reviews do not qualify. If requested please provide copy of the publication, and any other information relevant to the publication(s).

14. Case study / seminar / lecture (in house)	10 / hr. oral presentation 3 / hr. attendance
-----------------------------------------------	--------------------------------------------------

Attendance or presentation at "in house" CE activities or programs. Presentations covering less than 1hr but greater than 30 min. should

claim the maximum 10 points. Presentations of 30 min or less claim 5 CPD points. Similarly for attendance, a claim of 3 and 1.5 points respectively. If requested please provide details of subject, date, place, and time. If a claim for participation in web-based tutorials has been included please provide details of the, topic, presenter, URL, dates and times etc.

15. Formal lecture or clinical tutorial (University, Polytechnic)	5/lecture, 30/yr. max.
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Includes lectures given as part of a structured program of teaching at a University or Polytechnic over and above normal laboratory employment. If requested please provide the name of the number of lectures, an outline of each lecture and the name of the Institution.

16. Examiner / moderator / structured reading assessor (SRA)	20/examination/yr. 10/moderation/yr. 10/as SRA/yr.
--------------------------------------------------------------	----------------------------------------------------------

Appointment as either examiner or moderator for Medical Laboratory Science (or related) examinations conducted on behalf of the NZIMLS, NZ Universities or Polytechnics and other organisations. Suitable claims include examination of NZIMLS Fellowship treatises and reviews submitted as part of the structured reading programme. If requested please provide copy of the examination paper and other relevant details.

17. Professional service (NZIMLS Council, MLTB, SIG convenor etc.)	10 / yr. max. or 2 / meeting
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The following activities are examples of service to the profession:

- Administration of the profession's affairs through the NZIMLS Council. Includes co-opt's to Council sub-committees.
- Appointees to the MLTB and MLTB sub-committee co-opt's.
- Convenors of NZIMLS Special Interest Groups.
- Membership of NZIMLS annual scientific meeting, organising committees.
- NZIMLS representatives on Board's of Study (or equivalent) of tertiary teaching institutions.
- Preparation of SIG workshops etc.

A maximum of 10 points per annum or 2 points per meeting/activity. If requested please provide the relevant details to support claims..

18. Others (specify)	on application
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Claims not covered in other sections of this schedule. Please provide relevant documentation that may be helpful to the committee assessing claims under this section.

Programme information - taken from the CPD booklet Things to do

1. **Enrol** - if not a current financial Member of the NZIMLS please complete the membership application form and post together with a cheque or credit card details to the NZIMLS. Enrolments will be accepted at any stage throughout the year although the start date of each three year term will be back-dated to commence on the 1st of April in the same year of enrolment. If you are a current member of the NZIMLS and wish to enrol in the programme please complete the enrolment included and forward to the NZIMLS. Membership application and enrolment forms are also available at www.nzimls.org.nz

2. **Yearly submissions** - at the end of each year (around Feb-Mar), you should record your claims on the submission sheets (included in this booklet and downloadable from www.nzimls.org.nz) and forward to the Executive Officer of the NZIMLS (PO Box 505, Rangiora). Completed submission forms can be emailed, faxed or mailed. Please do not send supporting documentation with your yearly submissions sheet (see audits, below) and only submit claims for the years in which you are (or have been) enrolled in the programme. Once your submissions have been reviewed your CPD points total will be able together with your NZIMLS membership details through the website. Access to your records is through the use of your email and NZIMLS membership number .
3. **Records** - evidence to support CE activities must be kept by you and may be requested if you are selected to participate in the yearly audit process. Because of this it is recommended that as you attend meetings or take part in other CE events you keep written proof of attendance/participation. This may take the form of a Certificate of Attendance (which are often provided by the organisations running CE events) or other forms e.g. receipts of registration, program etc. If you are doubtful about the suitability of a meeting as a claim for CPD points, enquire with the organisers of the meeting or contact the NZIMLS Executive Office. Your CPD record is confidential, although it is possible that information about participation in the program may be required in the future by the NZ Registration Board.
4. **Audits** - approx 10% of all submissions will be audited yearly. If you are selected to participate in this process, you will be asked to provide documentation to support you claims. Failure to provide proof of attendance at a meeting or proof to support claims may result in a reduction in the yearly points claim. If selected for the audit please ensure that you send only copies of your original documents. Once the audit process has been completed you will be notified of the outcome.

It is hoped that this proposal for the restructuring of the CPD programme will meet the anticipated requirements of the Health Profession's Competency Assurance Act due for release in 2003.

My thanks to those who submitted comments for the group assigned the task of conducting this review. The group was made up of:

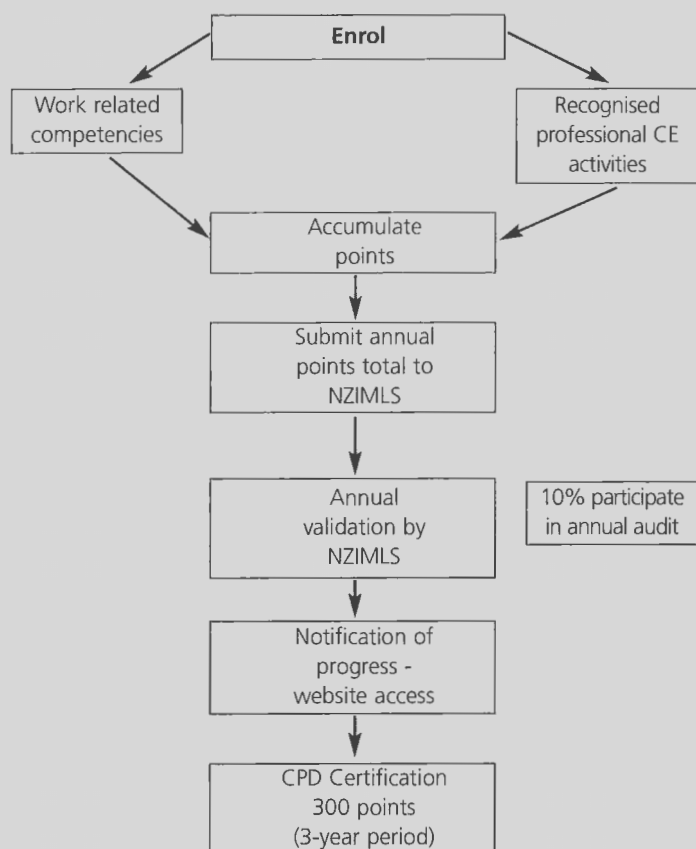
Anne Thornton (University of Otago, Medical School, Wellington, NZIMLS Council representative.)
 Chris Kendrick (Massey University - Chairman)
 Graeme Broad (Medlab Hamilton)
 Jan Parker (Southern Community Laboratories)
 Keith Wright (Taumarunui Hospital Laboratory)
 Kevin Taylor (Canterbury Health Laboratories)
 Sheryl Khull (NZBS - Palmerston North)
 Shirley Gainsford (Valley Diagnostics)

Please direct any queries about the proposed changes to the programme to:

Fran van Til
 Executive Officer of the NZIMLS
 PO Box 505
 RANGIORA

Chris Kendrick
 NZIMLS President (Acting)

CPD in summary



NEW ZEALAND INSTITUTE OF MEDICAL LABORATORY SCIENCE

2003 Calendar

30 April 2003	Applications close for Fellowship examinations	nzimls@eenz.com
30 April 2003	Committee Annual Reports to be with the Executive Officer	nzimls@eenz.com
30 April 2003	All accounts to National Treasurer for auditing	nzimls@eenz.com
2/3 May 2003	Microbiology SIG Seminar, Palmerston North	Tina Littlejohn jandm@medlabcentral.co.nz
19/21 April 2003	NICE Weekend, Wairakei Resort Hotel, Wairakei	Grant Bush grantb@medbop.co.nz
10 May 2003	Immunology SIG Seminar, Nelson	Roger Linton rl@ultra.medlabsouth.co.nz
10 May 2003	Biochemistry SIG Seminar, Hamilton	Tony Mace tonym@pathlab.co.nz
23 May 2003	Applications close for QTA examinations	nzimls@eenz.com
1 June 2003	Nomination forms for election of Officers and Remits to be with the Membership (60 days prior to AGM)	nzimls@eenz.com
Mid June 2003	Material for the August issue of the Journal must be with the Editor	Rob Siebers Rob@wnmeds.ac.nz
22 June 2003	Nominations close for election of officers (40 days prior to AGM)	nzimls@eenz.com
11 July 2003	Ballot papers to be with the membership (21 days prior to AGM)	nzimls@eenz.com
18 July 2003	Annual Reports and Balance Sheet to be with the membership (14 days prior to AGM)	nzimls@eenz.com
25 July 2003	Ballot papers and proxies to be with Executive Officer (7 days prior to AGM)	nzimls@eenz.com
31 July/1 August 2003	Combined Haematology and Transfusions Science SIGs seminar, Christchurch	Linda Henshaw linda.henshaw@cdhb.govt.nz
31 July / 1 August 2003	Council Meeting, Christchurch	nzimls@eenz.com
1 August 2003	Annual General Meeting, Christchurch	nzimls@eenz.com
Mid September 2003	Material for the November issue of the Journal must be with the Editor	Rob Siebers Rob@wnmeds.ac.nz
6 October 2003	Council Meeting, Gold Coast, Australia	nzimls@eenz.com
6-10 October 2003	South Pacific Congress, Gold Coast, Australia	Fran van Til fran@eenz.com
5 November 2003	QTA examinations	nzimls@eenz.com
12/13 November 2003	Fellowship Part One Examinations	nzimls@eenz.com



Address to the public health microbiology graduates of the Pacific Paramedical Training Centre

Talofa lava, Kia Ora, Gud De Tru, Kam na Mauri, Kia Orana katoatoa, Talofa, and to the people of the Federated States of Micronesia - warm Pacific greetings.

Thank you to John Elliott, the Director, Dr Ron McKenzie, Chairman, and the Management Committee of the Pacific Paramedical Training Centre for the invitation, and to our laboratory technicians from the Pacific - its nice to see you here and congratulations on achieving your certificates.

This is also a good opportunity to congratulate and acknowledge the work and great contributions the Pacific Paramedical Training Centre has made to look after the health needs of our Pacific people since the 1980s.

There are now 20 laboratories that cover disciplines from haematology to diagnosis of the sexually transmitted diseases, and the public health microbiology assurance and quality management are good developments to ensure always best practice and clear outcomes.

New Zealand is part of the Pacific, we are all Pacific Islanders and New Zealanders have always had a lot of affection for our Pacific people, and thank you for the commitment. To our Pacific Island laboratory technicians - thank you for the contribution you make.

Prior to my coming in Parliament, I co-ordinated the South Pacific protection programme for 10 years. I have worked in all of your countries from the grass-roots level to the Government level, and from education and awareness programmes to developing models for consumer law. We visited many of the hospitals and laboratories and I am humbled by the difficult conditions that you all work in, and often the limited resources and constraints that you work with.

I also want to affirm the Pacific Paramedical Training Centre's principal for your programmes. *"They must be appropriate, affordable and sustainable for the health care setting in which they will be used"*. Healthy communities are building blocks for healthy nation building. On your return, please take our love to our people, and congratulations - we are all so proud of you.

Winnie Laban, Member of Parliament

Reply from the students

Member of Parliament, the Honourable Winnie Laban, members of the Pacific Paramedical Training Centre Committee, distinguished guests, ladies and gentlemen.

Dorothy Fisher said *"A mother is not a person to lean on, but a person to make leaning unnecessary"*. Henry Brooke continues *"A teacher affects eternity, he can never tell where his influence stops"*. But Berman said *"If I shoot the sun, I may hit a star"*, therefore *"To be of use in the world, is the only way to happiness"* by Hans Christian.

At the beginning of this month Mr John Elliott said *"Now that I have introduced myself, it is now your turn"*. It was only the beginning. When the course was completed, it was like yesterday that I came, today we conversed, and tomorrow I will be leaving. Ladies and gentlemen, it is a great pleasure for me, on behalf of the Public Health Microbiology participants, to thank every one of you for accepting the invitation to our end of course presentation.

First of all, I would like to thank the PPTC for its numerous contributions towards the improvement of the laboratory services in the Pacific region, the New Zealand Government through the NZODA, the WHO for sponsoring this course, the Ministry of Health, tutors from the laboratory department at Wellington Hospital, any organisation who may have contributed in one way or the other, and last, but not least, the former head of this institution who still comes and provides tutorials, Mr Mike Lynch.

Coming to New Zealand was a wonderful experience for us. We really enjoyed our stay in this beautiful and colourful country, unfortunately it was a bit too cold for us at times. However, I can assure you all that not only have we enjoyed our stay here, but we also achieved the purpose of what we were here for. Outbreak of infectious diseases in the Pacific region is a major concern to our Public Health systems. It affects the social and well being of our fellow countrymen. It also affects the status of our fragile economies. This is where we as Public Health laboratory officers come into the scene.

The clinical and Public Health laboratories play a crucial role during outbreaks of any infection. The laboratory may be the only one in the country that can quickly provide the information needed to develop appropriate treatment policy during an epidemic. During an outbreak, the laboratory has four primary goals:

- ◆ Initial identification of the organism causing the outbreak.
- ◆ Initial determination of the anti-microbiological susceptibility patterns.
- ◆ Monitoring for changes in anti-microbiological susceptibility patterns.
- ◆ Defining the duration and geographical extent of the epidemic.

Ladies and gentlemen, having said that I can assure you all and especially the PPTC, that we have achieved what we came for. We will put in practice everything we have learned. Sometimes it will be difficult for us due to the economical status of our countries, but like Mike Lynch once told us *"Think outside what you have learned or what you know"*. I am very confident that when we go back we will be calling ourselves the laboratory scientists of the Pacific region. As Mike Lynch would repeatedly tell us *"Call yourself a laboratory scientist. Have confidence in yourself"*. Thank you Mike for your encouragement! Finally, I would like to thank past contributions from people like Dr Ron Mackenzie, Mr Mike Lynch, and others who have spent so much time and effort in improving the laboratory services of the Pacific region. We are here today to witness the closing of one of the courses, once again I would like to thank you all.

Malao Kalomuana, Laboratory Technician, Lenakel Hospital, Tanna, Vanuata



Students attending Public Health Microbiology Course September/October 2002. Left to right: Mrs Matanoanoa Iroa (Cook Islands), Mr Dominic Tiliwebug (Yap, Federated States of Micronesia), Mr Sero Kalkie (Vanuatu), Mrs Toligi Iese (Tuvalu), Mr Malao John Koalomuana (Vanuatu), Mr Baibuke Tauro (Kiribati), Mr Tamati Fau (Samoa).



Miss Winnie Laban Member of Parliament for Mana, who presented certificates to students attending Public Health Microbiology Course, September/October 2002, presenting certificate to Tamati Feu, Tupuatamasese Moele National Hospital Laboratory Apia, Samoa.

Microbiology SIG Meeting

2nd/3rd MAY 2003
PALMERSTON NORTH

Yes, it is that time of year again, time to organise your registration for the

Microbiology event of the year!

Palmerston North is not known for its beaches, stunning views, tropical weather or operatic society, BUT, we do know how to organise a great meeting. Some of you have survived our hospitality before with the Flockhouse experience. With your participation we hope to make this an equally memorable event.

The 2003 seminar will be held in the middle of the city allowing delegates easy access to the best accommodation and entertainment that Palmerston North can offer.

BUT
WE NEED **YOU**



So, write those talks for the Saturday session, get your registrations in the post so you don't miss out.

Friday- we plan to start at about 6pm with a couple of speakers followed by a light supper.

Saturday- start about 9am, finish about 4:30pm

7pm dinner

Further details will be posted out.

Microbiology SIG Meeting Registration

Name Phone

Address Fax

..... E-mail

Cheques payable to: MSIG

Friday 2 May 2003

Registration fee

\$15 NZIMLS members \$20 Non-members

Saturday 3 May 2003

Registration fee

\$65 NZIMLS members \$85 Non-members

Talk Title

Subject (if not clear from title)

Length of Talk Equipment required

First time speaker Yes No

Attending Dinner Yes No

Special Dietary Requirements

Please return to: Tina Littlejohn , Medlab Central, PO Box 293, PALMERSTON NORTH
Phone 06 952 3120 E-mail jandm@medlabcentral.co.nz By 18 April 2003



The Nelson region, famous for its beautiful golden beaches, tranquil National parks, NewZealand centre for the arts and crafts, and a climate to rival any other (2,400 hours of bright sunshine per annum, making it the sunniest city in NZ)
Now that takes some beating - But wait !!

NZIMLS ISIG ANNOUNCES THE 2003 IMMUNOLOGY SPECIAL INTEREST GROUP MEETING

**Saturday 10th May 2003
Trailways Motor Inn. Nelson NZ.**

Please register your interest immediately by completing your details below and contacting via address / fax below.

REGISTRATION:

Name Phone
Address Fax
..... E-mail

REGISTRATION FEES -Cheques payable to ISIG

NZIMLS Members \$ 30

Non Members \$ 37.50

Evening Dinner \$ 30

Special dietary requirements ?

Accommodation: A limited number of rooms are available on site for both Friday and Saturday nights. If this is required please indicate your requirements. Accommodation accounts are to be settled individually, but onsite bookings to be made now. The cost of these rooms is \$99 per room/night and can be shared. Trailways is located very close to the town centre. Many other accommodation venues are available if you prefer to make your own arrangements.

Number of Rooms required: Friday Saturday

I wish to share accommodation with:

Session Registration : Remember we expect to see something from every region. Please help make our meeting one to remember!

Talk title

Subject

Length of Talk Equipment required

Special requests???

Further details will be posted out to ISIG members and interested parties. Details will be posted on the NZIMLS website www.nzimls.org.nz

Please return by fax or post to: Rodger Linton, MedlabSouth, PO Box 25-091, Christchurch.
Phone (03) 3630824 ext 888. Fax (03) 3630803
Email : rl@ultra.medlabsouth.co.nz

Nelson
Live the day, ISIG 2003

Fourteenth Annual
NICE WEEKEND

**A Transfusion Science educational opportunity
organised by the TSSIG**

at Wairakei on 2-4 May 2003

The NICE Weekend (National Immunohaematology Continuing Education) is an educational meeting for all people working in Immunohaematology and/or blood services. As usual it will be held at the Wairakei Resort Hotel.

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

The registration fee is \$250, reduced to \$220 for current financial members of the NZIMLS. Your registration fee entitles you to:

- two nights (Friday 2 May and Saturday 3 May) accommodation on a share twin basis
- breakfast, morning and afternoon teas, and lunches on Saturday and Sunday
- dinner on Saturday night. (Dress theme is HOLLYWOOD)
- fun activities on Friday night.

Transport costs will be your own responsibility.

Accommodation on other nights and other meals can usually be arranged directly with Wairakei Resort Hotel. This is also your own responsibility.

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

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

Because participant numbers are limited to the FIFTY registrations preference will be given to NZIMLS members. We will fax your application form back to you on receipt, to let you know that your registration has been received. If you don't hear from us we have not heard from you.

If you have any questions contact

Grant Bush

Medlab BOP

Tauranga

ph 07 5798234

email; grantb@medbop.co.nz

NICE WEEKEND

2-4 May 2003

A Transfusion Science Education Opportunity

Organised by The TSSIG

Please register me for the 2003 NICE Weekend

Surname:		First Name:
Address for receipt:		
E-mail:		Do you agree to your email address being published in the NICE Weekend booklet? <input type="checkbox"/> Yes <input type="checkbox"/> No
Phone:	Fax:	Will you be leaving the weekend early on Sunday? No <input type="checkbox"/> Yes <input type="checkbox"/> Estimated time _____

Paper or Poster: (Circle) Title:

A brief abstract of your presentation MUST accompany your registration form . No abstract no registration!!
Email your abstract if possible.

Is this your first N.I.C.E Weekend? Yes No

Registration Fee	- \$ 250	\$
Or for NZIMLS members	- \$ 220	
Private Room Surcharge	- \$ 125	\$
I wish to share a room with _____		_____
Late Registration Fee (payable after 4 th April)	- \$ 50	\$
I enclose a cheque, made out to "NICE WEEKEND" for the amount of:		\$

Applications received after Friday 4th April 2003 can only be accepted if accompanied by the late registration fee. The Private Room Surcharge is payable only if you wish to have a room to yourself.

Signature:

Please send form and cheque to Grant Bush, Transfusion Lab Medlab BOP P.O.Box 130, Tauranga. Note registration is limited to 50 participants and preference will be given to NZIMLS members . Your form will be faxed back to you promptly to confirm your accepted registration.

Registration received and accepted	Date:
Number:	Signed:



Seminar

Biochemistry

Special Interest Group

Not to be missed by Today's Medical Laboratory Scientists

Where	Novotel Tanui, Hamilton
When	Saturday 10 th May 2003
Registration	9.30 – 10.00am

Proffered Papers...

Each Laboratory to present a paper

An award for the best proffered paper has been kindly sponsored by



ABBOTT Diagnostics Division

Costs: -

Registration	Members	\$55.00
	Non members	\$75.00

Dinner:	BBQ Theme	\$35.00
	<i>Cash Bar available</i>	

Accommodation:	Novotel Tanui - to be arranged individually on 07 838 1366
	Per room, per night, (halve the price, with 2 people per room!)
	\$157.50 (GST inclusive and including Breakfast)
	\$135.00 (GST inclusive and excluding Breakfast)

The above accommodation pricing is for rooms at the seminar venue, there are other motels available with different rates. Please make your own accommodation arrangements.

If you would like to register for the BSIG seminar 2003, please complete the enclosed Seminar Reply form, and return to Fran van Til by 28th April. Alternatively, you can register via the internet at www.eenz.com



BSIG Seminar Registration Form

Novotel Tanui, Hamilton
Saturday 10th May 2003

Registration Form

First Name: _____

Surname: _____

Laboratory: _____

Laboratory Address: _____

Contact Phone Number: _____

Email Address: _____

Registration Fees:

\$55.00 NZIMLS Members

\$75.00 Non-Members

On Line Registration available: www.eenz.com

Seminar Dinner: \$35.00 per person

\$TOTAL _____

Please make cheques payable to NZIMLS-BSIG Seminar

Any special dietary requirements: _____

Please return this form and payment to:

Fran Van Til
Executive Officer NZIMLS
P.O. Box 505
RANGIORA

Registration to be forwarded, please, by the 28th April 2003

Individuals to arrange their own accommodation with the Novotel Tanui
on 07 838 1366 or at other accommodation of their choice



BSIG Seminar

Novotel Tanui, Hamilton
Saturday 10th May 2003

PROFFERED PAPER

Presenter:

Oral Presentation

Poster

Title of Presentation:

Abstract provided: Yes

No

Equipment required:

Overhead projector

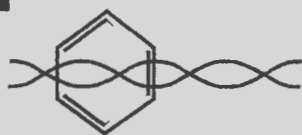
Slide projector

PowerPoint (Windows Laptop provided)

**Please return this form to: Tony Mace, Pathlab Waikato, PO Box 9115, Hamilton
by 28th April 2003**

Biochemistry

Special Interest Group



Current members of the committee are: Trevor Walmsley (Christchurch), Rob Siebers (Wellington), Tony Mace (Hamilton) and Nicky Thomas (Auckland).

We currently ensure that there is an annual Special Interest Group Meeting - the 2003 SIG meeting is in Hamilton (10th May) and being organised by Tony Mace. In the past few years the SIG meetings have been in Rotorua, Nelson, Wellington and Christchurch and have regularly attracted over 100 delegates.

From time to time we are also requested to supply names of members to help set, mark and moderate the Institute examinations (QTA and Fellowship) and to review the BMLS programs from Massey, Otago Universities and Auckland University of Technology.

I like to harness the wide range of skills available from members working in the small provincial laboratory, main centre laboratory, hospital laboratory, or community laboratory in setting the examinations

If you are interested in putting some of your expertise back into the profession or have ideas you would like to share please contact: Trevor Walmsley, Canterbury Health Laboratories, Christchurch. Trevor.Walmsley@cdhb.govt.nz

Haematology

Special Interest Group

HSIG Questionnaire

Journal - Blood, 1 October 2002 - Volume 100, Number 7 pg. 2399-2402.

Use of peripheral blood instead of bone marrow to monitor residual disease in children with acute lymphoblastic leukaemia

Questions

1. What type of test is typically performed at the completion of remission induction therapy, and what are the shortfalls of this test?
2. What does "MRD" mean?
3. What was the aim of this study?
4. What was the criterion for inclusion to this study?
5. At what limit was detectable MRD defined?
6. With patients with B-lineage ALL, was MRD more or less prevalent in bone marrow than in peripheral blood?
7. In T-lineage ALL, all cases had detectable MRD in peripheral blood and in bone marrow.

True or False?

8. What is the suggested finding of MRD in the peripheral blood?
9. In this study, the presence of MRD in peripheral blood detected more aggressive leukaemia's with higher a higher risk of recurrence.

True or False?

10. In this study, it is suggested that the use of peripheral blood should not be used for the monitoring of patients with T-lineage ALL instead of Bone marrow aspirations.

True or False?

Turn to page 40 for answers

SPECIAL INTEREST GROUP MEETING

A COMBINED EFFORT OF HSIG / TSSIG
(Haematology and Transfusion Science Special Interest Groups)
in association with NZIMLS
31st July - 1st August 2003
at Chateau on the Park
in CHRISTCHURCH

With topics that overlap the interests of haematology, coagulation and immunohaematology, this 1 1/2 day seminar makes a worthwhile update and get together!

ALSO, this years AGM of the NZIMLS will be held at a breakfast meeting on Friday 1st August.

A programme and details for registration will be sent out to all laboratory managers as soon as confirmed.

Book Reviews

Cases in Medical Microbiology and Infectious Disease (3rd edition, 2003) by Peter Gilligan, Lynn Smiley, and Daniel Shapiro. Published by the American Society for Microbiology Press.

Ordering Information: Blackwell Publishing Asia, PO Box 378, Carlton South, Victoria 3053, Australia. Cost (GST incl): A\$ 126.50

This book is primarily intended for medical students but would also be very suitable for those studying for the Bachelor of Medical Laboratory Science degree. The text consists of 68 clinical cases grouped in 7 sections, representing infections of a particular organ system (genitourinary tract, respiratory tract, etc). Each case is accompanied by very good colour illustrations and is followed by a case discussion and list of references.

The cases are prefaced by an excellent chapter titled "A Primer on the Laboratory Diagnosis of Infectious Diseases", which should be required reading for all undergraduate health science students. There is also an extensive glossary of medical terms at the end of the book.

I can highly recommend this book, not only to students of medical microbiology and infectious diseases, but also to their teachers!

Reviewed by Dr Michael Humble, Senior Lecturer, Wellington School of Medicine and Health Sciences

Human Molecular Biology Laboratory Manual (1st edition, 2003) by S Surzycki. Published by Blackwell Publishing (UK).

Ordering Information: Blackwell Publishing Asia, PO Box 378, Carlton South, Victoria 3053, Australia. Cost (GST incl): A\$ 126.50

The first impressions of this book are that it is well written, concise and readable. The course time-tabling is straight forward, although suffers from the sessions being extremely variable in length, with some time outside of the structured laboratory sessions also required. This may not suit a course taught in a series of afternoon or evening sessions, but may work better for a short term (two week) intensive course. Unfortunately, this variability is common to most formal instruction courses of this kind. As noted in the preface, this course can be shortened, using some sections to design a shorter course. Alternatively, extra preparation can occur, so laboratory sessions are shortened or combined to save time.

Most sections of each experiment are explained well, and there appears to be adequate background material presented to enable students who read the text to understand why they are performing each section of each experiment. Although most aspects are well explained, and a lot of background information is given, some small but significant pieces of information are missing. This information is possibly covered in greater detail in the author's other laboratory manual, which may be useful as a secondary text that the class can refer to, with a single copy being adequate as a reference.

Where new or recently discovered information is presented, this is covered in good depth while accepted and older information tends to be glossed over. For example, when assaying DNA quality and quantity, the reasoning behind using 230/260/280 nm ratios is explained carefully and in depth, but no reasoning is given for phosphate buffered saline (PBS) being acceptable as a diluent, with TE and water being unacceptable. Given that this manual is promoted as a basic text for students with little, if any, background in molecular biology, this dichotomy is disappointing.

Specific points of note are:

Page 13: A good proportion of the DNA isolated in Experiment 1 is likely to be bacterial in origin.

Page 13: As Corex tubes are particularly expensive and glass (breakable), the use of them in a student lab could prove uneconomic. A more viable alternative would be to use 30 mL Teflon-FEP tubes (eg Nalgene cat no.3114-0030). As these also have leak-proof screw-capped closures, laboratory safety will be enhanced as phenol will not be able to escape.

Page 15: steps 19 & 20. It is highly unlikely that high molecular weight DNA will dissolve within this time frame. Repeated pipetting will also shear the DNA into smaller fragments.

Page 17: step 7. High molecular weight DNA will not dissolve to the concentrations expected in this time frame at room temperature. It would be better to incubate at 65°C for this time, and omit the repeated pipetting.

Page 25: last line should read "with protruding 3'hydroxyl groups."

Page 35: Agarose gel electrophoresis. Staining gels with ethidium bromide (EtBr) after electrophoresis is preferred in most laboratories for a number of reasons. Primarily, as noted in this book, EtBr is a mutagen and suspected carcinogen. Under HSNO, it is also a trackable substance. Post run staining allows for easier containment and disposal of used stain, as smaller volumes of buffer are involved. Incorporating the dye into the gel when pouring leads to contamination of the running buffer and the gel box. The running buffer must then be decontaminated before disposal, and the gel boxes must be cleaned. Incorporating the dye into the gel can also cause problems with a phenomena known as band shifting, where some fragments migrate more slowly than they should, and appear to be larger than they actually are. During DNA fingerprinting or profiling exercises, this can give rise to miss-leading or inconclusive results. Incorporating the dye into the gel does save a small amount of time (10 to 15 min), but the disadvantages probably outweigh this. Post run staining is straight forward. The gel is immersed in running buffer containing approximately 10 µg/mL EtBr, and left sitting for 10 min. Gently shaking is not required, but may be used. The gel may then be visualised immediately, or can be de-stained in excess running buffer for a further 5 to 10 min to reduce background fluorescence.

Page 58: Given that the author describes CDP-star blots giving the best results after overnight incubation, it seems unusual the application of this substrate is not carried out at the end of lab session 4, with the exposure to X-ray film performed the next day. Also, leaving a membrane sitting in buffer C for extended periods of time is likely to give rise to elevated background levels.

Page 66: 20 min for this hybridisation appears to be very short. This may need to be verified experimentally before class use.

Chapter 3 finishes with a court transcript from the OJ Simpson trial, describing a practical use for this technology.

Chapter 5. Storage of DNA at -20°C is at odds with previous instructions, but storage at this temperature is probably preferable than either 4°C or room temperature.

Page 125: Agar plates containing ampicillin should be used within 7 days of preparation, and in this experiment, it would be preferable to have them prepared no earlier than the previous day.

Page 126: an alternative protocol for cleaning electroporation cuvettes would be: Immerse immediately in 70% ethanol (EtOH). Wash well with clean 70% EtOH. Store in clean 100% EtOH, dry before use, and sterilise by inverting them over a UV transilluminator for 5 min.

Page 127: plate 100 μL of cells ($1:10^6$) on one plate. Centrifuge remaining cells gently (6,000rpm, room temp, 3 min). Pour off most of supernatant (all except 100 μL). Resuspend cells in remaining volume, and plate on one plate).

Page128: step 3. I can understand the pressure of time in this course, but this is simply bad technique. Cells should be purified by streaking onto selective media, and inoculated using sterile loops. Even with antibiotic present in the media, it is possible to still get contaminants growing out of apparently sterile toothpicks.

Page132: re-suspension of the cells in an isotonic solution (150mM glucose, 100mM Tris, 10mM EDTA) before adding the lysis solution (II) gives better plasmid purification, especially in the hands of students, by allowing the more thorough and even re-suspension of cells, which leads to better, more even lysis. Keep the volumes of solution II and the ammonium acetate solutions the same, but add 600 μL isopropanol to compensate for the additional volume.

Page 136: apparent typo describing adding four tubes into thermal cycler, when only three have been prepared.

Chapter 6. Computer analysis of DNA. This chapter appears to be well written and straight forward.

Chapter 7. Determination of Human telomere length. The same DNA could be used as was prepared in the first exercise, or this experiment could be run as a complete practical course.

Page 186: steps 6-8. An overnight hybridisation is standard. Rather than removing the probe after 2hr, there appears to be no reason that it could not be left hybridising overnight. The following laboratory period would start by removing the hybridisation buffer containing the probe, and starting at step 2, p187.

Page187: step 4. It is better, particularly in a teaching situation, for the antibody to be diluted into buffer before the blocking buffer is tipped off. It is recommended that step 4 is carried out before step 3.

Page 187: step 5. Increasing the time of incubation has little if any effect on the background. One hour is routinely used in some applications.

Chapter 8. RNA isolation. The isolation of RNA from biological samples is fraught with difficulties when compared to DNA isolation. The molecule itself is many times more fragile than DNA, and as the author notes, particular care is required during isolation. It is doubtful that this procedure would add value to a basic course, as PCR, which is the basis for performing the whole experiment, is covered extensively in Chapter 4. Having noted that, this chapter appears to be well written and the experimentation is straight forward.

Generally this book is well written, with clear, concise instructions. It contains a number of practical experiments that illustrate how common modern molecular biological techniques are used in "practical" settings, in this case, forensics. It appears suitable as a primer for a basic course, but obviously, the course would require extensive leadership from an experienced molecular biologist.

The experiments described would break down into a smaller course very easily, as the experiments consist of:

1). Preparation of DNA	Two laboratory periods
2). DNA fingerprinting: Multi-locus analysis	Five laboratory periods
3). DNA fingerprinting: Single locus analysis	Two laboratory periods
4). PCR amplification of DNA	Two laboratory periods
5). DNA sequencing and analysis	Five laboratory periods
6). Telomere length determination	Six laboratory periods
7). RT-PCR of human genes	Two laboratory periods

Most of the experimentation described in this text would be able to be performed without regulatory approval. However, Chapter 5 would require approval due to the cloning involved when preparing the sequencing library. This work would also have to be carried out within

the confines of a PC2 laboratory within a restricted (transitional or containment) facility.

Reviewed by Glenn Wall-Manning, Dental Research Group, Wellington School of Medicine and Health Sciences.

A-Z of Haematology (1st edition, 2003) by Barbara Bain and Rajeev Gupta. Published by Blackwell Publishing (UK).

Ordering Information: Blackwell Publishing Asia, PO Box 378, Carlton South, Victoria 3053, Australia. Cost (GST incl): A\$ 105.60

Barbara Bain's books have an excellent reputation amongst haematologists and medical laboratory scientists alike. There would be very few haematology departments that do not possess a copy of either "Blood Cells – A Practical Guide" or "Bone Marrow Pathology". However, in this new book, co-authored by Rajeev Gupta, Barbara Bain's familiar preceptive approach, using concise coloured charts and diagrams, has been dispensed with. Instead, the authors have further developed the glossary concept, which has been such a useful feature of the earlier Bain texts, particularly the CD-ROM based "Interactive Haematology Imagebank".

The "A-Z of Haematology" uses a dictionary format to provide an easily accessible reference guide to all of those difficult to recall haematological definitions and terms. The text covers the full breadth of haematology and blood transfusion terminology, but also dabbles in the areas of biochemistry, cell biology and general medicine. Line drawings and monochrome photos are used to further elucidate some concepts. Both laboratory and clinical haematology are covered, and a strength of the book is an emphasis on the newer developments in haematology, particularly molecular haematology. For those who may ponder the *CBFB-MYH11* fusion gene and the associated clinical and cytogenetic abnormalities, this excellent book will help you to sleep easier. All readers will welcome the inclusion of the WHO classification of the haematological malignancies, and those working in the immunophenotyping laboratory will relish the comprehensive listing of CD numbers and the associated information.

This is a compact (233 page) book which contains a wealth of information in a concise format. It will aid readers in coming to grips with the technical and clinical terminology of Haematology, and would be a particularly useful reference to have at hand when undertaking journal reading. Highly recommended for all haematology laboratories, but will also have a place in cytogenetic departments.

Reviewed by Robin Allen, Haematology Laboratory, Waikato Hospital, Hamilton

Web Page

Internet Sites for Medical Scientists

The best textbook I ever bought was a PC, which was put online. With this there were unlimited sites to visit and unlimited knowledge to be obtained. It is my wish that readers will try some of these sites and also share with others the sites on the Internet that they have found useful. As interest grows, each publication of the journal will include those sites that readers submit. These will be placed into categories that will be speciality specific, or a "general" category depending on the site information.

I hope that readers think a little outside the square and can include topic sites on a variety of issues pertinent to Medical Sciences. Such issues might be writing a CV, health and safety, laboratory humour, writing technical papers etc. Feel free to submit any site you think others will enjoy (send to address below).

If you are looking for good search engines, try the following:

Google.com
Vivisimo.com
Copernic.com

Happy internetting,

Graeme Broad DMLS, DipBs
Projects Manager, Medlab Hamilton.

Sites for you to try this issue are:

1. Medical laboratory observer, www.mlo-online.com (interesting and different.)
2. www.ascp.org
3. www.medscape.com (password required, easy to sign up.)
4. www.pathguy.com (Ed Friedlander's site. Diverse and interesting.)
5. <http://info.med.yale.edu/labmed/resources/related.html>
6. www.path.upmc.edu/Cases.html (from University of Pittsburgh school of Medicine.)
7. www.mic.ki.se/Diseases (from Karolinska Institutet.)
8. www.aacb.asn.au/educ/case/conlist.html (AACB conundrums.)
9. www.pathology.med.umich.edu/cases (select "default.htm" to get to cases.)
10. www.ncbi.nih.gov/entrez/query.fcgi (PubMed and Medline)
11. www.medal.org (Medical algorithm project, >3900 algorithms available.)
12. www.aacc.org/edlinks (AACC online educational resources.)
13. www.ashteachingcases.org/kyle (Haematology cases.)
14. www.kcom.edu/faculty/chamberlain (Medical Microbiology.)
15. www.mic.ki.se/medimages.html (Medical images and illustrations.)
16. www-sci.lib.uci.edu/~martindale/Medical.html (A "Virtual" medical centre.)

Answers to HSIG questionnaire

1. Bone Marrow samples. The shortfalls of BM is that the frequency of monitoring is limited (esp. in children) by the discomfort and practical difficulties posed by bone marrow aspiration.
2. MRD = 'Minimal Residual Disease'
3. Aim was to study the residual disease in children with ALL by the use of peripheral blood instead of bone marrow.
4. Criterion was that the leukaemic cells express an immuno-pheno type suitable for flow cytometric studies of MRD at the time of diagnosis.
5. 0.01% (or more)
6. More prevalent
7. True
8. That MRD is dependent on specific biologic features of the leukaemic cells, rather than the physical disruption of the blood/bone marrow barrier.
9. True
10. False

New products and services

New antibiotic disk diffusion reader offered by bioMérieux Australia

The BIOMIC® AST System for interpreting zone diameters goes further than currently available zone readers. Its reading time is significantly quicker and the colour digital camera copes with opaque media such as Chocolate and Charcoal Agar, and difficult growth patterns such as alpha hemolysis.

An exciting feature of the BIOMIC² is its ability to interpret accurate MICs from the continuous agar gradient around each disk. This feature has received 510(k) approval from the US-FDA as substantially equivalent to reference MIC methods

The robust software is in its 7th version. It is easy to use and includes Expert analysis, epidemiology reports and QC checking. This system provides the flexibility to change test antibiotics at any time. A built-in LIS (Lab-Information-System) interface is included.

High resolution colour culture plate images are saved for a day to enable review, eliminate the need to re-find plates, and to archive any interesting images. Endpoint measurements are editable on-screen.

The system comes with IDTree' software, capable of providing 95% accurate species identification for over 80% of isolates based on NCCLS-M35 simple rapid methods. Think of it as an interactive laboratory quality manual.

The BIOMIC® AST System offers fast zone reading of all common plate media, validated MIC results, and a full software package.

For more information contact:

Jane Speirs

bioMérieux NZ Pty

Tel: 0800 284 825

Fax: 0800 284 835

Email: clinical@biomerieux.com.au

Web: www.biomerieux.co.nz

responsive and flexible in a fast changing market, to be complemented by the stability of an established company.

Mr Fowler said, "This exceptional small firm/large firm strategic alliance gives In Vitro Technologies a strong financial position, and the ability to deliver timely benchmark solutions for our clients' needs." "We deliver safe, secure solutions through our global alliance partners. In Vitro Technologies is highly selective about the companies we work with, and ensures a strict adherence to the highest ethical standards."

In Vitro Technologies' alliance partners include Alifax S.P.A., DiaSorin, Fumouze, Nova Biomedical, and Tecan Laboratory Specimen Distribution Systems.

Biotek acquisition brings cutting edge technologies to New Zealand

In Vitro Technologies last week acquired Biotek in a deal that will provide the local scientific community with innovative diagnostic solutions.

Biotek, based in Auckland, has operated in New Zealand for over 20 years as a national distributor for medical and clinical diagnostic solutions.

The acquisition will give the company and its clients access to a much larger range of advanced solutions, through In Vitro Technologies' widespread network of alliance partners, including blue chips such as DiaSorin, Nova Biomedical, Wampole and Alifax.

In Vitro Technologies' Managing Director, Brian Fowler, said the acquisition will mean New Zealand will have better access to diagnostic solutions not currently available in this country.

Mr Fowler said, "Biotek had the right mix of a good corporate culture, an extensive network, strong relationships, and outstanding employees. The acquisition will mean that they have access to the very latest and best solutions for their clients."

JJ Richards, an Australian waste and environmental management company, holds a substantial equity position in In Vitro Technologies, and will provide the company with the capital funding and infrastructure support to ensure the venture is successful.

The In Vitro Technologies and JJ Richards alliance gives In Vitro Technologies the unique advantage as a small company able to be

Abstracts of articles in the British Journal of Biomedical Science. Official publication of the British Institute of Biomedical Science

Abuzakouk M, Feighery C, Jackson J. Tumour necrosis factor blocking agents: a new therapeutic modality for inflammatory disorders. *Br J Biomed Sci* 2002;59(3):173-9.

Abstract. Development of anti-tumour necrosis factor-alpha (anti-TNF alpha) treatment offers the potential to alter radically the course of inflammatory diseases such as rheumatoid arthritis and Crohn's disease using modalities directed against a specific inflammatory mediator. Controlled randomised trials in these diseases demonstrate clinical benefit associated with significant improvement in patients with severe active joint and intestinal disease, often when conventional therapies are unsuccessful. To date, anti-TNF alpha therapy has been well tolerated and shows a favourable safety profile. This review considers the nature of this therapy and current evidence of its clinical benefit and adverse effects.

Puli V, Clarke SC. Clinical aspects of pneumonia. *Br J Biomed Sci* 2002;59(3):170-2.

Abstract. Pneumonia is a serious medical condition and a major cause of morbidity and mortality worldwide. It has many infectious aetiologies, although bacterial and viral forms are most common. Our understanding of pneumonia has improved significantly during the course of the 20th century but the overall disease burden has changed little. Although antibiotics have helped to reduce the mortality associated with some types of pneumonia, the level of morbidity remains constant. Furthermore, the existence of antibiotic-resistant bacteria worldwide is becoming an increasing problem in treatment. This essay describes the different types of pneumonia from a clinical perspective and highlights the problems associated with the condition.

Windsor JJ, Macfarlane L, Hughes-Thapa G, Jones SK, Whiteside TM. Incidence of *Blastocystis hominis* in faecal samples submitted for routine microbiological analysis. *Br J Biomed Sci* 2002;59(3):154-7.

Abstract. Over a one-year period, 1390 faecal samples were submitted to Aberystwyth Public Health Laboratory for routine microbiological examination. All were stained using a commercial trichrome method. *Blastocystis hominis* was detected in 96 (6.9%), making it the most common parasite found in the study. Of the *B. hominis*-positive specimens, 73% were missed on direct microscopy. Molecular typing of *B. hominis* has revealed extensive genetic diversity in morphologically identical strains and thus detection by microscopy alone may not be sufficient to confirm the role of this organism in human disease.

Yakoob J, Fan XG, Peng XN, Hu GL, Zhang Z. *Helicobacter pylori* cagA and vacA cytotoxin genes in Changsha, China. *Br J Biomed Sci* 2002;59(3):150-3.

Abstract. Cytotoxin-associated protein (cagA) and the vacuolating cytotoxin (vacA) encoded by cagA and vacA genes are virulence determinants of *Helicobacter pylori*. In earlier studies among Chinese patients, all *H. pylori* strains were cagA-positive and vacAs1a/m2 type. Here, we determine the cagA, vacA and allele status of *H. pylori* strains isolated from patients with upper gastrointestinal symptoms in Changsha, China. Forty strains of *H. pylori* isolated from patients with peptic ulcer disease between March 1997 and August 1999 were recovered from storage at -80 degrees C and studied by the polymerase chain reaction (PCR) for cagA and vacA genotypes. CagA was positive

in 75% of *H. pylori* isolates. Patients with peptic ulcer demonstrated cagA in 83% (15/18), compared with 68% (15/22) patients with superficial gastritis. vacAs1 allele was carried in 82.5% (33/40) isolates, of which 52.5% (21/40) were subtype vacAs1a/m2 and 17.5% (7/40) were subtype vacAs1b/m2.

Agewall S, Persson B, Lindstedt G, Fagerberg B. Smoking and use of smokeless tobacco in treated hypertensive men at high coronary risk: utility of urinary cotinine determination. *Br J Biomed Sci* 2002;59(3):145-9.

Abstract. Guidelines for the treatment of hypertension underline the central importance of strenuous efforts to reduce the prevalence of smoking, as epidemiological studies consistently have demonstrated that smoking increases the risk of cardiovascular disease and death by some two- or three-fold. Accuracy of a questionnaire is examined against the ability of urinary cotinine determination to distinguish between men exposed to tobacco (94 smokers [25%], 30 snuff users [8%]) and men not exposed (n = 257), all of whom were treated hypertensives and were associated with at least one of the following factors: smoking, diabetes mellitus, serum cholesterol > or = 6.5 mmol/L. Main outcome variables in this cross-sectional study of 381 men were cotinine concentration and cotinine:creatinine ratio in overnight urine samples (decision limits: 2 $\mu\text{mol/L}$ and 1.0 mmol/mol, respectively); tobacco use according to questionnaire; and follow-up examination by questionnaire of alleged non-smokers with high urinary cotinine levels. Questionnaire sensitivity was 85%, whereas the urinary cotinine assay showed 98% sensitivity and 99% specificity. Fourteen (15%) out of 94 patients may have used tobacco without reporting it in the questionnaire. In conclusion, cotinine measurement substantially improved the discrimination between smokers and non-smokers in men with multiple risk factors for cardiovascular disease.

Wocial B, Ignatowska-Switalska H, Berent H, Dutkiewicz-Raczkowska M, Kuczynska K, Chodakowska J, et al. Do catecholamines influence the level of plasma leptin in patients with pheochromocytoma? *Br J Biomed Sci* 2002;59(3):141-4.

Abstract. The relationship between plasma leptin and catecholamine concentrations during chronic and acute catecholamine excess is studied. Patients with pheochromocytoma, divided according to gender, were examined under basal conditions (n = 18) and at selected time-points during surgical removal of the tumour (n = 12). Appropriate controls were used (n = 23) for the basal study. Plasma leptin was determined by radioimmunoassay (RIA) and plasma noradrenaline (NA) and adrenaline (A) by high-performance liquid chromatography (HPLC). Statistical evaluation employed Student's t-test, Wilcoxon test and Spearman's correlation coefficient. Gender-related differences in plasma leptin in normal subjects was confirmed, and these were maintained in the patients. Pheochromocytoma patients had normal plasma leptin levels in the basal state and decreased levels following the massive catecholamine surge provoked by surgery. Plasma leptin concentration did not correlate with plasma NA or A in either group studied. In the patients with pheochromocytoma, acute but not chronic catecholamine excess affected plasma leptin, suggesting a role for sympathetic activity in modulating leptin release.

Diggle MA, Clarke SC. Semi-automation of the polymerase chain reaction for laboratory confirmation of meningococcal disease. *Br J Biomed Sci* 2002;59(3):137-40.

Abstract. Demand for accurate high-throughput detection and characterisation of medically important bacteria has increased dramatically within research and clinical laboratories. Liquid-handling robots have been developed to achieve high levels of accuracy and reproducibility. Assay automation can play a key role in the modern diagnostic laboratory and the data presented here shows that automated PCR is comparable with manual methods. Importantly, automation is preferred when high-quality results cannot be guaranteed using manual methods. This is particularly important when results are required quickly for public health management.

Other articles without abstracts

Moore JE, Millar BC. Need for improved molecular biology training for biomedical scientists in NHS microbiology laboratories. *Br J Biomed Sci* 2002;59(3):180.

Honda M, Matsushita S, Murayama O, Millar BC, Moore JE, Matsuda M. Cloning and sequence analysis of the *recA* gene in urease-positive thermophilic campylobacter (UPTC). *Br J Biomed Sci* 2002;59(3):166-9.

Moore JE, Reid A, Millar BC, Jiru X, McCaughan J, Goldsmith CE, et al. *Pandora* sp. isolated from a patient with cystic fibrosis: problems associated with laboratory identification. *Br J Biomed Sci* 2002;59(3):164-6.

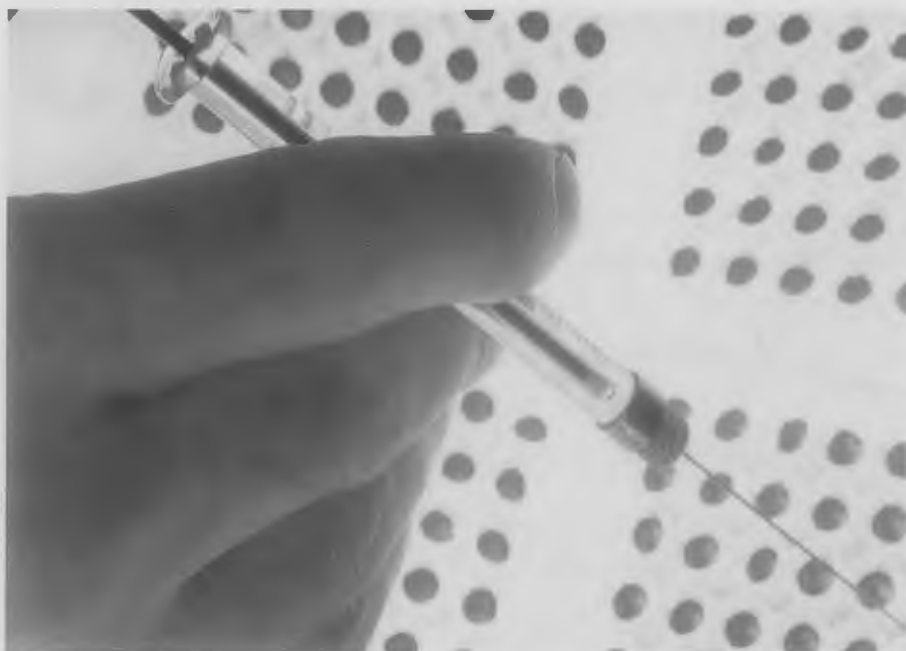
Smith SI, Otuonye MN, Omonigbehin EA, Nkoth A, Okany CC, Ariyo F, et al. Prevalence of *Campylobacter* species among HIV/AIDS patients in Nigeria. *Br J Biomed Sci* 2002;59(3):162-3

Clarke SC, Diggle MA, Edwards GF. Multilocus sequence typing and *porA* gene sequencing differentiates strains of *Neisseria meningitidis* during case clusters. *Br J Biomed Sci* 2002;59(3):160-2.

Matsuda M, Eda Y, Isobe K, Moore JE. Plasmid profiles of urease-positive thermophilic campylobacter (UPTC) strains isolated in Europe and Asia (Japan). *Br J Biomed Sci* 2002;59(3):158-60.

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AIMS NZIMLS South Pacific Congress 2003

AIMS NZIMLS
South Pacific Congress
6-10 October 2003
Conrad Jupiters
Gold Coast, Queensland

Call for Abstracts

*Authors are invited to submit abstracts for oral and/or poster presentation by
1st July 2003 for consideration by the scientific program committee*

Conditions of Submission

1. Abstracts may be submitted on any topic relevant to medical laboratory science. The organising committee reserves the right to reject unsuitable topics.
2. Abstracts should be descriptive and concise. They should be thoroughly checked for spelling and grammar before submitting.
3. Abstracts should be 250 words in length and **not** contain references, tables or figures.
4. The abstract should be arranged as follows:
 - * Objective
 - * Statement of Findings
 - * Key Conclusions
5. The "Presenters/Authors" section must show the surname/s and initials and affiliation, in that order. The presenter must be indicated in CAPITALS as distinct from co-authors. Titles, degrees and awards are not to be shown. For Affiliation, street address, postcode, state and/or country are not required unless outside Australia and New Zealand, when only the city and country are required.
 - eg. SMITH J Y, Westmead Hospital, Sydney (*presenter - surname in capitals*)
 - eg. Jones D H, St Vincents' University Hospital, Dublin, Ireland
6. An 80 word biography is required to enable the Chairman to introduce the presenter, should the abstract be accepted.
7. Receipts of abstracts will be acknowledged. Authors will be advised by **Friday 25 July 2003** whether their abstracts have been accepted.
8. Successful abstracts will be published and distributed to delegates at the conference. AIMS and NZIMLS reserve the right to publish in their respective Journals.

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The South Pacific Congress is held every four years and is hosted alternately by the New Zealand Institute of Medical Laboratory Science and the Australian Institute of Medical Scientists. A provisional program is published in this issue and is available on our website www.aims.org.au. For further conference information please contact:

Ms Fran van Til
fran@eenz.com

South Pacific Congress 2003 Preliminary Program
 WEDNESDAY 8 OCTOBER 2003

Opening and welcome

Fellowship presentations and Awards

Saül Foley Lecture

Professor Allan Cripps (Pro Vice-Chancellor - Research, University of Canberra)

Morning Tea

PLENARY SESSION

Therapeutic Applications of Cell Signalling

Dr Jo Trapani (University of Melbourne)

Lunch

1330-1500

TECHNOLOGY SYMPOSIUM

Major Sponsor Involvement

Afternoon Tea

<p>1530-1700</p> <p><i>Pathology Reporting - HL7</i> Klaus Veil (University of Ballarat)</p> <p><i>LOINC Coding</i> Dr Stan Huff (Intermountain Health Care, Utah)</p> <p><i>XML</i> Speaker TBA</p>	<p><i>Laser Microdissection Microscope</i> Dr Margaret Cummings (Royal Brisbane Hospital)</p> <p><i>Cofocal Microscopy</i> Grace Chojnowski (Queensland Institute of Medical Research)</p> <p><i>Image Analysis</i> Pasqual Banford (University of Queensland)</p>	<p><i>Near Patient Testing</i> Dr Lindsey Taylor (The Prince Charles Hospital, Brisbane)</p> <p><i>Portable Coagulation Analyzers</i> Dr Michael Ray (Haemostasis Research Laboratory, The Prince Charles Hospital, Brisbane)</p>	<p><i>Benchmarking Project</i> Prof Stewart Bryant (Monash University)</p> <p><i>Electronic Documentation</i> Lynn Nelson (Douglass Hanly Moir Pathology)</p> <p><i>Lowering Laboratory Costs</i> Paul Schreckenberger (University of Illinois, Chicago)</p>	<p>SYMPOSIUM ELECTRONIC PATHOLOGY</p> <p>SYMPOSIUM HISTOTECHNOLOGY</p> <p>SYMPOSIUM POINT OF CARE</p> <p>SYMPOSIUM LOWERING LABORATORY COSTS BY CONTROLLING UTILISATION</p> <p>SYMPOSIUM PAEDIATRIC PATHOLOGY</p>
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"A Rash Investigation"

South Pacific Congress 2003 Preliminary Program
THURSDAY 9 OCTOBER 2003

0900-1030 **BIOTECHNOLOGY - OUR NEW OPPORTUNITY**
Biotechnology opportunities in Australia Speaker TBA
Biotechnology growth Speaker TBA (Emerging Technologies, Dept of Innovation and Information, Queensland Government)

Morning Tea

SOUTH PACIFIC BIOTECHNOLOGY BOOM

1100-1230 *Converting biotechnology into clinical diagnostics* Mel Bridges (Pan Bio)
Diagnostic and therapeutic uses of dendritic cells Prof Derek Hart (Mater Medical Research Institute)
Role of Pathology Laboratory in Research Prof Ian Gardner (CRC-Queensland University of Technology)

Lunch

1330-1500	IMMUNOLOGY <i>Dendritic Cell Therapy</i> David Ritchie (Malaghan Research Institute, New Zealand)	BIOCHEMISTRY <i>Biosensors</i> Dr Andrew St John (AI Scientific)	MOLECULAR PATHOLOGY <i>Genetic testing for haemochromatosis</i> Dr Lorraine Westacott (Queensland Medical Laboratory)	HISTOCHEMISTRY <i>Immunohistochemistry</i> Keith Miller (UCL Medical School, UK)	MICROBIOLOGY <i>Identification and characterization of non-fermenting gram-negative bacilli</i> Paul Schreckenberger (University of Illinois, Chicago)	TRANSFUSION <i>Nucleic Acid Testing</i> Catherine Hyland (Australian Red Cross Blood Transfusion Service, Brisbane)
	<i>Adoptive Immunotherapy</i> Rajiv Khanna (Queensland Institute of Medical Research)	<i>Microarray Technology</i> Dr Glen Boyle (Queensland Institute of Medical Research)	<i>Molecular pathology of haematological disorders</i> Dr John Rowell (Royal Brisbane Hospital)	<i>Microsatellite Instability Testing & DNA Repair Protein</i> Dr Barbara Leggett (Royal Brisbane Hospital Research Foundation, Clinical Research Centre)	Speaker TBA	<i>Progesa System</i> Bruce MacDonald (Australian Red Cross Blood Transfusion Service, Brisbane)
	<i>Elispot & Tetramer Technology</i> Cameron Turtle (Mater Medical Research Institute)	<i>Protein Chip</i> Andrea McCracken (Advanced Labs)	<i>Chronic Leukaemia</i> Dr Gillian Rozenberg (Prince of Wales Hospital)	Speaker TBA	Speaker TBA	<i>Current Status of Plasma Products</i> (CSL Limited)

Afternoon Tea

1530-1700	IMMUNOLOGY <i>Proffered Papers</i>	BIOCHEMISTRY <i>Proffered Papers</i>	HAEMATOLOGY <i>Proffered Papers</i>	HISTOLOGY <i>Proffered Papers</i>	MICROBIOLOGY <i>Proffered Papers</i>	BLOOD BANK <i>Proffered Papers</i>
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South Pacific Congress 2003 Preliminary Program
FRIDAY 10 OCTOBER 2003

0900-1030	INFECTIOUS DISEASES <i>Emerging multiresistant infections</i> Paul Schreckenberger (University of Illinois, Chicago)	JOHN WHITELEY MEMORIAL LECTURE <i>Innate Immunity</i> Robyn Minchinton (Australian Red Cross Blood Transfusion Service, Brisbane)	BREAST PATHOLOGY <i>Current status of breast cancer diagnosis</i> Dr Di Cominos (Sullivan Nicolaides Pathology) <i>Recent advances in breast cancer treatment</i> Dr David Grimes (Wesley Medical Centre, Brisbane)			
1100-1230	MOLECULAR DIAGNOSIS OF INFECTIOUS DISEASE <i>TB Testing & PCR</i> Chris Gilpin (Mycobacterium Reference Laboratory, The Prince Charles Hospital, Brisbane)	TRANSFUSION Pam Hudson (Institute of Clinical Pathology & Medical Research - Westmead Hospital)	THROMBOSIS & HAEMOSTASIS <i>Novel snake venom components</i> Dr Paul Masci (University of Queensland, Southern Clinical School)	FORENSIC SCIENCE <i>Forensic Medicine</i> Ass Prof Leo Freney (Forensic Science - Queensland Health Scientific Services)	MANAGEMENT <i>Relation between ISO17025 & ISO9001:2001</i> Kaye Watson (Queensland Medical Laboratory)	CYTOLOGY & HISTOLOGY <i>Pitfalls in Breast Cancer Diagnosis</i> Dr Di Cominos (Sullivan Nicolaides Pathology) <i>Herceptin/Her-2 survey</i> Dr Margaret Cummings (Royal Brisbane Hospital)
	<i>RT PCR For Infectious Diseases</i> Dr Theo Sloots (Sir Albert Sakzewski Virus Research Centre)	Speaker TBA	<i>New anticoagulants</i> Dr Tim Brighton (St George Hospital)	<i>SNP Technology in Forensic Medicine</i> Prof James Dale (Queensland University of Technology)	<i>Quality Assurance - The New Zealand Perspective</i> Speaker TBA <i>Mobile Laboratory</i> Speaker TBA	<i>Herceptest/Her-2 survey</i> Dr Adrienne Morey (St Vincent's Hospital, Sydney)
<i>Lunch</i>						
1330-1500	TROPICAL HEALTH <i>Scabies</i> Dr Greg Lawrence (Queensland Institute of Medical Research)	INFERTILITY <i>Preimplantation Genetic Diagnosis</i> Dr Cynthia Roberts (Sydney IVE)	HAEMATOLOGY <i>Topic TBA</i> Dr Robyn Rodwell (Mater Hospital, Brisbane)	TOXICOLOGY <i>The role of the analyst in the regulation of horse and greyhound racing</i> Dr Cheryl Foster (Racing Science Centre, Queensland)	EDUCATION <i>Future of Education For Medical Scientists</i>	CYTOLOGY & HISTOLOGY <i>Cahretinin expression in renal cells</i> Dr Vin Williams (Path Centre)
	<i>Box Jellyfish</i> Dr Jamie Seymour (James Cook University)	<i>Male Infertility - Causes and Treatments</i> Keith Harrison (Queensland Fertility Group)	<i>Recent advances in laboratory diagnosis of cancer</i> Dr Mike McGuckin (Mater Medical Research Institute)	<i>Sport Toxicology</i> Speaker TBA <i>Occupational Toxicology</i> Speaker TBA		<i>ICC in fluid diagnosis - current status</i> Dr Paul Shield (Sullivan Nicolaides Pathology) <i>Immunohistochemistry</i> Keith Miller (UCL Medical School, UK)
1530-1700	Malaria Vaccine Prof Michael Good (Queensland Institute of Medical Research)					
<i>Afternoon Tea</i>						
CLOSING SESSION - DEBATE: Registration of Medical Scientists in Australia						

South Pacific Congress 2003 Preliminary Workshop Program

Monday 6 October 2003

Full Day Workshop

WS1: Haematology Morphology (*Gillian Rozenberg, The Prince of Wales Hospital*)

Monday Morning

WS2: Shift Work and Wellbeing (*Carmel Bofinger, Simtars; Simon Smith, University of Queensland, Joe Kelly, Queensland Public Sector Union*)

WS3: Parasitology (*Co-ordinator Bob Dow, Queensland University of Technology*)

WS4: Foetal-maternal Haemorrhage (*Speakers TBA*)

WS5: Effective Scientific Writing (*John Stirling, Flinders Medical Centre*)

Monday Afternoon

WS6: Basic Biochemistry (*Tony Badrick, Sullivan Nicolaides Pathology*)

WS7: Snake Venom Detection (*Tim Carroll, CSL Limited*)

WS8: Management (*Title & Speakers TBA*)

Tuesday 7 October 2003

Full Day Workshop

WS9: Basic Blood Transfusion (*Tim Carroll, CSL Limited*)

Tuesday Morning

WS10: Heparin Associated Thrombocytopenia (*Dr Peter Wood, The Prince Charles Hospital*)

WS11: Management (*Title and Speakers TBA*)

WS12: Flow Cytometry (*Graham Chapman, Becton Dickinson Biosciences Australia*)

WS13: Emerging Antibiotic Resistance - The Laboratory Challenge (*Narelle George & Nick Nuttall, Royal Brisbane Hospital*)

Tuesday Afternoon

WS14: Paediatric Haematology Morphology (*Gillian Rozenberg, The Prince of Wales Hospital*)

WS15: Immunohistochemistry (*Keith Miller, UCL Medical School, UK*)

WS16: Laboratory Identification of the genus *Bacillus* (*Narelle George & John Bates, Royal Brisbane Hospital*)

Monday 6 - Friday 10 October 2003

WS17: Surfing Workshop! Learn to Surf with the Gold Coast Surfing School

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Winning the Publications Game (2nd Ed.) by Tim Albert.
 Radcliffe Medical Press, Oxford 2000
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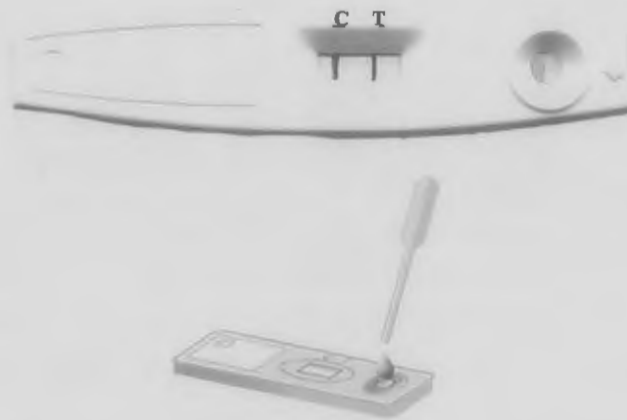
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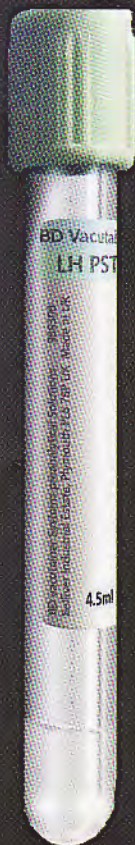
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