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Auto-fluorescence properties of proteins incubated with monosaccharides - an \textit{in vitro} study

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Abstract

Non-enzymatic glycation forms advanced glycation end-products (AGEs), which may influence pathogenesis of diabetic complications and their measurement may be of great use in disease management and the prevention of complications. One way of doing this is by measuring their auto-fluorescence, but the properties of these metabolites are not clear. This study investigated the possible auto-fluorescence of collagen IV, elastin and albumin during incubation with glucose and/or fructose \textit{in vitro} over a 12 week period; these investigations were duplicated separately in the presence of urea and creatinine to mimic the presence of non-protein nitrogenous (NPN) wastes.

Auto-fluorescence was observed when collagen IV was incubated with glucose separately and with glucose and NPN wastes combined. No auto-fluorescence was seen when albumin or elastin were incubated with glucose or when each of the three proteins was incubated with fructose. It is possible that AGEs caused the auto-fluorescence and this may be useful in detection of diabetic complications and its management. The effects of urea and creatinine on the auto-fluorescence could not be clearly established therefore further research is required.

\textit{Key words:} auto-fluorescence, diabetes mellitus, diabetic complications, glycation.

Introduction

Diabetic complications are major causes of morbidity and mortality and there is evidence to suggest that many diabetic complications are mediated by early glycated proteins and/or AGEs formed by non-enzymatic glycation of proteins (Gugliucci 2000). However, not all glycation products have been isolated and those already characterised are complex and heterogenous (Raj \textit{et al} 2000). The chemical nature of AGEs \textit{in vivo} is unclear because these products are present in low levels and are liable to chemical hydrolysis (Huebschmann \textit{et al} 2006). The measurement of glycated proteins and AGEs has the potential to be of great significance in management and prevention of diabetic complications (Ahmed and Thornalley 2007) but according to Ahmed (2005) the mechanisms underlying their formation remain unclear. The analysis of serum AGEs in human diabetics has been difficult because of the absence of a recognised standard or established unit, and these AGEs are found in low concentrations in tissue proteins (Ahmed \textit{et al} 2002). Techniques such as the enzyme-linked immunosorbent assay only detect individual AGEs while other methods require pre-analytical steps that may alter or convert Amadori adducts (products of non-enzymatic condensation of glucose with reactive amino groups) to AGEs thereby affecting accuracy and specificity (Lapolla \textit{et al} 2005).

Studies have mostly focused on non-enzymatic glycation of proteins by glucose with comparatively little attention paid to glycation by other monosaccharides such as fructose, possibly due to the fact that glucose is the most abundant sugar in blood. Fructose is perceived to be safer than sucrose, particularly in diabetes mellitus since it does not adversely affect blood glucose regulation, at least in the short term. The amount of fructose in the diet has increased but the effects of long-term fructose consumption have not been adequately studied in humans and it may be more harmful than is recognised (Gaby 2005). The first stages in the reactions of glucose or fructose with amino acids are similar and lead to formation of a Schiff base. In the second part; glucose reactions form Amadori products while fructose reactions form Heyns products and both products eventually give AGEs (Schalkwijk \textit{et al} 2004). \textit{In vitro} studies show that fructose
is a more potent glycating agent than glucose and is up to 10 times more efficient at forming AGEs (McPherson et al 1988). Studies on the role of fructose in the development of diabetic complications by Sakai et al (2002) also show that fructose accelerates the production of AGEs more than glucose. Kawasaki et al (1998) and Herbert et al (1999) reported that fructose may play a role in lens damage in diabetic rats. This in vitro study investigated possible auto-fluorescence of proteins incubated with glucose and fructose separately, and combined, the latter to ascertain synergistic effects since these monosaccharides are both present in the body.

Fluorescence is an expanding technique in medical science, and has been used for measurement of AGEs since some of these have fluorescent properties (Schmitt et al 2004; Januszewski et al 2005; Lapolla et al 2005). However, the fluorescence of individual glycated products needs also to be clearly established. Furthermore, fluorescence specificity can be compromised in the presence of other fluorescent substances such as NADPH (reduced nicotinamide adenine dinucleotide phosphate), non-protein adducts, glucose, or lipid-derived oxidation products that fluoresce, or the fluorescence can be interfered with by non-protein tissue components (Schmitt et al 2004). This study was therefore extended to investigate the possible effects of NPN wastes on auto-fluorescence of glycated products. Various trials have indicated the potential for using skin auto-fluorescence as a tool in assessment of diabetic complications (Meerwalt et al 2005; Rutgers et al 2006; Meerwalt et al 2007). The current study explored the auto-fluorescence properties of collagen IV and elastin when incubated with glucose in vitro since these proteins are extracellular matrix components in various tissues (Yamamoto et al 2002). The concentrations of albumin, collagen and elastin used in the study were physiological while the levels of glucose, fructose, urea and creatinine mimicked physiological and pathological states.

## Materials and methods

### Preparation of reagents

The water used in preparing the various solutions was deionised using NANOpure® Water System (Barnstead, USA) and autoclaved using Tomy ES-315 (Tomy Seiko, Japan). All the chemicals were of analytical grade and weighing was carried out on an electronic balance (Molecular Solutions, USA). Phosphate-buffered saline powder (Sigma-Aldrich, Australia) was dissolved in deionised water to make 10 mM pH 7.4, which was confirmed by radiometer (Pacific Laboratories, Australia). This buffer was used to make preparations of human proteins (Sigma-Aldrich, Australia); collagen IV, elastin and albumin.

### Experiments

In the first set of experiments, glucose and fructose (Sigma-Aldrich, Australia) were incubated separately with each of the protein solutions while in the second set, glucose and fructose combined were again incubated with each of the proteins. The third set of experiments involved addition of urea and creatinine (Sigma-Aldrich, Australia) to each protein-monosaccharide incubation. All preparations were done aseptically in sterile falcon plastic tubes (Interpath, Australia) and the solutions were left to dissolve overnight at 4°C after which they were sterilised by passing through a micropore filter.

The preparations were made to give the following working concentrations: albumin 45 g/L, collagen 800 ng/L and elastin 800 ng/L. The glucose and fructose concentrations were 5, 15, 25 and 35 mmol/L and 200, 400, 600 and 800 μmol/L, respectively, while urea and creatinine concentrations were 5 and 30 mmol/L and 100 and 1000 μmol/L respectively. The final working concentrations of proteins were formulated to simulate physiological conditions while those of monosaccharides and NPN wastes mimicked physiological and pathological conditions.

The preparations were incubated in a water-bath at 37°C for 12 weeks in the dark. The water bath temperature was monitored daily, and weekly auto-fluorescence measurements were carried out using an FS 3000 fluorescence spectrometer (Perkin-Elmer, England).

### Control of microbial contamination

In addition to sterile filtration and use of an aseptic environment, visual inspection for growth in the laboratory and experimental tubes was done daily. Safe (Ajax Chemical, Australia), was added to the water-bath to prevent bacterial growth and to maintain an aseptic environment. Sterile fluorimetric cells were used for each measurement and the volumes withdrawn for analysis were discarded after measurement. The working bench was sterilised before and after analyses and measurements were carried in the presence of a Bunsen flame. Samples from all the tubes were cultured on blood agar (Oxoid, USA) on the first day, in week six and on the final day of experiment.

### Fluorescence measurements

Quinine sulphate (BDH chemicals, Australia) used as the standard was prepared weekly prior to fluorimetric analysis by dissolving in 0.05 M H₂SO₄ (Chem Lab, Australia) to working concentrations of 0, 0.5, 1, 2 and 5 mg/L. A pre-scan was carried out using the full range of monochromator limits from 200 to 800 nm. The excitation/emission slit width combination of 2.5 and 5.0 nm gave maximum intensity. The maxima excitation and emission wavelengths for the standard were 352...
nm and 447 nm, respectively. Effects due to Rayleigh and Raman scatterings were removed as per operator’s manual. Samples of 3 mL were withdrawn weekly from the incubations for fluorescence analysis. New fluorimetric cells were used for each measurement to avoid carry-over and the measurements were done in triplicate and the mean fluorescence value was calculated.

**Data handling**

The results are expressed as the mean of three measurements and the data is presented as figures in which the means of auto-fluorescence are shown weekly. The data for each set of weekly auto-fluorescence measurements were compared to baseline measurements (first week) and data from weekly auto-fluorescence measurements in proteins incubated with various concentrations of monosaccharides were compared to controls (without glucose and/or fructose). The experiments in which fructose was added were compared to those which had glucose added. The auto-fluorescence of incubations of proteins with monosaccharides in the presence of NPN wastes was compared to experiments which did not have NPN wastes.

**Results**

No microbial growth was seen in agar plates in any of the experiments and the fluorescence of the standard remained constant throughout the 12 week period.

**Auto-fluorescence of proteins incubated with various glucose concentrations**

No auto-fluorescence was seen when albumin and elastin were incubated with glucose. However, auto-fluorescence was observed in some of the tubes in which collagen IV was incubated with glucose and in some tubes with collagen IV incubated with glucose and NPN wastes (Figs 1, 2 and 3). Collagen IV incubated with glucose auto-fluoresced with maxima excitation and emission at 350 nm and 440 nm, respectively. Auto-fluorescence of proteins incubated with various fructose concentrations

No auto-fluorescence was seen when albumin and elastin were incubated with various fructose concentrations. Auto-fluorescence was, however, observed in some of the experiments in which collagen IV was incubated with fructose and glucose combined, and when collagen IV was incubated with fructose and glucose combined plus NPN wastes (Figs 4, 5 and 6).

![Figure 1](image1.png) **Figure 1.** Auto-fluorescence of human collagen IV incubated with various glucose concentrations during the 12 week period.

![Figure 2](image2.png) **Figure 2.** Auto-fluorescence of human collagen IV incubated with various glucose concentrations and 5 mmol/L urea and 100 μmol/L creatinine during the 12 week period.

![Figure 3](image3.png) **Figure 3.** Auto-fluorescence of human collagen IV incubated with various glucose concentrations and 30 mmol/L urea and 1000 μmol/L creatinine during the 12 week period.
The auto-fluorescence, if any, of individual species of glycated metabolites and AGEs has not been fully studied. This study incubated collagen IV and elastin, which are extracellular matrix proteins, and albumin which is a serum protein with glucose and fructose, to mimic glycation in vivo. Urea and creatinine were also added to the incubation of the proteins with monosaccharides to ascertain if they interfered with auto-fluorescence. It was important to mimic in vivo physiological conditions hence incubation was for 12 weeks to allow for formation of glycation products at 37°C and pH 7.4. Previous studies have used similar experimental conditions (Gopalkrishnapillai et al. 2003).

We were cognisant of the fact that contamination by micro-organisms could result in the metabolism of monosaccharides and proteins and possibly decreasing their levels. It was also hypothesised that such metabolism could produce auto-fluorescence, or metabolites that interfere with auto-fluorescence. The literature cites micro-organisms with fluorescence properties e.g. Pseudomonas aeruginosa (Cornelis and Matthijs 2002) hence it was necessary to use sterile solutions and to sterilise all the preparations by autoclaving prior to addition of proteins. Since proteins are denatured by heat (Bischof and He 2005) the solutions containing proteins were sterilised by passing through a micropore filter. Coupled to these preventative measures, each experimental tube was cultured for micro-organisms at the start, middle and conclusion of the study. Since no microbial growth was observed it is assumed that the auto-fluorescence observed is attributed to glycated products and this is strengthened by the absence of auto-fluorescence in baseline tubes. Although the body contains different proteins and carbohydrates, this in vitro protocol allowed for the study of glycation of individual proteins by specific monosaccharides. We were aware that metabolites can potentiate or inhibit one another in vivo; hence in this study we investigated the combined effects of glucose and fructose on glycation and the combined effects of urea and creatinine on the auto-fluorescence of proteins incubated with those monosaccharides.

Auto-fluorescence of proteins incubated with glucose

The auto-fluorescence that was observed in the twelfth week when collagen IV was incubated with glucose (Fig. 1) suggests that auto-fluorescence was dependent on the concentration of glucose since no auto-fluorescence was seen when collagen was incubated with low concentrations of glucose. Furthermore, this auto-fluorescence appears to increase from week 10 suggesting dependence on time. Most studies have used fluorophores to conjugate glycated molecules in vitro followed by quantitation of these products but few studies have looked at auto-fluorescence. This study investigated auto-fluorescence of glycated proteins without chemical modification and this perhaps gives a better picture of these products in vivo in diabetes mellitus and the associated diabetic complications.

Products of elastin or albumin incubated with glucose did not auto-fluoresce; it is possible that the products
of these glycations have no fluorescent properties. We recommend in future studies to extend the incubation time since glycation is a slow process (Lapolla et al 2005). The presence of auto-fluorescence in collagen IV experiments but not in elastin could be explained by the few ε-amino groups in elastin compared to collagen and non-enzymatic glycation is dependent on the number of ε-amino groups in proteins (Yamamoto et al 2002). It is also probable that a weak auto-fluorescence was present but it was below the detection of the instrument.

In this study no literature was found on auto-fluorescence of AGEs specifically pertaining to glycation of human; collagen IV, elastin and albumin. Indeed, results from the collagen IV experiments suggest that glycation of this protein could be related to glucose concentration and time, and if this is the case, then further studies are needed to establish the use of such auto-fluorescence in monitoring glycaemia and complications of diabetes mellitus. Meerwaldt et al (2004) studied skin auto-fluorescence and concluded that auto-fluorescence may be a convenient and rapid tool for the assessment of long-term diabetic complications. This study demonstrated auto-fluorescence of collagen IV glycation products in vitro and as collagen IV is an extracellular matrix protein (Yamamoto et al 2002), the auto-fluorescence which other studies observed in the skin, could in part be due to glycated collagen.

**Auto-fluorescence of proteins glycated by fructose**

In this study no auto-fluorescence was observed when elastin or albumin was incubated with fructose. However, auto-fluorescence was seen in the twelfth week when collagen IV (Fig. 4) was incubated with high levels of glucose and fructose combined. The magnitude of this fluorescence appears similar to that obtained when collagen IV was incubated with glucose (Fig. 1). Since no fluorescence was obtained when collagen IV was incubated with fructose, this suggests that the auto-fluorescence observed could have been due to glycation by glucose. Sakai et al (2002) studied the role of fructose in development of diabetic complications by incubating collagen IV with 200 mmol/L of glucose or fructose and suggested that fructose accelerated the production of AGEs more than glucose as the fluorescence intensity was higher in fructose than in glucose incubations. Oimomi et al (1989) incubated collagen with 50, 100 and 200 mmol/L glucose or fructose and reported that fluorescence increased as concentrations of glucose or fructose increased, but fluorescence intensity was higher in the fructose experiment. In this study auto-fluorescence was not observed in the experiments in which proteins were incubated with fructose and it is possible that the variations in observations are due to the massive differences in concentrations of collagen and fructose used in the different studies. The reference range of fructose is 55-333 μmol/L in serum (Wu 2006) and in our study we sought to mimic in vivo glycation. Hence we used physiological levels (200 μmol/L) and pathological levels (600 μmol/L) of fructose while higher levels were used in other studies. Demonstration of auto-fluorescence of glycation of proteins using high concentrations of proteins and fructose may be possible in vitro but may not be consistent with in vivo levels even in pathological states.

**Effects of urea and creatinine on auto-fluorescence of proteins incubated with the monosaccharides**

A complication of diabetes mellitus is impairment of renal function characterised by increased levels of nitrogenous wastes in the blood (Jerums et al 2003). This study investigated the effects of physiological and pathological levels of urea and creatinine on the auto-fluorescence of proteins when incubated with glucose and/or fructose. The data suggest that NPN wastes increase the auto-fluorescence of collagen IV glycation products as the auto-fluorescence observed was higher in experiments which had NPN wastes (Figs 2 and 3). Perhaps future studies could look at the contributions of individual NPN wastes and ascertain their relative contribution to fluorescence. In this study we found only one article (Mendez et al 2007) regarding the effects of urea on fluorescence of AGEs and it reported that urea decreased fluorescence of glycated proteins. The differences between the results in our study and those of Mendez et al (2007) could be due to the differences in protocols used. In our study we used human proteins, glucose, fructose, urea and creatinine dissolved in phosphate buffered saline and fluorescence analysis carried out at 37°C. Mendez et al (2007) dissolved bovine albumin and glucose in phosphate buffered saline while urea was dissolved in distilled water, equal volumes were incubated, and fluorescence analysis carried out at 24.4°C. It is possible that the two studies measured fluorescence at two different final pHs and this could have affected the results. In our study we also used urea and creatinine combined as they co-exist in vivo while Mendez et al (2007) used urea only.

**Limitations of the study**

The aim of the study was to investigate whether glycated proteins auto-fluorescence. Future work would need to quantify the findings of this study using large sample numbers and relating the auto-fluorescence to the severity of diabetes and its complications. Under in vivo conditions the level of glucose is not constant and proteins and monosaccharides in vivo exist together, but in this study we deliberately mimicked controlled hyperglycaemic conditions using individual proteins incubated with individual monosaccharides and a combination of glucose and fructose. The study was designed to control the variables so that the glycation products of individual monosaccharides could be studied. There are many proteins and monosaccharides in vivo which are implicated in glycation and it is worth studying auto-fluorescence, if any, of proteins such as immunoglobulins as a result of glycation.

Non-enzymatic glycation of proteins is a slow process with the first stage reversible; only a small portion of the Amadori glycated proteins further react to form irreversible AGEs, therefore the majority of glycation products in the body are Amadori glycated proteins. Literature that pertains to whether the Amadori glycated proteins, which are formed in the early stages of the glycation reaction, emit auto-fluorescence or interfere in the measurement of
auto-fluorescence of AGEs is scarce, hence further studies are needed.

**Conclusion**

This study demonstrated the auto-fluorescence of human collagen IV incubated with glucose *in vitro*, which appears to be dependent on concentration of glucose and time. If this auto-fluorescence is due to AGEs then such measurements could be useful in monitoring diabetes mellitus and diabetic complications. Some studies have reported that fructose is more reactive *in vitro* compared to glucose but this was not seen in this study, perhaps owing to the fact that in this study lower levels of fructose and physiological concentrations of proteins were used while in other studies much higher levels were used. The data from this study suggest that NPN wastes increase auto-fluorescence when collagen IV is incubated with monosaccharides but further studies are needed to confirm this finding. Collagen IV is an extracellular matrix protein and studies need to be targeted at investigating collagen AGEs in the skin to develop a non-invasive technique for management of diabetes mellitus.

**Acknowledgements**

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**References**


Multiskilling or deskilling? Workplace influences on the quality of multidisciplinary medical scientists

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Abstract
Pathology laboratories are increasingly organised according to the capabilities of the automated analytical equipment that they use. One of the consequences of this and other economic trends is the use of multidisciplinary scientists in the laboratory. Some commentators have associated multidisciplinary scientists with a decrease in scientific standards (i.e. deskilling). This pilot study surveyed 38 multidisciplinary scientists and 21 single discipline scientists in order to determine whether multidisciplinary practice in medical science might contribute to deskilling, or if the so-called deskilling process were avoidable. The survey identified inadequate training, supervision, and competency assessment of multidisciplinary scientists as potential contributors to deskilling. These factors appeared to be related to the workplace and to the multidisciplinary job design, not to multidisciplinary practice per se. As such, these factors are modifiable and therefore avoidable. A larger scale study would shed further light on the factors that this pilot study has identified as potential contributors to deskilling.

Keywords: Laboratory personnel, staff development, in-service training, medical science, scientist, pathology, professional status.

Introduction
The departmental structure of pathology laboratories that has existed since the pre-automation era is evolving into a more integrated structure that is sample based (Vining 1993; Wilding 1995; Hewett 1999). This has resulted from the capabilities of the automated analytical systems that are currently available. Laboratory instruments now carry test menus that cross the traditional boundaries between departments of the pathology laboratory (Ash 1996; Young et al 1996; Zinder 1995). An implication of this reorganisation and the need for cost containment in the health care sector is that laboratory managers require multidisciplinary scientific staff (i.e. medical scientists with knowledge and skills relevant to not just a single pathology department) to operate these integrated laboratories (Young et al 1996; Keaton 1996; Weinstein 1995) rather than the traditional specialist scientist, who is confined to a single department within the pathology laboratory.

The problem with the modern analytical technologies, which cross the traditional boundaries of pathology departments, is that they often require less scientific expertise to operate, and thus may lead to deskilling of medical scientists operating such instruments. The rationale at the core of such fears is that loss of expertise will accompany the multiskilling process and that the multiskilling process is actually a euphemism for deskilling (CAMRT 1995).

Such deskilling of medical scientists may be also accompanied by a de-professionalisation of the medical science profession (McGregor and Moriarty 2003a; Weekes 2002) and thus result in a lowering of the standard of services provided by pathology laboratories (MacDonald and Treloar 1996; Swaminathan 1995; Richardson 1999; Weekes 2002). There is little data to suggest that these concerns regarding deskilling are based on anything other than the supposition that breadth of knowledge can only be attained at the expense of depth of knowledge. In fact, very little has been published on multiskilling in the health services generally over recent years.

There are two major factors that could potentially contribute to deskilling of both specialist and multidisciplinary medical scientists. The first of these is the decrease in the level of analytical expertise required

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in the laboratory which, according to Isaacs (1995), is a largely inevitable consequence of technological progress. The second factor is the preparation of scientists in the workplace through supervised workplace training, ongoing professional education and competency assessment (O’Leary and Guerin 1994; Schwartz 1994; Mullins 1996). Any decrease in standards that arises from lack of attention to these details is an avoidable outcome. Thus, there are elements in the preparation of both multidisciplinary scientists and specialist scientists that may contribute to deskilling. These factors have been reported to cause dissatisfaction (Douglas and Wood 1984; Nolan et al 1995) and have been linked with decreased professional status (McGregor and Moriarty 2003a). Further, the link between job satisfaction and the work performed has been found to be weaker in multiskilled medical scientists (Akroyd et al 1992; McGregor and Moriarty 2003b).

This pilot study surveyed a sample consisting of both multidisciplinary scientists and single discipline (specialist) scientists in order to determine whether there were significant differences in workplace preparation and job design between the two groups that would tend to predispose multidisciplinary scientists to deskilling more than single discipline scientists.

**Materials and methods**

**Sample population**

The participants in this survey consisted of a sample of medical scientists employed in pathology laboratories. A total of 109 survey questionnaires were mailed out to 16 laboratories Australia wide, with the exception of the Australian Capital Territory. These laboratories included seven public laboratories and nine privately operated laboratories. Initial contact with the participants was made via the supervising scientist or laboratory manager at each laboratory. This contact was made by telephone to assess the availability of suitable staff for the study and to obtain an estimate of the number of eligible staff at each site. Following initial contact, a package consisting of a covering letter describing the inclusion and exclusion criteria (refer to Table 1) and an appropriate number of survey questionnaires were sent to the contact person at each site. The contact person was asked to distribute the surveys to scientific staff who fitted the inclusion criteria for both multidisciplinary and single discipline scientists who represented a wide range of experience, including both recent graduates as well as more experienced staff. Laboratories with an individual response rate of less than 50% were followed up by telephone or mail.

The study was limited to those disciplines that form the “core services” area of a large central laboratory and to small peripheral or regional laboratories. The disciplines included clinical biochemistry, haematology/coagulation, blood bank and microbiology. The histology discipline was therefore omitted from the inclusion criteria for this survey as multidisciplinary scientists do not usually rotate through that area.

On receipt of the returned questionnaires, the sample population was divided into two subsets, multidisciplinary scientists and single discipline (control) scientists according to Table 1. Questions assessing demographic characteristics were included in the survey to confirm the distribution of scientific experience.

**Table 1. Inclusion and exclusion criteria for multidisciplinary and control scientists.**

<table>
<thead>
<tr>
<th>Multidisciplinary sample</th>
<th>Inclusion criteria:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Must be employed as a medical scientist.</td>
</tr>
<tr>
<td></td>
<td>• Must work, on a routine basis, in at least two of the following disciplines: clinical chemistry, haematology/coagulation, blood bank or microbiology.</td>
</tr>
<tr>
<td></td>
<td>Exclusion criterion:</td>
</tr>
<tr>
<td></td>
<td>• Must not have a designated management role (e.g. Head or Deputy Head of Department).</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Single discipline (control) sample</th>
<th>Inclusion criteria:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Must be employed as a medical scientist.</td>
</tr>
<tr>
<td></td>
<td>• Must work in only one of the following disciplines: clinical chemistry, haematology/coagulation, blood bank or microbiology.</td>
</tr>
<tr>
<td></td>
<td>• Must have worked in that discipline for a period of not less than two years, except in the case of recent graduates.</td>
</tr>
<tr>
<td></td>
<td>Exclusion criterion:</td>
</tr>
<tr>
<td></td>
<td>• Must not have a designated management role (e.g. Head or Deputy Head of Department).</td>
</tr>
</tbody>
</table>
Instrumentation

The research instrument consisted of a two part questionnaire (parts A and B). Part A sought demographic information such as nature of employment (i.e. single or multidisciplinary), educational qualifications, state in which employed, laboratory experience, and a number of questions regarding workplace training and the type of work performed. Part B surveyed the participants’ opinion on the adequacy of their preparation for unsupervised work (such as adequacy of workplace training and personal opinions of their competency). The majority of questions in this section were in multiple choice format with four point Likert scale responses provided. The response range provided was from ‘strongly agree’ to ‘strongly disagree’. A copy of the complete questionnaire, as used in the survey, is available from the authors on request.

Several of the questions in the questionnaire were asked more than once. These questions required different responses at each iteration to control for acquiescent response sets (Brink and Wood 1988). Where the respondents’ answers indicated a clear misunderstanding of a question, that particular response was omitted from the study. Respondents were given the opportunity to refrain from answering any question that they did not consider applicable to them.

Statistical methods

Since the data obtained from the survey included both numerical and ordinal data sets, separate statistical techniques were required for each type of data set. Sample means for the numerical data sets were calculated, along with 95% confidence intervals (CI) for the population mean. It was assumed that the samples were normally distributed (Bland 1990). The values of the sample means were compared using the two-sample t test. The F-test was used to determine the t test method to be used (i.e. assuming equal or unequal variance). The ordinal data sets were analysed as estimates of proportions. Where the distribution of the data permitted (i.e. np, n(1-p) >5: n = sample size; p = proportion), 95% CI for the population proportions were calculated using a normal approximation (Bland 1990).

Results

Fifty-nine scientists from 14 of the laboratories returned the questionnaire for an overall response rate of 54%. The majority of the responses were received from multidisciplinary scientists (64%), the remainder from ‘control’ single discipline scientists. The response rate for the multidisciplinary group was 72%; the response rate for the control group was 38%. Responses were received from multidisciplinary and control scientists representing both private and public laboratories. No responses were received from two laboratories to which surveys were sent; one was a single discipline public laboratory department, the other a regional public laboratory. Laboratories were categorised to four types; the response rates from these are shown in Table 2. Respondents were employed in Queensland (n=25), New South Wales (n=11), Victoria (n=5), Tasmania (n=8), South Australia (n=4), Western Australia (n=3) and the Northern Territory (n=3).

Table 2. Distribution of questionnaire responses sorted by laboratory type.

<table>
<thead>
<tr>
<th>Laboratory type</th>
<th>Multi-disciplinary scientists</th>
<th>Single discipline scientists</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n %</td>
<td>n %</td>
</tr>
<tr>
<td>Private: central</td>
<td>8 21</td>
<td>12 57</td>
</tr>
<tr>
<td>Private: hospital</td>
<td>16 42</td>
<td>1 5</td>
</tr>
<tr>
<td>Private: regional/peripheral</td>
<td>8 21</td>
<td>0 0</td>
</tr>
<tr>
<td>Public: hospital</td>
<td>6 16</td>
<td>8 38</td>
</tr>
<tr>
<td>TOTAL</td>
<td>38 100</td>
<td>21 100</td>
</tr>
</tbody>
</table>

The levels of experience reported by the respondents ranged from less than one to more than 30 years. Both multidisciplinary and control scientists were grouped into four categories according to their total scientific experience (Table 3). A range of specialty areas were also represented (Table 4).

Table 3. Summary of total scientific experience reported by the multidisciplinary and control groups.

<table>
<thead>
<tr>
<th>Total scientific experience (years)</th>
<th>Multi-disciplinary</th>
<th>Control</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n %</td>
<td>n %</td>
<td>n %</td>
</tr>
<tr>
<td>&lt;2</td>
<td>9 24</td>
<td>1 5</td>
<td>10 17</td>
</tr>
<tr>
<td>2-5</td>
<td>10 26</td>
<td>4 19</td>
<td>14 24</td>
</tr>
<tr>
<td>5-10</td>
<td>6 16</td>
<td>4 19</td>
<td>10 17</td>
</tr>
<tr>
<td>&gt;10</td>
<td>13 34</td>
<td>12 57</td>
<td>25 42</td>
</tr>
<tr>
<td>TOTAL</td>
<td>38 100</td>
<td>21 100</td>
<td>59 100</td>
</tr>
</tbody>
</table>

Table 4. Distribution of multidisciplinary and control group samples by personal scientific specialty.

<table>
<thead>
<tr>
<th>Personal specialty</th>
<th>Multi-disciplinary scientists</th>
<th>Single discipline scientists</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n %</td>
<td>n %</td>
</tr>
<tr>
<td>Blood Bank</td>
<td>4 10</td>
<td>2 9</td>
</tr>
<tr>
<td>Clinical Biochemistry</td>
<td>9 24</td>
<td>8 38</td>
</tr>
<tr>
<td>Haematology/Coagulation</td>
<td>14 37</td>
<td>6 29</td>
</tr>
<tr>
<td>Haematology/Coagulation and Blood Bank</td>
<td>2 5</td>
<td>0 0</td>
</tr>
<tr>
<td>Haematology/Coagulation and Microbiology</td>
<td>2 5</td>
<td>0 0</td>
</tr>
<tr>
<td>Microbiology</td>
<td>5 13</td>
<td>5 24</td>
</tr>
<tr>
<td>All disciplines</td>
<td>2 5</td>
<td>0 0</td>
</tr>
<tr>
<td>TOTAL</td>
<td>38 100</td>
<td>21 100</td>
</tr>
</tbody>
</table>
Respondents were asked to estimate the length of training that they had received in each discipline prior to commencing unsupervised work in that discipline. The differences between the mean training period that was reported by each multidisciplinary experience group was significant (p ≤0.05) (Fig. 1). A similar change in mean training period per discipline was observed in the control group (Fig. 2), however, this was not statistically significant (p>0.05).

**Figure 1.** Changes in mean training period per discipline for multidisciplinary scientists.

Error bars show 95% confidence limits.

**Figure 2.** Changes in mean training period per discipline for single discipline (control) scientists.

Error bars show 95% confidence limits.

The majority of the multidisciplinary scientists (79%) had been trained as such from their first employment after graduation. There was no significant difference between the mean training period reported by this group and that of the remaining multidisciplinary scientists who provided other reasons for multidisciplinary training (p>0.05). There was also no significant difference between the training periods for each of the four disciplines included in the study (p>0.05).

In part B of the questionnaire, respondents were asked to provide their opinions of the adequacy of their workplace training, supervision, working conditions and the level of confidence that they had in their basic duties. The responses of the multidisciplinary scientists to these questions are provided in Table 5. Of these, only the first question regarding the level of organisation and supervision of the training was relevant to the control sample for the purpose of this study. Nineteen percent of the control group agreed that the workplace training that they had received was poorly organised, poorly supervised and did not meet their individual needs and levels of experience.

Twenty-nine percent of the multidisciplinary sample (95% CI 14.5-43.3%) indicated that they were not assessed for competency in each of the disciplines prior to commencing unsupervised work. The same proportion indicated that they were not assessed for competency on an ongoing basis. A further 21% of the multidisciplinary sample indicated that they had experienced ongoing competency assessment in either a continuous or other informal ongoing manner. The respondents who indicated informal means of ongoing competency assessment cited methods such as continuous review by peers and superiors as competency assessment. In comparison, 5% of the control group indicated that they were not assessed for competency prior to working unsupervised and 21% were not assessed for competency in an ongoing manner. Only two (10%) of the control sample indicated an informal method of ongoing assessment.

Multidisciplinary scientists reported a mean of 28% of their total working time being spent in each discipline. However, the mean percentage spent working in specialty disciplines was 47%. The mean proportion of time spent working in non-specialty disciplines was significantly less (17%) (p<0.001). The mean percentage of time that the multidisciplinary sample reported as being spent working supervised (or at least not alone) in each non-specialty discipline was 7% (95% CI 5.3-9.1%). Further, approximately 54% reported that the percentage of time spent working under supervision was less than 5% of their total working time in at least one of the non-specialty disciplines that they work in. Figure 3 illustrates the level of supervision for the multidisciplinary scientists with various levels of experience.
Participation in external quality assurance programs (QAP) by the multidisciplinary sample was approximately divided into three even groups. The first group (37%, 95% CI 21.5-52.2%) indicated that they participate in QAP exercises in all of the disciplines in which they worked. The second group (34%, 95% CI 19.1-49.3%) participated in QAP exercises only in their specialty discipline. Approximately 24% (95% CI 10.2-37.2%) of the multidisciplinary scientists indicated that they participated in external QAP in more than one, but not all, of the disciplines in which they worked. The final 5% (n=2) indicated that they did not participate in any external quality assurance activities in any discipline. The participation rate in QAP exercises for the control sample was 100%.

Of the entire multidisciplinary sample, only four respondents (12%) indicated that they had attained a tertiary qualification that exceeded the minimum entry requirements to the profession (Whitfield et al 1993). None of the multidisciplinary sample indicated that they had obtained a professional qualification offered by any of the relevant societies (e.g. Member of the Australian Association of Clinical Biochemists (MAACB) or Fellow of the Australian Institute of Medical Scientists (FAIMS)). In contrast, six (29%) of the control group indicated that they had attained a postgraduate tertiary qualification in addition to the minimum entry requirement degree. In addition, 19% of the control sample indicated that they held full membership of either the Australian Association of Clinical Biochemists or the Australian Society for Microbiology.

**Discussion**

The results of this pilot study indicate that there appear to be changes in the way that workplace training of multidisciplinary medical scientists is conducted. Of particular concern was the shorter supervised training periods provided for the least experienced scientists, in each discipline (Fig. 1). While a similar decrease in training period was observed in the control group (Fig. 2) it was not statistically significant. However, a significant difference between the means of the control subgroups was unlikely to be detected because both of the control subgroups in question were small in size and had relatively large standard deviations (compared to the mean value) (Bland 1990).

---

**Table 5. Multidisciplinary scientists’ responses to questions in part B of the survey questionnaire.**

<table>
<thead>
<tr>
<th>Question</th>
<th>Agree</th>
<th>Disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Your on-the-job training program was poorly organised, poorly supervised and did not meet individual needs and levels of experience.</td>
<td>9</td>
<td>24 29</td>
</tr>
<tr>
<td>2. Your on-the-job training provided adequate preparation for unsupervised work as a multidisciplinary medical scientist</td>
<td>37</td>
<td>97 1</td>
</tr>
<tr>
<td>3. Your training has provided you with adequate confidence to fulfi your sign-out (i.e. result verification) requirements in a manner that befits your responsibility to patient care in each of the laboratory disciplines that you work in.</td>
<td>35</td>
<td>95 2</td>
</tr>
<tr>
<td>4. You have sufficient knowledge of quality control principles to ensure that any batch of patient results will be precise and accurate within expected limits in each of the laboratory disciplines that you work in.</td>
<td>37</td>
<td>100 0</td>
</tr>
<tr>
<td>5. When quality control or mechanical problems occur, you are able to troubleshoot the most frequently occurring problems of the test methods and instrumentation that you use regularly</td>
<td>37</td>
<td>100 0</td>
</tr>
<tr>
<td>6. You have attained an adequate knowledge of pathology testing to recognise the effects of pre-analytical, analytical and post-analytical variables (e.g. haemolysis reagent quality control failure and clerical errors respectively) in each of the laboratory disciplines that you work in.</td>
<td>35</td>
<td>95 2</td>
</tr>
<tr>
<td>7. The percentage of time spent working in each of the laboratory disciplines is adequate to maintain your skills at an acceptable level for your work in each discipline.</td>
<td>28</td>
<td>74 10 26</td>
</tr>
<tr>
<td>8. Your competency in each laboratory discipline is at least equivalent to that of the full-time staff in each of those disciplines who perform the same tests.</td>
<td>27</td>
<td>71 11 29</td>
</tr>
<tr>
<td>9. Multidisciplinary staff should participate in quality assurance exercises in each laboratory discipline that they work in.</td>
<td>37</td>
<td>97 1</td>
</tr>
</tbody>
</table>
The decrease in the supervised training period that was seen in both samples coincided with a decreased level of organisation, supervision and attendance to the needs of the individual. Similar proportions (24% and 19% respectively) of both multidisciplinary and control samples reported their training as poorly supervised, poorly structured and not meeting their individual needs or level of experience. Because a high proportion of the multidisciplinary group were trained as multidisciplinary scientists in their first job (84%), it is inferred that these results reflect the workplace training of graduate scientists. While not rigorously eliminating the possibility of site- or employer-related bias, the wide range of responses, both geographically and by laboratory type, indicates that such a bias is unlikely.

In addition, more than half of the multidisciplinary scientists with less than two years experience indicated that their training was poorly organised, poorly supervised and did not meet their individual needs. This indicates that the workplace training, as experienced by the more recently graduated members of the multidisciplinary sample, was not as well organised or supervised as the training received by the more experienced multidisciplinary scientists.

Despite these findings, the majority of the multidisciplinary sample indicated that the workplace training that they had received provided adequate preparation for unsupervised multidisciplinary work. Similarly, responses to more specific questions of respondents' abilities to recognise erroneous results and factors that interfere with results were also overwhelmingly affirmative (Table 5). However, the training detailed above would seem to indicate that it was barely adequate in preparing these graduates for multidisciplinary work and therefore must be questioned.

Hunter and Losciuto (1993) conducted a large survey in the United States to identify areas where supervisors' expectations of newly graduated laboratory staff (medical technologists) were not met by their capabilities. In that survey, supervising scientists were asked to rank a number of laboratory duties and competencies in order of importance and also to rank them in order of likelihood that a new graduate could perform such tasks. The largest differences between importance and likelihood were found in the competencies involved in performing analytical tests, teamwork and preventive and corrective maintenance. These competencies specifically included analysis of quality control data, maintaining accuracy and precision in the testing system, the recognition of equipment malfunctions, prioritisation of work, and recognition of factors affecting measurement. The recently graduated scientists in this survey, who had the benefit of post-graduate workplace training, expressed confidence in the areas identified by Hunter and Losciuto (1993) (Table 5). Thus, the training programs that the respondents in this survey experienced, despite the observed shortcomings, would appear to have provided them with adequate confidence to fulfil their basic duties.

First person expression of self-confidence, however, does not provide either objective or adequate indication of competency in the laboratory. Objective assessment of competency is an essential process in the training of scientists (Mullins 1996). Furthermore, this is necessary for each of the disciplines in which the multidisciplinary scientist is required to work. However, the population mean of the proportion of multidisciplinary scientists who were not assessed for competency prior to commencing unsupervised work could be as high as 43% (from the current study). In comparison, only one respondent from the control sample indicated that they had not been assessed for competency prior to working unsupervised. One respondent from the multidisciplinary sample indicated informal assessment of competency, such as tacit approval from senior staff that their skills were adequate, prior to their commencement of unsupervised work. Another respondent commented that the method of training and competency assessment that they had experienced consisted of the informal process of “see one, do one, equals competent”.

Similar proportions (20% and 30% respectively) of both the control and multidisciplinary samples indicated that they were not assessed for competency in an ongoing manner. Again, there were responses suggesting that the assessment of competency was an informal process. Processes such as continuous review of competency by peers and senior staff in the form of feedback were cited as informal methods of ongoing competency assessment. These results are suggestive of a range of informal and formal methods being used, in practice, to assess and monitor the competency and performance of scientific staff. Unfortunately, the data do not permit any inference on the adequacy of these informal methods of assessment or a comparison with more formal assessment methods.

Further to the idea of ongoing competency assessment is the development and maintenance of skills in each of the laboratory disciplines associated with multidisciplinary scientists. The continual development of understanding and skills relating to the analytical process, as well as the clinical applications of the results that are produced, is fundamental to the development of scientific expertise. It is in this development of expertise that multidisciplinary scientists are potentially at a disadvantage. The proportion of time that multidisciplinary scientists spent in each discipline was considerably less than that reported by the control sample. This was evident by the proportion of multidisciplinary scientists who indicated that their skills were less than equivalent to the single discipline scientists who performed the same tests in each discipline (Table 5). This was despite the expectation that multidisciplinary
scientists are required to produce results that are equivalent to those produced by single disciplinary scientists (NPAAC 1999; Woo and Henry 1994).

Inequity between the skills of multidisciplinary scientists and single discipline scientists appeared to be exacerbated by the limited time that multidisciplinary scientists have available to learn new skills and reinforce existing ones. Twenty-six percent of the multidisciplinary sample (95% CI 12-40%) indicated that they did not spend adequate time in each discipline to maintain their skills at an acceptable level. The data further indicated that the amount of time that multidisciplinary scientists spent working supervised in each discipline was not sufficient to learn new skills and to maintain current skills. The National Association of Testing Authorities and the Royal College of Pathologists of Australia recommend that non-routine scientists spend at least one day per month in each discipline under the supervision of routine scientific staff (preferably senior staff) in each discipline (Allred and Steiner 1994). This is the equivalent of 5% of the total working time for a full-time multidisciplinary scientist. However, greater than 50% of the multidisciplinary sample indicated that they spent less than 5% of their time in at least one of the disciplines that they did not consider to be a specialised field.

This presents a significant threat to the level of competency that these scientists can acquire in these non-specialty disciplines. The distribution of the time that is spent working under supervision in non-specialty disciplines is critical to whether that time is productive or not. There needs to be a balance between the learning of new skills and repetition to reinforce existing skills. Further, in order to maximise learning, it is also necessary to identify the areas where further training is required for each individual so that greater efficiencies in the process of ongoing training can be achieved. Individual laboratories must identify the role that they require their multidisciplinary scientists to play in order to determine what skills and level of background knowledge those scientists require (Reilly 1996). For example there is a need to determine whether multidisciplinary scientists will be restricted to low level tasks: such as routine analysis, or whether they will also be required to provide high level “value-adding” roles, such as interpretative clinical consultation (Burke 1995; Pannall 1995; McDonald and Smith 1995). It is important then, to identify the roles and the individual skill and knowledge sets that are required of multidisciplinary scientists so that learning can be efficiently focused on those areas. It was expected from this study that the more recently graduated scientists would be subjected to higher levels of supervision than their more experienced colleagues. However, the multidisciplinary scientists in the subgroup with less than two years total scientific experience reported the highest proportion of unsupervised work (Fig. 3). That proportion is significantly higher than that reported by the groups with two to 10 years of experience and is similar to that reported by the group with greater than 10 years experience. When the personal specialty is excluded from the percentage of unsupervised work in each discipline, the multidisciplinary group with less than two years experience had a mean proportion of unsupervised work that was comparable to that of the single discipline group. This low level of supervision implies that the skills of these recent graduates are being perceived by their supervisors as being comparable to those of single discipline scientists. The high proportion of unsupervised work reported by the recently graduated multidisciplinary scientists means that they are at a disadvantage in the acquisition of expert knowledge and technical proficiency and are unlikely to develop the same skill levels as the single discipline scientists in each discipline.

Two domains of learning contribute to the development of expert knowledge and technical proficiency: training and education. Training involves the acquisition of the necessary psychomotor skills required to perform a task, while education implies the development of cognitive understanding of the system in which the scientist works (Woo and Henry 1994). The development of expert knowledge domains such as understanding of the clinical significance of the results that they produce is dependent upon workplace exposure to problem solving events (Pannall 1995; Bryant 1996; Dominiczak and Hooper 1996; Sibber 1984). This means that multidisciplinary scientists can and must develop expert knowledge in each discipline, but only through frequent exposure to the problems and procedures of each discipline and from frequent contact with experienced staff in each discipline. An introductory training period sufficiently provides recently graduated scientists with the necessary skills to perform multidisciplinary tasks. However the education of multidisciplinary scientists is an ongoing process and requires experience in each discipline. Premature removal of supervision and working contact with single discipline scientists threatens the education process of inexperienced multidisciplinary scientists.

Beyond formal assessment of competency and supervised on-the-job work experience, participation in external quality assurance activities (proficiency testing) is a secondary means of assessing the quality of laboratory staff and the training that they have received (Lunz et al. 1987). It has been recommended that all staff, including non-routine staff such as multidisciplinary scientists, be involved in the testing of external quality assurance materials (Allred and Steiner 1994). However in the current study, only 42% of the multidisciplinary scientists reported participation in external quality assurance activities in each of the disciplines. Most of
the remaining multidisciplinary scientists indicated that they participated in such exercises in some but not all of the disciplines in which they worked. The remaining 5% of the multidisciplinary sample indicated that they did not participate in any external quality assurance activities at all. This is despite an almost unanimous agreement from both the multidisciplinary and control samples that multidisciplinary scientists should participate in quality assurance exercises for each discipline in which they worked.

In this study there were more single discipline scientists with tertiary and professional qualifications than there were multidisciplinary scientists. These data may be biased, though, as several of the control respondents who reported additional tertiary and professional qualifications originated from a single disciplinary department. Thus, it is possible that such data may represent a unique culture in that particular department that promotes further study, rather than an overall trend for single discipline scientists to pursue further study more than multidisciplinary scientists. However, there are two possible explanations for such a difference in postgraduate study patterns, should it exist. Firstly, many multidisciplinary scientists are located in regional centres and do not have the benefit of access to academic facilities or resources (McKenzie et al. 1996). In this study, however, only 20% of the multidisciplinary sample indicated that they were employed in a peripheral or regional laboratory. Secondly, it is possible that multidisciplinary scientists are unable to dedicate large amounts of their working time to develop a specialisation that can be pursued as a postgraduate course of study, due to the nature of their employment. However, professional qualifications with a general focus, such as some of the Masters degree programs offered by tertiary institutions and the general fellowship offered by the Australian Institute of Medical Scientists, provide an opportunity for experienced multidisciplinary scientists to obtain a professional qualification. Barriers that impede the development of expert knowledge and competency will interfere with opportunities for professional development and promotion.

Conclusion

The aspects of multidisciplinary practice that have been identified in this pilot study as potential contributors to deskilling arise from the multidisciplinary job design, rather than multidisciplinary practice per se, and are consequently avoidable. It is therefore the responsibility of employers and the professional associations to accept that multidisciplinary practice requires more careful planning and ongoing commitment. Of particular concern are the issues concerning the induction and career path articulation of recently graduated scientists. These must be further investigated in a larger study and addressed if professional standards are to be maintained in the multidisciplinary era of the practice of medical science.

References


AIMS has initiated a scholarship programme for the RCPA/AIMS Morphology Workshop.

In 2009 there will be up to TWO scholarships available for all financial members of the Institute. Both will be for the workshop held on 3-4 July 2009, at Westmead Hospital, Westmead, NSW.

This workshop has been held at least twice a year for the last 18 years. It is organised through the RCPA QAP in Haematology office by a group of AIMS members and Haematologists. The workshop is now acknowledged as the premier workshop of its type, not only in Australia but also in the Asia Pacific Rim. It is a ‘wet’ workshop held over two full days.

CONDITIONS

Applicants would be expected to have some basic knowledge and the scholarship is particularly suitable for members who either do not have resources for continuing education available to them or have a need for retraining due to rationalisation or multiskilling in their workplace.

Previously unsuccessful applicants are encouraged to apply.

VALUE

The value of each scholarship will not exceed $1000. The exact value will depend on the applicant’s travel requirements.

DEADLINE

Tuesday 14 April 2009

SEND TO

AIMS National Office
PO Box 1911
MILTON QLD 4064
Phone: 07 3876 2988
Fax: 07 3876 2999
Email: aimsnat@aims.org.au

AIMS SCHOLARSHIPS

NSM 2009
12-16 October 2009

Five scholarships of $1,000 each will be offered in the categories below to financial members of AIMS to attend the AIMS NSM 2009. This year three Remote Attendee Scholarships, one First Time Presenter Scholarships and one Young Scientist scholarship are offered. Applicants must be current members of AIMS and must have held membership for at least six months at the time of the application. Affiliate, retained or student members are not eligible to apply. For full details and application forms see the AIMS website www.aims.org.au or contact National Office.

APPLICATIONS CLOSE AT 4.00 PM QUEENSLAND TIME ON TUESDAY 14 APRIL 2009.
The patient in this case study was a male diagnosed with infantile nephrotic cystinosis at the age of eleven months. Nephrotic cystinosis is a rare autosomal recessive disorder resulting in the accumulation of cystine crystals primarily in the kidney as well as other organs, including the bone marrow. These crystals are almost never seen in the peripheral blood. Cystinosis presents between six and twelve months of age. The clinical characteristics include failure to thrive, progressive renal failure, loss of muscle function, photophobia and fair hair. Diagnosis is made by measuring the level of cystine in peripheral blood white cells.

By the age of eleven years, the patient’s condition had progressed to renal failure requiring peritoneal dialysis and frequent blood transfusions. At the age of thirteen, he received a renal transplant, the kidney being donated by a family member. He was then started on a regimen of immunosuppressive therapy.

By the age of twenty the patient was experiencing neurological abnormalities. He had difficulty in walking and swallowing, loss of memory and progressive loss of speech as well as diminished intellectual function. He continued to receive immunosuppressive therapy for his renal transplant.

At the age of twenty-six he presented to the Casualty Department. He had cervical and mediastinal lymphadenopathy and splenomegaly. A full blood count was performed with the following results:

Hb 115 g/L, WBC 5.4 x 10^9/L and platelet count 197 x 10^9/L. The peripheral blood film revealed the presence of circulating blast cells. A bone marrow biopsy was performed. The bone marrow was hypercellular with 70% blasts. The blasts had a high N/C ratio; the nuclei were variable from round to irregular and folded in shape. They contained one to four distinct nucleoli. Immunophenotyping was performed with the following results:

CD45+, HLA-DR-, CD19+, cytoCD79a+, cytoCD3+, CD2+, CD5+, CD7+, CD38+ and CD117+.

CD4, CD8. A diagnosis of T-cell lymphoblastic lymphoma/leukaemia was made.

CD2, 5 and 7 are the most commonly expressed markers in T-cell lymphoma/leukaemia. CD3 is often present in the cytoplasm but not on the surface. CD4 and CD8 may be expressed or may be negative.

Co-expression of CD79a and CD117 has been described on primitive T cell lineages however the expression of CD19, normally a B cell marker, is unusual.

A cytogenetic analysis on the available cells revealed a 46, XY karyotype. Subsequent fluorescence in situ hybridisation (FISH) studies showed no evidence of BCR-ABL 1 gene rearrangements.
Post Transplant Lymphoproliferative Disorders (PTLD) are a well-known complication of immunosuppressive treatment after solid organ transplantation. Any lymphoma/leukaemia that occurs in the post-transplant population is considered to be a type of PTLD. The median time from transplant to diagnosis is fifteen years. The majority of post transplant lymphoma/leukaemias are B cell in origin and are associated with EBV infection. T-cell variants are very rare. The patient in this study was EBV positive.

The risk factors of PTLD are intensity of immunosuppression, type of organ transplanted, Epstein-Barr virus (EBV) seronegativity and the duration of the immunosuppression. EBV seronegativity pre-transplant is a powerful predisposing factor for the development of PTLD. Studies show that EBV seronegative patients experience a 10-76 fold greater incidence of PTLD when compared to seropositive counterparts.

The patient in this study died suddenly, two months post chemotherapy induction.

Address correspondence to:
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Department of Haematology
Prince of Wales Hospital
Barker Street
Randwick NSW 2031
Email: gillian_rozenberg@yahoo.com

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THE AIMS FELLOWSHIP PROGRAM

A modular structure has been developed comprising two compulsory and two elective modules to be completed for each discipline. Considerable flexibility is provided to the study format, subject modules that can be selected, and the timeframe for completing the program. Mentoring arrangements are made as required for each candidate.

The programme also retains a viva voce examination. A dissertation may not be required at the end stage if, during the previous five years, the candidate has published a paper in a relevant peer reviewed journal or successfully completed a research degree thesis approved by the Examinations Council.

The new model also provides for Members to undertake any module without formally entering the Fellowship programme. APACE certificates are awarded and 40 APACE points accrued for successfully completed modules; compulsory modules completed attract advanced standing for subsequent enrolment into the Fellowship program within a five year period.

The Fellowship provides an attractive and highly competitive option to academic postgraduate degrees at a fraction of the cost.

I encourage Members to consider the Fellowship as the preferred option for advancing their knowledge and career prospects.

Richard Hanlon
Chair, Examinations Council
We were saddened to learn of the passing, in December 2008, of AIMS Life Member and former President, Gordon Ingham Pratt.

Gordon Pratt was born in England in 1923. He left Grammar School at the age of sixteen, having reached school leaving certificate standard, and commenced work as a “laboratory boy” at the Public Health Laboratory, Derby. During the next two years he was taught by the chief technician of the laboratory, and attended evening classes and meetings and lectures of the Institute of Medical Technology (now the Institute of Biomedical Science). At the age of 18 he was drafted into the RAF Medical Services and served as a laboratory technician for five years. On returning to civilian life he obtained membership of the Institute of Medical Technology. He then spent six months assisting research on an artificial kidney before taking charge of a laboratory attached to a 100 bed hospital.

In 1951 he came to Australia to a position as senior technician in the Public Health Department at Melbourne University, and in February of 1952 he joined the then Society of Laboratory Technicians of Australasia, as AIMS was then called.

In 1958 he moved to the position of laboratory manager at Preston and Northcote Community Hospital, a position he held until 1965, when he took up the position of laboratory manager at the University of Melbourne Austin Campus.

Gordon Pratt made an outstanding contribution to the Institute during his 57 year membership. He was Federal President for eight years, from 1963 to 1970. He was also President of the Victorian Branch for a number of years.

Mr Pratt was instrumental, with the late Betty Wilson, in the establishment of the Institute’s Fellowship program, and was chair of the Postgraduate Education Committee (PEC) from 1969 to 1978. It is reported that at one stage of his membership he held the positions of Federal President, Victorian Branch Chair and Chair of the PEC. He was awarded Life Membership of AIMS in 1977.

In retirement Gordon Pratt continued to maintain an interest in the profession and the education of new medical scientists. In May 2002 he visited the new laboratories for the RMIT Medical Laboratory Science program at Bundoora which had been recently relocated from the city campus.

Those who knew him remember him with great affection. He was an outstanding President, a man of considerable personal presence and great courtesy, and an excellent speaker. The current members of AIMS owe a great deal to the vision and dedication of Gordon Ingham Pratt.
New South Wales State Medical Congress 2009

Australian Institute of Medical Scientists National Scientific Meeting 2009

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Monday 12 & Tuesday 13 October 2009

Conference Sessions
Wednesday 14 to Friday 16 October 2009

Conference Dinner
Thursday 15 October 2009

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MEDICAL SCIENCE - TODAY AND TOMORROW
Allergy and Asthma: Practical diagnosis and management
Edited by Massoud Mahmoudi
Soft cover, 385 pages
AU$70.00

Allergy is one of the most commonly heard terms used in hospitals and in general practice. Inquiring about drug and latex allergy has become a routine part of history taking for new patients. Hay fever, food allergy, bee stings and asthma are familiar terms to many individuals and common reasons for frequent visits to the doctor or hospital emergency department.

Allergy and Asthma: Practical Diagnosis and Management has concisely but comprehensively collated the salient insights and concepts in allergy medicine in one easy to follow volume. It is a compilation of contributions from 47 recognised experts in the fields of allergy and immunology and is edited by the internationally respected Professor Massoud Mahmoudi, (who also contributed six chapters) Clinical Professor of Medicine, Division of Allergy and Immunology, University of California.

Allergy and Asthma: Practical Diagnosis and Management is designed as a primary reference for front-line general practitioners, primary healthcare providers, and in teaching the diagnosis and management of allergy-based diseases to medical students.

As expected Allergy and Asthma: Practical Diagnosis and Management includes chapters ranging from a thorough review of the immunological basis of allergy, the history and physical examination of the allergic patient, allergic diseases, and diagnosis and management of allergy. There are six chapters dedicated specifically to asthma. What sets this book apart is the inclusion of uncommonly discussed but important topics including pollution, cough, pseudoasthma, sick building syndrome, complementary and alternative therapies, and allergy in the elderly. A valuable feature that will assist readers to remain up to date, is the inclusion after each chapter, of an evidence-based medicine section. This discusses an important study finding or publication, relevant to that chapter, that has added to our knowledge and understanding of allergic disease.

Allergy and Asthma: Practical Diagnosis and Management is a very ‘hands on’ text, meant to be kept at hand and used often due to its direct practicality to the physician. It also has a direct practical application to Medical Laboratory Scientist, with a clear discussion of the diagnostic testing available for allergic diseases, including their limitations. It is easy to read, has a large number of helpful figures and tables, and is fully referenced.

This volume is highly recommended to all health professionals.
Dr Bevan Hokin,
Director of Pathology,
Sydney Adventist Hospital
Wahroonga, New South Wales

Atlas of Orthopaedic Pathology, Third Edition
Lester Wold, K. Krishnan Unni, Franklin Sim, Murali Sundaram
Saunders Elsevier, 2008
Hardcover, 548 pages
ISBN: 978-1-4160-5328-6
AU$275.00

The third edition of the Atlas of Orthopaedic Pathology is a comprehensive clinicopathological summary of the major orthopaedic conditions and a useful addition to the working library of practising pathologists and others.

This volume is striking for its clarity and simplicity. Each chapter is consistent in its layout. The information is clearly set out in point form using the headings:

- Clinical signs
- Clinical symptoms
- Major radiological features
- Radiological differential diagnosis
- Major pathological features, both macroscopic and microscopic
- Pathological differential diagnosis
- Treatment options

There is also a schematic skeletal diagram, showing the distribution of the condition and a histogram of age incidence data.

The radiological and histological illustrations are plentiful and of the highest quality.

This text is much more comprehensive than the name ‘atlas’ suggests, and would be a very useful volume to be kept close at hand for the reporting pathologist. Those who would find it most useful include general pathologists, specialist histopathologists who receive a few orthopaedic specimens as part of their daily workload, radiologists, pathology and orthopaedic registrars, and histopathology laboratory staff. Although not comprehensive enough for
a specialist orthopaedic pathologist, it could still form a useful part of his or her library for teaching.

Purchasers of this volume should be aware that it is not an exhaustive text and does not claim to be. Although joint diseases are dealt with in the format described above, some joint conditions which are commonly seen in this practice, such as changes after joint replacement, do not appear to be included – or if they are, were not easily or intuitively found in the otherwise thorough index. Further, some differential diagnoses are listed but not illustrated, especially in joint pathology.

This third edition includes additional chapters on tumour-like conditions as well as updated references for most chapters. The layout of chapters is logical; it is well referenced and indexed, and the included CD-ROM contains all the book’s excellent illustrations in downloadable format that may be included in the reader’s own electronic presentations.

This volume is highly recommended to the target audience.

Dr Bevan Hokin (Director of Pathology), and Dr Fay Chambers (Pathologist)
Sydney Adventist Hospital,
Wahroonga, New South Wales

Insulin – A voice for choice
Dr Arthur Teuscher
Karger, 2007
Soft cover, XIV+82 pages
ISBN: 978-3-8055-8353-4
US$28.00

This unusual work is a blend of medical history, clinical practice, research and a possible touch of conspiracy.

The book commences with a clear overview of insulin therapy that is concise and easily understood. The following section provides a brief but complete history of insulin, and introduces the pivotal concept that the earlier “animal insulins” (bovine or porcine) and the later development of “human insulins” and insulin analogues are different.

Insulin hypoglycaemia in all its manifestations is discussed extensively. The hazards of “human” insulin hypoglycaemia are presented by case study, along with reports of “human” insulin-induced hypoglycaemia being associated with road traffic accidents, ‘dead-in-bed’ syndrome, violence and emotional instability.

Research findings are presented that demonstrate that “human” insulin and “animal” insulins are not the same, building a strong case that the recombinant technology-sourced “human” insulin is in fact not identical to the human insulin, and in susceptible patients is dangerous, compared with the older “animal” insulins.

While not actually making a conspiracy allegation, the author demonstrates the power of the big drug companies in the case of the promotion of the so-called “human” insulin in three ways:

- The aggressive marketing of “human” insulin and the withdrawal from the market of “animal” insulin to the point where it is almost impossible to obtain “animal” insulin in many countries;
- The use of the Brand name “Humulin” was approved by the FDA contrary to the FDA’s own long-standing regulations that disallow fanciful names or false and/or misleading claims embedded in the name. (“Humulin” suggests “human” when the insulin is in fact is synthetic recombinant DNA-sourced, insulin that is not human identical).
- The FDA’s short 4-month review of the first medical product of biotechnology, when the average time for approvals was two or more years, suggests an “unusual enthusiasm by FDA staff for the product”.

This remarkable book concludes with a Chapter on Advocacy where the authors seek to retain the availability of animal-sourced insulin, providing clinicians the option to use either Humulin or “animal” insulin. The key message is that “human” insulin is not suitable for all patients, so there should be a choice.

While an unusual book, the case is well argued, and while the case is presented passionately, it is also balanced. Full referencing of the text provides additional credibility.

Dr Bevan Hokin,
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Wahroonga, New South Wales

Leishmania – After the Genome
Edited by Peter J. Myler and Nicolas Fasel
Caister Academic Press, 2008
Hardcover, 306 pages
ISBN: 978-904455-28-8
€150.00

This book represents a most thorough and comprehensive review of current research into the genetics, biology, host-parasite interactions and developments in treatment of Leishmaniasis. The chapters are contributed by many eminent researchers in the field, and thus it contains the most recent research and developments relating to this organism.
The first chapter discusses epidemiological trends in Leishmaniasis, and provides an excellent introduction into the epidemiology, geographic range, prevalence and manifestations of the disease. The second chapter covers genome structure and content, and is an informative and extremely thorough analysis of the content of the genomes of the three Leishmania species which have been sequenced, including the content, protein coding sequences, RNA genes and putative protein genes. Intraspies relationships and the relationships to the genomes of other Trypanosomatids are also discussed. The next chapter discusses the regulation of gene expression, which interestingly occurs post-transcriptionally in Leishmania by pre-mRNA processing. It includes discussions of mRNA stability and translation, protein stability and post translational control.

The fourth chapter is a fascinating review of Leishmania proteomics, including mechanisms by which drug resistance develops and putative vaccine targets and protein markers in patient serum which may serve as diagnostic tools in the identification and monitoring of disease. Metabolomics is the subject of the following chapter, providing discussion of the methods and implications of findings in this very new area in Leishmania research, which is providing new insights into virulence, disease process and drug and vaccine targets. Chapter six discusses the differentiation of Leishmania from amastigote to promastigote, and the role of environmental factors such as temperature and pH in this process. This chapter includes a comprehensive discussion of methods by which the Old World and New World species may be axenised.

The following two chapters are focused on drug discovery and resistance in Leishmania. The metabolism of Leishmania is discussed in the context of the development of new treatments, followed by the genotypic and phenotypic aspects of antimicrobial drug resistance.

Surface proteins are the subject of chapter nine. This chapter comprehensively covers all known types of surface proteins including those of unknown function. A short section discusses surface proteins in the context of parasite-host interactions.

Parasite-host interactions are discussed more thoroughly in chapters ten and eleven. The chapter on the biology of Leishmania-sandfly interactions was particularly interesting, taking the reader from sandfly distribution worldwide through their biology, the life cycle of Leishmania within the sandfly, vector competence and finally molecular interactions of sandflies with the parasite. The following chapter discusses cellular and molecular interactions between the parasite and the human macrophage, discussing these through all stages from phagocytosis to the mechanisms by which the parasite manipulation of transcription within macrophages. This chapter includes a short section on comparisons of these interactions with other Trypanosomatids.

Chapter twelve is a review of host responses to Leishmania infections, discussing cytokine responses as well as the role of cytokine inhibitors and T cells in immune reactions to infection. These responses are discussed in the context of both experimental models and observations made in human infections.

Leishmaniasis is becoming a disease of increasing relevance in Australia due to large numbers of migrants from endemic areas, infections in soldiers returning from both Iraq and Afghanistan, and the recent discovery of a Leishmania species infecting marsupials in the North of Australia. This book represents a most valuable reference for any Scientist who wishes to expand their knowledge and understanding of current research into this important parasitic infection. I feel that it is a must for the library of any individual undertaking research into this disease.

Richard Bradbury
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Lifestyle Medicine

Garry Egger, Andrew Binns, Stephan Rossner
McGraw-Hill 2008
Soft cover, 307 pages
ISBN: 978-0-0701-3817-9
AU$60.00

The introductory chapter of Lifestyle Medicine includes a cartoon of a chubby patient chatting with his doctor and saying: “Yes, I believe in prevention. So can you give me a pill that will prevent me from having to exercise, eat less and stop smoking and drinking?”

Many Australians believe that they have an adequate understanding of lifestyle issues that impact on their health – but they keep smoking, drinking to excess of health recommendations for men and women, not exercising even for a half hour each day and eating themselves into an obesity epidemic. Many health professionals, if not a part of the problem themselves, are puzzled by the increasing incidence of preventable disease directly attributable to
Human Cancer Viruses: Principles of Transformation and Pathogenesis

Edited by J Nicholas, K-T Jeang and T-C Wu
S Karger AG
Hardcover, XII + 244 pages
ISBN: 978-3-8055-8576-7
€151.50

The first edition of Human Cancer Viruses: Principles of Transformation and Pathogenesis is one of a series of volumes on Translational Research in Biomedicine produced by Karger in 2008. The aim of the series is to present contemporary information in biomedicine with a translational orientation. The mission of this book is to present a review of human viral oncology as a cohesive topic. The original idea for this text came from a long-standing collaboration between many of its authors in the teaching of viral oncology to postgraduate students at the John Hopkins School of Medicine. Translational research remains a relatively new research topic, therefore the universal definition of translational research remains unclear to many. However, it has been said that ‘the goal of translational research is to implement in vivo measurements and leverage preclinical models that more accurately predict drug effects in humans.’ The authors of this text take a holistic view on translational research that transcends the boundaries between laboratory bench and bedside research. Edited by 24 internationally renowned scientists, this text is logically presented in 16 sections. It contains a total of 12 chapters, 9 tables, 26 monochromatic and 9 colour figures.

Since the discovery of a tumour-causing virus, Rous sarcoma virus, almost 100 years ago, studies of oncogenic viruses have made enormous contributions to our understanding of crucially important aspects of molecular and cellular biology. This book provides an up-to-date overview of the six major viruses that cause human cancers, human T lymphotropic virus type 1, human papillomavirus, hepatitis B and C viruses, human herpesvirus type 8. Each chapter contains an up-to-date review on fundamental principles that underlie the theme, to be followed by their clinical applications and underlying cellular and molecular mechanisms. Understanding the mechanisms leading to cellular transformation and oncogenesis by these viruses, in addition to the roles of particular viral proteins in these processes and the normal virus life cycle, is essential for the development of highly directed and specific therapeutic and anti-viral treatments. Each chapter is presented and expressed in simple language and uses an uncomplicated interpretation; therefore it is comprehensible to non-molecular biology practitioners. Each major virus type involved in oncogenesis has been addressed effectively. The use of figures has further clarified key concepts.

This text is well-researched and aims to provide a comprehensive overview of human oncogenic viruses, with respect to their molecular biology and epidemiology and to the clinical aspects of disease, therapy and prevention. It contains an appropriate level of detail for both scientists who engage in clinical research and clinical practitioners. This book is recommended for postgraduate students, postdoctoral researchers, scientists and clinicians who wish to understand the mechanisms leading to cellular transformation and oncogenes by these viruses as a basis for the development of anti-viral treatments. The references and author index sections make it possible to identify key papers required for further investigation.
The writing style of the text is appropriate for the target audience. The cost for this text is justifiable for such well-compiled information.

Captain Dennis Mok MAIMS MASM AFAIM
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Progress and Challenges in Transfusion Medicine, Hemostasis, and Hemotherapy
Edited by Rüdiger E Scharf
Softback 407 pages
29 tables, 27 colour illustrations, 31 black and white diagrams
ISBN 978-3-8055-8659-7
€68.00

Progress and Challenges in Transfusion Medicine, Haemostasis and Haemotherapy is a compilation of the lectures and presentations given at the 2008 Joint Congress of the German Society for Transfusion Medicine and Immunohematology and the Interdisciplinary European Society for Hemapheresis and Hemothrapy held in Düsseldorf in September 2008. There is a strong emphasis on haemostasis, blood component therapy, therapeutic apheresis and haematological oncology in this nicely illustrated and presented volume. Each article reviews and summarises the latest research undertaken by the author and his or her collaborators in their speciality and represents the State-of-the-Art in each particular field. Emerging and newly applied laboratory technologies are discussed as are newer modalities of treatment and therapies still in their research phases.

The book is comprised of 32 articles in total and these are grouped into 13 categories and 3 main disciplines, namely, haemostasis, immunohematology and haematology. There is considerable overlap between the three disciplines as well as discussions which span the fields of immunology and microbiology. This volume is necessarily Eurocentric as almost all the authors live and work in Germany, Austria, Switzerland or France and some of the methods discussed in the presentations may not yet be in use outside of the E.U.

Although each chapter is an appropriately scholarly treatment of the topic under discussion it is worth noting that there are many examples of a slight displacement of English grammar with the Germanic or Gallic rendering of certain turns of English phrasing. Some sentences may require a second read but this doesn’t impair the gist of what the author is trying to say. Some examples are “Already 10 years ago...(page 189)”, “Since a long time ago...(page 200)”,”In case that the most common weak D types can be excluded... (annotation page 204)”. There was an “und” spotted on page 289. In any case, whether the articles were written in the native tongue of the author and then translated into English or written directly into English is essentially immaterial. The reader simply has to make a slight adjustment for the way certain passages are expressed.

Progress and Challenges should not be viewed as a textbook nor a comprehensive treatise of the topics discussed. It is what it says it is, the “take-home message” of the Joint Congress. This is not to say that we are dealing with a lightweight treatment here, quite the contrary in fact. A lot of knowledge is assumed and the fundamentals of for example, the clotting cascade or contact factor activation, are not discussed in those articles dealing with haemostatic mechanisms. The articles are the content of the presentations given at the Congress and these were presented to a high-powered audience who would not have needed a reiteration of the basics. It is evident that in several cases the authors were constrained by the editor who pared down the content of the articles. One only has to recall one’s own experiences with attention spans at conferences to appreciate why this might have been necessary. Nevertheless, there is some very interesting material on offer in this book and any scientist working in haematology, haemostasis, immunology or blood banking will find the articles in at least one of the 13 sections of great interest.

There is an excellent article on the use of genotyping in resolving serologically ambiguous blood groups and another truly fascinating article on the research efforts to mass produce in-vitro, engineered red blood cells which are inert with respect to the ABO and D systems. Imagine! This would have been the stuff of science fiction 25 years ago!

A point to note however; there is no index, just the table of contents. The reader has to browse the contents pages to locate the articles of interest.

Who would buy or read this book? It would be widely read by scientists who are themselves engaged in similar research efforts or by medical specialists who treat patients with haematological disorders. Medical scientists wishing to update their current theoretical knowledge and MLS students undertaking post-grad courses would also benefit. But would they buy it? Probably not. Their institute or university’s library would though and a worthwhile acquisition it would be too.

Gerard Carter MAIMS
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Pulmonary Pathology 1st Edition
A volume in the series Foundations in Pathology.
Edited by Dan S Zander and Carol F Farver
Hard cover, 852 pages
AU$159.00

The scope and increasing complexity of modern pathology is such that general pathology books are limited in the coverage able to be afforded each subspecialty of this subject. This has resulted in the production of the
Foundations in Diagnostic Pathology series that provide single volumes dedicated to a description of the pathology and cytopathology of a major organ or system. In this publication on pulmonary pathology, Drs Zander and Farver have brought together a wide ranging team of eminent contributors from the United States, Canada, the United Kingdom, Europe and Pakistan. The result of the combined effort by the authors is a comprehensive text book that is a thorough treatise of respiratory histopathology, respiratory cytology and contemporary diagnostic laboratory methods.

The textbook comprises 40 chapters which is a clear indication to the reader when scanning the chapter list how the many facets of respiratory pathology have been teased apart for specific attention in this publication. The editorial style that has been adopted makes good use of headings that direct the reader to each condition discussed. The standard organisation throughout provides in order, a definition of each condition studied followed by clinical, radiological and pathological features, differential diagnosis, ancillary methods and where applicable, prognosis and therapy options. At the conclusion of each section within any chapter, the information for each condition is summarised under bullet points into two colour coded fact sheets—one for epidemiology and clinical features and the other for pathologic features and recommended ancillary testing.

The first two chapters address the anatomy of the respiratory system, the place of the lung biopsy in the diagnostic workup of respiratory patients and technical pitfalls associated with biopsy specimens. The third chapter presents a refreshing view of the science and art of histopathology with an overview of a pattern based approach to the diagnosis of benign, inflammatory and neoplastic respiratory diseases. The subsequent chapters address specific aspects of respiratory pathology and each of these will be briefly mentioned here to demonstrate the extent of the coverage of this subject. Chapters 4 through to 6 address developmental and paediatric disorders and lung neoplasms in infants and children. Chapters 7 to 9 cover vascular disease, pulmonary haemorrhage and acute lung injury. Chapters 10 to 15 address infectious diseases and for this reviewer these chapters represent the highlight of the publication for the extent of the information on usual and uncommon infectious agents encountered in respiratory specimens. Separate chapters are dedicated to bacterial, mycobacterial, fungal, viral and parasitic infections. Chalmydial Mycoplasmal, Rickettsial and Ehrlichial infections are combined in the last chapter on infections.

Chapters 16 to 25 include interstitial, environmental, iatrogenic, emphysematous disease of small airways and transplantation pathology.

Chapters 26-35 address benign, precursors of malignancy, malignant neoplasms and pleural diseases including inflammatory and fibrosing pleural processes, mesothelioma and pleural involvement by extra pleural malignancies.

Chapter 36 addresses pulmonary manifestations of systemic disease and chapters 37-40, cover exfoliative and fine needle aspiration cytology followed by diagnostic methods and techniques including immunohistochemistry, immunofluorescence and immunologic testing.

The text is supported by more than 180 colour and black and white plates that show consistent clarity of detail and are coupled with informative legends. While most of the images of tissue sections are of haematoxylin and eosin stained examples, good use is made of macrophotographs, radiologic images, electron micrographs and images of special stains including histochemistry and immunohistochemistry that further complement the information within the text. There are 44 tables of supporting information that provide summaries of useful clinical and pathological data in addition to the fact sheets.

References are included at the completion of each chapter and these are conveniently organised under headings related to the conditions as they are described in the text. The text is supported by a well developed index that is coded in a style that can direct the reader to the full description of the subject of inquiry or alternatively to the fact sheet boxes or information in tables.

This is a very well priced text book that is highly readable and one that would be of value to students of pulmonary pathology, practicing histopathologists and scientists with an interest in respiratory disease. The clinico-pathological correlations and the radiological consequences that are described should be of interest to respiratory clinicians, radiologists and surgeons as well. The succinct and comprehensive style that has been achieved by the editors will make this book a valuable addition to personal and reference libraries.

Vincent Williams
Associate Professor
Curtin University of Technology
Faculty of Health Sciences
School of Biomedical Sciences
Perth, Western Australia
Cellular Diagnostics  
Basic Principles, Methods and Clinical Applications of Flow Cytometry  

Edited by Ulrich Sack, Attila Tarnok, Gregor Rothe  
Karger, 2009  
Hard cover, 738 pages  
US$179.00

The preface states that this text is an updated version of the 2006 German handbook Zelluläre Diagnostik. The original German text has been translated into English thanks to a grant from the “Wallace H. Coulter Foundation” which possibly explains why the book contains duplicate biographies of WH Coulter.

The intention of the book “is to provide a comprehensive and detailed compilation of all aspects of flow cytometry (FC)” and it certainly has a course subject text format. The text is divided into 4 major sections. There are contributions from a total of 66 authors, with the editors themselves making an appearance as sole or contributing author on several occasions. There is a detailed up to date reference section at the end of each chapter.

Section one: History and Methodological Principles (8 chapters, 189 pages) dedicates the first two chapters to the development of FC to seventeen colour flow cytometry with the next six covering the instrumentation of FC, fluorochromes and the range of FC applications. Internationally recognised bodies that provide guidelines for this science are briefly mentioned. There are several tables comparing current flow cytometer specifications and the authors have also included the webpage addresses of the manufacturers. The chapter on cell sorting is the only chapter in the book not referenced. Although there is only a brief mention of compensation in the text, the reader is directed to websites for more detailed information.

Section two: Characterization and Phenotyping of Cells (9 chapters, 134 pages) contains a chapter on the investigation of a dynamic reference range for lymphocytes in the peripheral blood of healthy children to 16 years of age. The remainder cover isolation of peripheral blood, endothelial and mesenchymal progenitor cells and myeloid dendritic cells. The last two major sections cover the current applications of flow cytometry in a diagnostic or reference laboratory. Sections two, three: Analysis of Cell Function (7 chapters, 177 pages) and four: Diagnostic Indications (13 chapters, 220 pages) are mostly independent of each other and follow the format of: introduction, a step by step work instruction and data analysis in isolating and identifying the population of interest. Each chapter also contains a troubleshooting section and chapter summary. With this format, there is a repeat of information on specimen type, collection and storage information, instrument set-up.

This book is intended as a bench-top text for the scientist involved in the diagnostic or research laboratory flow cytometry (FC) centre. The work instructions are perhaps more detailed than needed for those already in a diagnostic/research laboratory where protocols have already been established but may be useful in the set-up or development of new protocols.

All chapters were informative and easy to read, with numerous tables and figures. The chapter on diagnosis of Non-Hodgkin’s Lymphoma contains a figure on the effects of specimen aging which appears mislabelled. Some authors have included the manufacturer and item product number within the antibody tables making tracking of such items hassle free. There is a very comprehensive chapter on fluorochrome selection and combination.

While I found most of the stated 184 figures and 117 tables fitted with the accompanying text, more detailed labelling of figures would benefit the newcomer to the field. The inclusion of more colour dot plots in diagnostic chapters would have been beneficial. There are some acronyms not listed in “Abbreviations”.

As a relative newcomer to the field of FC, from a haematology background, I found that the authors have succeeded in the delivery of a text that is informative and providing a basic grounding in FC methodology and application. FC use has evolved into a science that can not be contained into a single volume and once the novice has progressed to more diagnostic application, more comprehensive, specific texts would be required. This book would be valuable in the laboratory library as an initial contact for any scientist moving into the world of FC and as a quick reference to FC applications.

Ruth Eastment  
Haematology Scientist  
Mater Health Services - Pathology  
Brisbane
Following is a list of books available for review by resource consultants and members of the Institute with particular expertise in the field.

The reviewer is invited to retain the complimentary copy of the book once the review is received.

As per our agreement with the book publishing companies, complimentary books are submitted to the Institute provided that all reviews are published in the Australian Journal of Medical Science. These reviews must be of a high quality as buying decisions and the reputation of the book and author are important considerations.

Books not requested will be allocated at discretion of the Editors for the Australian Journal of Medical Science. Reviews should be 300 to 700 words depending on the volume of the book. Time limit for return of review is six weeks.

Requests to: Australian Institute of Medical Scientists, PO Box 1911, Milton, Qld 4064. Tel: (07) 3876 2988. Fax: (07) 3876 2999. Email: aimsnat@aims.org.au


13. **FNA Cytology in the Diagnosis of Lymphoma** authors L Skoog and E Tani. Karger. 77 pages.


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Call for Abstracts close date:
Friday 29 May 2009
Questions relating to the *Auto-fluorescence properties of proteins incubated with monosaccharides – an in vitro study*. Page 2 of this issue.

1. Elisa based methods only detect individual AGEs while other methods require pre-analytical steps that may produce AGEs thereby affecting accuracy and specificity.  
   True/False

2. Fluorescence specificity can be compromised by the presence of other fluorescent substances or can be interfered with by non-protein tissue components.  
   True/False

3. Samples from all the tubes were only cultured on blood agar on the final day of experiment.  
   True/False

4. New fluorimetric cells were used for each measurement to avoid carry-over with the measurements done once per sample.  
   True/False

5. Auto-fluorescence was never observed in the tubes in which collagen IV was incubated with glucose.  
   True/False

6. Auto-fluorescence appears to increase from week 10 suggesting dependence on time.  
   True/False

7. Most studies have used fluorophores to conjugate glycated molecules in vitro this study investigated auto-fluorescence of glycated proteins without chemical modification.  
   True/False

8. Previous papers have studied skin auto-fluorescence and concluded that auto-fluorescence may be a convenient and rapid tool for the assessment of long-term diabetic complications.  
   True/False

9. This study sought to mimic in vivo glycation hence used human physiological levels and pathological levels of fructose only while other studies used much higher levels.  
   True/False

10. This studies data suggests that NPN wastes has no impact on the auto-fluorescence of collagen IV glycation products.  
    True/False

Name: __________________________________________  Membership No: ____________________________

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AJMS APACE Questions, AIMS National Office, PO Box 1911, Milton Qld 4064. Facsimile: 61 7 3876 2999
Questions relating to Multiskilling or deskilling? Workplace influences on the quality of multidisciplinary medical scientists. Page 8 of this issue.

1. The link between job satisfaction and work performed has been found to be weaker in single discipline medical scientists.  
   **True/False**

2. For statistical purposes it was assumed that the samples were normally distributed.  
   **True/False**

3. The response rate for both the multidisciplinary group and the control group was close to 50%.  
   **True/False**

4. Approximately a quarter of the multidisciplinary scientists indicated that they did not participate in external QAP for all of the disciplines in which they worked.  
   **True/False**

5. Significantly more multidisciplinary than control samples reported poor training.  
   **True/False**

6. The survey found the workplace training for the more recently graduated multidisciplinary scientists was not as well organised or supervised as when the more experienced multidisciplinary scientists were trained.  
   **True/False**

7. The proportion of multidisciplinary scientists who were not assessed for competency prior to commencing unsupervised work was not statistically different from the control sample.  
   **True/False**

8. The multidisciplinary scientists with less than two years experience reported the highest proportion of unsupervised work.  
   **True/False**

9. Premature removal of supervision and working contact with single discipline scientists threatens the education process of inexperienced multidisciplinary scientists.  
   **True/False**

10. The aspects of multidisciplinary practice that have been identified in this pilot study as potential contributors to deskilling arise from the multidisciplinary job design and are consequently avoidable.  
    **True/False**

Name: ___________________________ Membership No: ___________________________

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YEAR 2009


MARCH 13-15: XXV World Congress of Pathology and Laboratory Medicine, Pathology Update 2009 in conjunction with XXV WASPaLM. Sydney Convention and Exhibition Centre, Darling Harbour, Sydney NSW. Website: www.rcpa.edu.au/Continuing/PathologyUpdate.htm


MAY 15-17: NSW South West Division Conference, Orange. Website: www.aims.org.au.

JUNE 4-7: 14th Congress of the European Hematology Association, Berlin, Germany. Website: www.eha.eu/congress/

JUNE 5-7: Capricornia Medical Science Association Scientific Conference, Rydges Capricorn Resort, Yeppoon, Queensland. ‘Pathology Under the Palms - Tropical Medicine by the Sea’. Contact: richard_lord@health.qld.gov.au. Website: www.cmsa2009.com


CONVENTION & CONGRESS CALENDAR


AUGUST 18-21: New Zealand Institute of Medical Laboratory Science Conference, Marlborough Convention Centre, Blenheim. Contact: fran@nzimls.org.nz

AUGUST 25-28: National Serology Reference Laboratory, Australia, 26th NRL Workshop on Serology, Christchurch, New Zealand. Website: www.nrl.gov.au

SEPTEMBER 14-17: Australian Association of Clinical Biochemists, 47th Annual Scientific Conference. The Brisbane Convention & Exhibition Centre, Brisbane, Queensland. Website: www.aacb.asn.au/web/Meetings/Annual_Scientific_Conference/Brisbane_2009/


SEPTEMBER 28-30: IBMS Biomedical Science Congress. ICC, Birmingham. Website: www.ibmscongress.com

NOVEMBER 1-4: The Australasian Flow Cytometry Group 32nd Annual Meeting. Brisbane Convention and Exhibition Centre, Southbank, Brisbane. Contacts: grace.chojnowski@qimr.edu.au; paula.hall@qimr.edu.au. Website: www.afcg.org.au

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