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Laboratory information systems in clinical biochemistry in Australia

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Abstract

Computers and information technology in pathology have improved efficiency and security allowing more effective patient care. However the extent of utilisation of this technology in Australia is not clear. The aim of the study was to look at availability and utilisation of Laboratory Information System (LIS) in clinical biochemistry laboratories. Self-administered questionnaires were sent to senior staff of clinical biochemistry in NPAAC GX/GY classified laboratories in Australia. Questions ascertained whether the laboratory utilised a LIS and the functionality of the system. Of the 82 respondents, 97% have LIS and a large number have bi-directional interface on the main analysers, quality control validation programs and a LIS program to alert critical values. Ninety-three percent of respondents have results available electronically to the patient health-care team. The majority of laboratories auto-validate and accept general serum chemistry and immunoassay results using algorithms embedded in either middle-ware or the LIS. Management, chemical pathologist, senior scientist collectively or alone determine and update the auto-validation rules. Computer and biochemistry personnel are responsible for inserting auto-validation rules into the LIS. The use of computers and LIS’s appears universal and the future laboratory will rely more on interfaces for instrumentation, software programs for quality control, auto-validation, handling of critical values, and reporting of results. These attributes assist to make pathology pivotal to patient care and close to the patient care team.

Keywords: Information systems, computers, laboratories, clinical biochemistry

Introduction

Over the years we have witnessed the use of computers and information technology in pathology making dramatic improvements in efficiency in a number of areas such as data transfer, quality control and validation of results and resource management. Early use of computers was to interface mainframe analysers so that large amounts of data could be transferred (up-loaded) electronically to the Laboratory Information System (LIS), a uni-directional interface. Bi-directional interfaces were then developed so that requested tests were downloaded into the instruments. The download of requests and the subsequent upload of results removed many manual actions and improved security, accuracy and efficiency of data transfer. Apart from improved security and efficiency, fast transfer of data has resulted in shorter turnaround times for pathology results. Electronic data transfer allows results from pathology to be available in real time for the health practitioners to manage patient’s admission, treatment, and discharge.

The development and use of the LIS in quality control (Sax et al 1967) has allowed consistent application of rules e.g. Westgard Rules for acceptance or rejection of quality control results (Cembrowski and Carey 1989). Programs are available that permit insertion of comments to quality control results and to record actions taken in relation to out of limit values. The running means, standard deviations, and co-efficient of variations are now commonly calculated and compared against static values for given analytes as part of quality assurance. In addition the plotting of results by e.g. Levey Jennings charts allows trends to be observed and simultaneous plotting of several levels of quality control data on one graph permits a more informative review of the performance of an assay. This is now a common feature in clinical biochemistry.

A major development in the utilisation of the LIS in the core laboratory was the introduction of rules governing the acceptance of patient results without further intervention by staff. This provides uniformity of practice across all shifts (Berman 2006). These rule based algorithms also ensure the release of most patient results and maximise the efficiency of the mainframe automation (Goldschmidt 2002). These rules ensure that patient results outside predetermined ranges are reviewed by experienced staff before reporting and validated results are reported in a timely manner. The rules incorporate a review of results in relation to physiological range, critical limits, demographics (e.g. age,
sex, pregnancy), reference interval, and review of previous results (delta check). The rules may also incorporate the results of other analytes to create, for instance, ratios for more informative validation of analyte results e.g. urea and creatinine. In addition to acceptance of patients’ results rules may also be written to include comments on patient results. The process of auto-validation (auto-verification) is halted when the internal quality control falls outside acceptable limits. Friedman (2001) states that the LIS as part of information technology can compress the time and distance which has previously separated medical staff from the laboratory. Britt et al (2008) state that 97% of general practitioners now have computers and can thus have patient results downloaded.

Jones and O’Connor (2004) state that the best laboratory information management (LIMS) systems have the following attributes:

1. Recording of all requests for all tests
2. Online, real-time linking of the LIMS to automated analytical instruments
3. Automated validation of test results
4. Real-time recording of quality control data
5. Electronic delivery of results to clinical users
6. Implementation of decision support systems to enhance clinical outputs
7. Support of data analysis for audit, clinical risk management, disease surveillance and epidemiology (e.g. cancer registration, screening programmes, communicable disease reporting and external quality assessment data management).

This study looked at the first five attributes listed by Jones and O’Connor as these have a direct bearing on daily operations in clinical biochemistry laboratories in Australia.

Materials and methods

This study had ethical clearance from the Human Research Ethics Committee of Charles Sturt University, New South Wales, Australia. Self-administered paper questionnaires were sent to senior staff in charge of clinical biochemistry in NPAAC GX/GY classified laboratories (NPAAC 2007a). The 121 laboratories comprised both public and private, rural and metropolitan, hospital and stand-alone entities. The GX/GY laboratories were obtained from the NATA list of accredited laboratories (www.nata.asn.au/index.php/facilitiesandlabs/). The mode of contact was mail using a 4 time contact model which has been demonstrated to be effective in increasing the response rate by Fox et al (1988), Larson and Chow (2003), and Lapane et al (2007). The mailed packages followed that of McCoy and Hargie (2007) which was an adaptation of Fox et al (1988). The four-time contact method has also been advocated by a number of researchers (McCoy and Hargie 2007, Dillman 2007, and Dillman and Frey 1974). The first contact consisted of an introductory letter, questionnaire and self-addressed stamped reply envelope while the second was a reminder letter. The third contact consisted of another version of the introductory letter and the questionnaire while the fourth contact was another version of the reminder letter. The 4 contacts were approximately 6 weeks apart and mailing of the 4 contacts was personalized, a format advocated by McCoy and Hargie (2007). Personalization was indicated by a handwritten address in ink, signing of the introductory letter, the use of postage stamps rather than franking, letter addressed to the person rather than generic greeting, and inclusion of a business card. Envelopes bearing the crest of Charles Sturt University were used and the envelopes were individually stamped with the address hand-written.

The questionnaire had 5 sections, Section V Computers, consisted of 13 questions to ascertain whether the laboratory utilised a LIS and the functionality of the system including interfacing of analyzers, internal quality control, patient results and auto-validation. The responses were; ‘Yes’ or ‘No’ or ‘Not applicable’ and are expressed as percentages of responses. Some of the questions sourced for descriptive answers to allow capturing of opinions.

Results

Of the 82 respondents (one response per laboratory) to the survey (68% response rate), 97% had LIS. A large number of laboratories had a bi-directional interface on the main analysers and there was also a significant number with uni-directional interface (Table 1).

<table>
<thead>
<tr>
<th>Response</th>
<th>Bi-directionally interfaced</th>
<th>Uni-directionally interfaced</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Frequency</td>
<td>Percentage</td>
</tr>
<tr>
<td>Yes</td>
<td>79</td>
<td>97</td>
</tr>
<tr>
<td>No</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Not applicable</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>No response</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>82</td>
<td>100</td>
</tr>
</tbody>
</table>
Although the majority of laboratories have a quality control validation program a substantial number also responded negatively. Most of the laboratories also have a LIS program to alert critical values (2).

Table 3. Distribution of health-care teams to which results are made available electronically from the respondents’ laboratories

<table>
<thead>
<tr>
<th>Health-care team</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wards</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Doctors’ clinics</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>Wards and doctors’ clinics</td>
<td>62</td>
<td>76</td>
</tr>
<tr>
<td>Not applicable</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>No response</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>82</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 3 shows that 93% of respondents have results available electronically to the patient health-care team (wards, doctors’ clinics and external clinics). The majority of laboratories respondents (67/82) utilise auto-validation of results and use algorithms embedded in either middleware or the LIS (Table 4).

Table 4. Distribution of use of auto-validation of results in the respondents’ laboratories

<table>
<thead>
<tr>
<th>Response</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>67</td>
<td>82</td>
</tr>
<tr>
<td>No</td>
<td>9</td>
<td>11</td>
</tr>
<tr>
<td>Not applicable</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>No response</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>82</td>
<td>100</td>
</tr>
</tbody>
</table>

The responses indicate that the majority of laboratories accept general serum chemistry and immunoassay results by auto-validation (Table 5) and the responses in Table 4 indicate that management, chemical pathologist, senior scientist collectively or alone mainly determine the rules for auto-validation.

Table 5. Distribution of approximate percentage of results released via auto-validation for general serum chemistry and for immunoassays in the respondents’ laboratories

<table>
<thead>
<tr>
<th>Response</th>
<th>General serum chemistry</th>
<th>Immunoassays</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>Percentage</td>
<td>Frequency</td>
</tr>
<tr>
<td>&lt;30%</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>30%</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>40%</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>50%</td>
<td>11</td>
<td>14</td>
</tr>
<tr>
<td>60%</td>
<td>13</td>
<td>16</td>
</tr>
<tr>
<td>70%</td>
<td>15</td>
<td>19</td>
</tr>
<tr>
<td>80%</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>&gt;80%</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Not applicable</td>
<td>11</td>
<td>14</td>
</tr>
<tr>
<td>No response</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>82</td>
<td>100</td>
</tr>
</tbody>
</table>

A significant number of laboratories have computer staff that insert auto-validation rules into the LIS. In some laboratories this role is carried out by clinical biochemistry staff while in other laboratories computer and clinical biochemistry staff share this responsibility (Table 7). In most laboratories management, chemical pathologist, senior scientist and scientist are responsible for updating the auto-validation rules (Table 8).

Table 7. Distribution of category of staff who insert auto-validation rules into the LIS in the respondents’ laboratories

<table>
<thead>
<tr>
<th>Staff category</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Computer staff</td>
<td>34</td>
<td>41</td>
</tr>
<tr>
<td>Clinical biochemistry staff</td>
<td>12</td>
<td>15</td>
</tr>
<tr>
<td>Computer and clinical biochemistry staff</td>
<td>21</td>
<td>26</td>
</tr>
<tr>
<td>Not applicable</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>No response</td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>82</td>
<td>100</td>
</tr>
</tbody>
</table>
Table 8. Distribution of category of staff which up-date the auto-validation rules in the respondents’ laboratories

<table>
<thead>
<tr>
<th>Staff category</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Management group</td>
<td>11</td>
<td>13</td>
</tr>
<tr>
<td>Chemical pathologist</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Senior scientist</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Management group, Chemical pathologist</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Senior scientist</td>
<td>19</td>
<td>23</td>
</tr>
<tr>
<td>Management group, Chemical pathologist</td>
<td>16</td>
<td>20</td>
</tr>
<tr>
<td>Senior scientist</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Scientist</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Not applicable</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>Total</td>
<td>82</td>
<td>100</td>
</tr>
</tbody>
</table>

**Discussion**

The study has shown that LIS are utilised in most clinical biochemistry laboratories in Australia. These systems are used for: registering requests, interfacing instrumentation, quality control programs, and reporting patient results. Other functions of LIS include reflex testing, calculations involving patient results, adding interpretive comments, management (workload recording, budget, human resources and training), occupational health and safety, quality management, and data mining of patient results e.g. reference interval setting, discovery of unnoticed disease states.

It is essential for efficient patient care that staff are conversant with programs that: interface the instruments, validate results, search for results, process quality control, record telephoning, faxing, and printing of results. The extensive use of LIS in pathology with bi-directionally interfaced analysers and total laboratory automation in core laboratories has created an environment where patients’ results are available in a timely manner. The downloading of requests and uploading of the results into the LIS must be error free for maximum patient care.

The European Computer Driving Licence (ECDL) was adopted as the basic standard for NHS staff in England and Scotland (Jones and O’Connor 2004) and a similar qualification is desirable in Australia for pathology staff. Computer studies taught in AIMS accredited courses may take guidance from this NHS future requirement. The ECDL course is mapped in Australia to the ICAI11 Information Technology and Communications Training Package. Pathology scientists must ensure that their knowledge is adequate to ensure that the LIS are sufficient to provide optimal patient care.

**Interface**

Instrument interface is widely utilised in the laboratories (Table 1). The bidirectional interface defined by Strangio (accessed 27 March 2012) enables the demographics of the patient and the request groups to be down-loaded into an instrument. After analysis the result can be up-loaded into the LIS for validation and release, either electronically, hard copy or both. The use of the bi-directional interface obviates a number of manual steps e.g. keying in the laboratory identifier and tests to the analyser, selecting the rack position for the patient sample on the instrument, and keying patient results into the LIS. Keying in of results is prone to error given the number of key strokes for each group of analytes. Manual entry of patient results requires a second check of the entered results to ensure accuracy, which must be performed in a timely manner (not possible on sole scientist shifts), and is a requirement of NPAAC (AS ISO15189-2013). Manual entry of results has a significant time penalty while the bi-directional interface saves considerable staff time.

Table 1 indicates that a small number of laboratories utilise a uni-directional interface, possibly due to the fact that some instruments are only capable of uni-directional interface. Uni-directional interface allows results to be uploaded into the LIS but not down-loading of patient requests to the analyser. Therefore this requires programming the requests into the instruments. Manual programming has inherent problems including wrong laboratory identification numbers, incomplete requests being registered in the analyser and the necessity to check a print out of results against the primary tube. This wastes time and the intensive nature of manually registering patients’ requests into analysers lengthens the turnaround time for patient results thereby reducing efficiency.

**Internal quality control**

Table 2 shows that while 56% of laboratories have a quality control validation program in the LIS a substantial number (38%) do not. It is possible that such laboratories may utilise quality control programs on an analyser since many analysers have an option to insert quality control mean values and standard deviations to allow acceptance of assay performance. While this works well in day to day activity it does have medium and long term difficulties. For instance, the size of the instrument’s data base may be limiting with regard to the length of time that data can be stored. This may impact on review of trends in the data and on-going review of the mean and standard deviation. If that is the case then the quality control data needs to be archived on disc for future reference. Apart from the short and medium term concerns the periodic replacement of instruments requires that the data is transferred to disc, accessed perhaps via a personal computer, often by a proprietary program hence continued access requires the continued availability of this program. A further difficulty arises when there are several
instruments performing the same range of analytes in so far as the staff must ensure that each instrument has the same mean and standard deviation for each analyte.

Computerised review of internal quality control material has been in use since the mid-1960s (Sax et al 1967). The quality control program maintained a running mean, standard deviation and coefficient of variation for each test. Among the objectives of the program were a measure of accuracy and imprecision and to permit detection of deterioration of any component concerning the generation of results. The first computerised programs were developed to handle the increasingly large amount of data that early automated instruments e.g. the AutoAnalyser I and II (Technicon Corporation, Tarrytown NY) were capable of producing. NPAAC in Requirements for Pathology Laboratories (2007) states that:

"The laboratory monitors the validity of testing by employing internal quality control procedures using control materials appropriate to the methods and materials used in sample analysis. The frequency of control testing gives assurance that the method is in control at the time of testing."

In highly automated laboratories with greater than forty analytes on a major analyser using a minimum of 2 levels of quality control material for each 8 hour shift, at least 240 data points are produced and analysed per day. A computer program can plot these on a Levey Jennings chart (Levey and Jennings 1950). In addition the LIS can calculate the running mean and standard deviation for each analyte and compare these against assigned values. The calculations are not readily performed if the data is manually plotted. Westgard rules are often applied to the data and permit a subtlety of interpretation of the internal quality control which would be difficult to achieve in a manual appraisal. Various combinations of Westgard rules may be utilised e.g. 1, 2, 3, 4, 5, 6, 7 (Cembrowski and Carey 1989) and thereby accept or reject the quality control results and thereby allow auto-validation of patient results. However as Levey and Jennings point out ‘it remains for the analyst to study the cause and prevention of error’. In a large laboratory the LIS quality control program may have the capability of plotting results from one analyser against results from another analyser using e.g. Youden plot (Buttner et al 1978) for common analytes to demonstrate agreement between the two analysers.

Critical patient results

The responses in Table 2 indicate that 92% of the laboratories have a program to alert the staff to designated critical results. The volume of results which are produced by main frame analysers is usually high and the immunoassay analyser may also have a wide range of analytes. Many of these analytes have defined critical values and given the number of analytes and the number of rules for any given analyte it is essential that the LIS has embedded rules so that the result display can alert the scientist to critical results. Dighe et al (2006) cite Lundberg (1972) as the originator of the concept of critical (panic) values. Critical results may be defined as those which fall outside the reference interval to such an extent that they require intervention in the immediate term. The communication of these results to the appropriate health practitioner is an important duty for laboratory staff (Lundberg 1972).

Electronic transfer of results

The questionnaire sought information regarding electronic transfer of results to further elucidate the support offered by the LIS. In Table 3 it is shown that 93% of the respondents indicated that results are transferred electronically to wards and clinics. Such transfer provides more timely results than waiting for a hard copy and typically hard copy reports are produced only once or twice per day which results in delay. In addition hard copy reports are sometimes mislaid or delivered to the wrong unit or address whereas electronic results may be accessed from any terminal with a pathology result program. Delivery of electronic results ensures that patient management can be carried out in a shorter period compared to the wait for hard copy reports. Other forms of communicating results are paper documents, telephoning, faxing, messaging service text messaging, remote access to pathology system by dial-in or web access and access via a third-party data repository. Perhaps for maximum and effective communication of results the various methods need to be evaluated and any may be effective in certain circumstances.

Auto-validation

The immediacy of use of auto-validated results requires that the algorithm releasing the results should have been verified and that the program is tested for limits required for the release of results. Auto-validation of results only occurs when both analytical and physiological checks of the result have been performed. Analytical checks include acceptance of calibration and the acceptance of internal quality control. Physiological checks include the expected physiological range of concentrations for an analyte and a delta check which consists of reviewing the present result against the previous result (Young 1976). The limits for the range of auto-validated results for any analyte are also determined to highlight results which may potentially be erroneous. The algorithm for any analyte is usually set by senior staff in the laboratory and after consultation with stake-holders.

In Table 4 it is observed that the majority of laboratories utilise auto-validation of results with algorithms embedded in either middleware or the LIS. The algorithms will have been formulated by management, chemical pathologists/registrars/senior scientific staff, to enable the maximum number of results to be accepted without further review. The release of patient results by auto-validation rules in the
LIS or middleware gives laboratory staff increased time to review abnormal results.

A major benefit of auto-validation is that consistency in the process of reviewing and accepting patient results is achieved. Valdivie et al (1992) compared seven experts against the expert system developed in their laboratory and reported that only one of seven experts exceeded the ability of the expert system to detect abnormal cases and such observations reinforce the importance of expert systems. Similarly laboratories utilising rule based algorithms to accept patient results have embedded intellectual knowledge which is utilised at all times resulting in a constant level of review. Torke et al (2005) reported that that the introduction of auto-verification in their laboratory leads to a decrease in the total error rate of human review of patient results. Large inter-individual variation has been reported by Oosterhuis et al (2000). The staff reviewing the results can vary from the relatively inexperienced to the well experienced. There is also a variation in immediate backup consultation with evening shifts (e.g. 1600 to 2400 hours) and night shifts (e.g. 0000 to 0800 hours having less immediate contact with more senior staff. In these circumstances the use of an expert system is valuable. During the day shift the factor of fatigue due to the high number of results being presented can be alleviated by the use of an expert system.

The responses in Table 5 show that 62% of laboratories accept ≥50% of general serum chemistry results by auto-validation and that 33% accept ≥70% of patients' general serum chemistry results. The large variation in the percentage of results accepted by auto-validation may be attributed to differing algorithms in each institution and different patient mix. The responses to this question mirror published material (Valdivie et al 1992; Torke et al 2005). In Table 5 it is observed that 31% of laboratories accept ≥50% of immunoassay results and 19% accept ≥70% of patient immunoassay results by auto-validation. This is less than half of the results accepted for general serum chemistry by auto-validation. Tumour markers require comparison of the current with previous result and although this can be performed by LIS it may be considered prudent to review two or more results for a given patient. Likewise cardiac markers e.g. troponin I or troponin T may be more finely considered and many endocrine results may need review of clinical notes before release of results.

The rules for auto-validation are determined by the management team, chemical pathologist and senior scientist collectively or alone as shown in Table 6. It is interesting to note that scientists are involved in the determination of rules in 61/71 laboratories. Combined effort to insert rules by clinical biochemistry and computer staff was indicated by 21/67 laboratories (Table 7). It is important for the efficiency of the laboratory that clinical biochemistry staff (including the chemical pathologist) should have the ability to write or modify rules. This view is supported by Blick (1997) who stated that ‘An expert computer system must: (a) be easily modifiable by a non-computer programmer’. The computer staff may not have the time thus writing the rules should be taught to senior biochemistry staff. The responses shown in Table 8 on who updates the auto-validation of rules indicate that a team approach to updating the validation rules is the usual course of action within a laboratory.

**Conclusion**

The use of computers and LIS within the laboratory appears universal and the laboratory of the 21st Century relies on interfaces for instrumentation, software programs for quality control, auto-validation, result reporting including specific handling of critical values, and electronic reporting of results. These attributes have assisted to make pathology a central contributor to timely patient care and this facility has also linked pathology closely to the patient care team. The efficient use of programs in the LIS is a required skill and knowledge base for scientific staff.

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Idiopathic systemic capillary leak (Clarkson) disease

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Abstract

Idiopathic systemic capillary leak syndrome (ISCLS) or Clarkson disease is a disorder that can mimic polycythaemia vera (PV) on presentation. It is a rare disorder with only 150 cases described worldwide, and is characterised by severe hypotension, hypoalbuminaemia and haemoconcentration. The haemoconcentration can result in a high haematocrit, often >0.60 (RR 0.33 – 0.47), as well as an elevated white cell and platelet count; all features of PV. The relevant clinical and laboratory features of a case of ISCLS in a 52-year-old male are outlined in this case study.

Keywords: Clarkson disease, idiopathic systemic capillary leak syndrome, polycythaemia vera, haemoconcentration

Introduction

Idiopathic systemic capillary leak syndrome (ISCLS) is a rare disorder with only 150 cases described worldwide (Druy and Greipp 2010). It is likely to be under-recognised because the first episode may be fatal and the presentation full blood count (FBC) can be similar to polycythaemia vera (PV). It is attributed to the acute transient dysfunction of the vascular endothelium which controls the passage of fluid and macromolecules between the intravascular and interstitial spaces and is characterised by severe hypotension, hypoalbuminaemia and haemoconcentration.

The haemoconcentration typically leads to an elevated haematocrit (Hct) which is often greater than 0.60 (RR 0.33 – 0.47) as well as leucocytosis and thrombocytosis. There is circulatory insufficiency due to hypotension and the increased viscosity of the peripheral blood. Renal failure is a common feature and oedema may result in compartment syndrome. Thromboembolic events may also occur (Clarkson et al 1960, Marks and Shuster 1973).

Case report and results

The 52-year-old male patient's previous medical history was largely unsubstantiated as he had spent a lot of time working overseas. There was a history of meningococcal sepsis in 1998 and 2001 in the United Kingdom and Germany respectively but there was no microbiological evidence for confirmation. He also suffered an intra-cranial bleed in 2006 in China. He previously had a heavy alcohol intake, but this had ceased a few years ago. He is a non-smoker and is usually well.

There was no history of any haematological disorder, but a brother has lymphoma and is waiting for an allogeneic stem cell transplant.

He presented at the Emergency Department of a Brisbane hospital in July 2012, with a four day history of fatigue along with some diarrhoea and vomiting. On presentation he was drowsy and had a mottled skin rash. On examination he looked unwell with tachycardia and cyanosis but had a normal blood pressure.

Initial laboratory investigations are shown in Tables 1-4 and an image of his blood film is shown in Figure 1.

Table 1. Full blood count results on presentation

<table>
<thead>
<tr>
<th>16/07/12</th>
<th>Reference range</th>
</tr>
</thead>
<tbody>
<tr>
<td>11:40</td>
<td></td>
</tr>
<tr>
<td>Haemoglobin</td>
<td>258 (135-180 g/L)</td>
</tr>
<tr>
<td>Red cell count</td>
<td>8.04 (4.5-6.0 x 10⁹/L)</td>
</tr>
<tr>
<td>Haematocrit</td>
<td>0.76 (0.39-0.52)</td>
</tr>
<tr>
<td>Platelet count</td>
<td>231 (150-400 x 10⁹/L)</td>
</tr>
<tr>
<td>White blood cell count</td>
<td>39.8 (4.0-11.0 x 10⁹/L)</td>
</tr>
</tbody>
</table>

Table 2. Coagulation results on presentation

<table>
<thead>
<tr>
<th>16/07/12</th>
<th>Reference range</th>
</tr>
</thead>
<tbody>
<tr>
<td>INR</td>
<td>2.1 (0.9-1.2)</td>
</tr>
<tr>
<td>Prothrombin time</td>
<td>23 (10-13 s)</td>
</tr>
<tr>
<td>APTT</td>
<td>&gt;200 * (26-41 s)</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>4.0 (1.7-4.5 g/L)</td>
</tr>
</tbody>
</table>

* Post heparin infusion
Table 3. Initial biochemistry results

<table>
<thead>
<tr>
<th></th>
<th>16/07/12</th>
<th>Reference range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>134</td>
<td>135-145 mmol/L</td>
</tr>
<tr>
<td>Potassium</td>
<td>*</td>
<td>3.5-5.1 mmol/L</td>
</tr>
<tr>
<td>Chloride</td>
<td>97</td>
<td>100-110 mmol/L</td>
</tr>
<tr>
<td>Bicarbonate</td>
<td>20</td>
<td>22-32 mmol/L</td>
</tr>
<tr>
<td>Anion gap</td>
<td>17</td>
<td>4-13 mmol/L</td>
</tr>
<tr>
<td>Urea</td>
<td>7.7</td>
<td>2.1-7.1 mmol/L</td>
</tr>
<tr>
<td>Creatinine</td>
<td>284</td>
<td>73-108 umol/L</td>
</tr>
<tr>
<td>Urea/creatinine</td>
<td>27</td>
<td>40-100</td>
</tr>
</tbody>
</table>

* Potassium could not be measured due to sample haemolysis.

Table 4. Venous blood gas results (on room air)

<table>
<thead>
<tr>
<th></th>
<th>16/07/12</th>
<th>Reference range</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.07</td>
<td>7.35 – 7.45</td>
</tr>
<tr>
<td>PCO2</td>
<td>45</td>
<td>35 – 45 mmHg</td>
</tr>
<tr>
<td>PO2</td>
<td>75</td>
<td>75 – 100mmHg</td>
</tr>
<tr>
<td>O2 saturation</td>
<td>20</td>
<td>94-98 %</td>
</tr>
<tr>
<td>P50</td>
<td>39.4</td>
<td>24.0 – 28.0 mmHg</td>
</tr>
<tr>
<td>HCO3</td>
<td>23</td>
<td>22 - 33 mmol/L</td>
</tr>
<tr>
<td>ABE</td>
<td>-16.1</td>
<td>-3.0 – 3.0 mmol/L</td>
</tr>
</tbody>
</table>

ABE = Actual base excess

The patient was diagnosed with severe lactic acidosis, hyperviscosity and acute kidney injury. He was treated with IV rehydration, a 500 mL venesection and a heparin infusion and he responded well.

His FBC rapidly changed, with all parameters decreasing and returning to within the reference range by 48 h after admission (Table 5).

He was discharged on antibiotics and prophylactic heparin 5000 units BD and referred to the specialist haematology clinic two days later for investigation of his apparent polycythaemia. At the clinic, the haematologist noted that he was well looking, not cyanosed and there was no palpable hepatosplenomegaly.

Further laboratory tests were ordered to investigate the abnormal presentation FBC and these included tests for PV; JAK2 mutation studies, iron studies, haemoglobin studies and erythropoietin (EPO). The only abnormal result was an EPO of <1 mIU/mL (reference range 4.0 – 32.0).

He had follow up counts over the next few months (Table 6)

The haematologist reviewed all the results on the 5th December and commented that there was no need for ongoing clinical review but if the patient became unwell again, an urgent FBC needed to be done.

Four days later (9th December) the patient presented at Emergency and results are shown in Tables 7 & 8.

He was rehydrated over the next three days and again his results returned to normal – see Table 7.

Unfortunately this stabilisation was not sustained and his parameters increased dramatically the next day (Table 9). The treatment again consisted of intensive rehydration (six litres of normal saline and four litres of albumin) with the FBC parameters again normalizing.
Table 7. Full blood counts post-treatment in December

<table>
<thead>
<tr>
<th>Date</th>
<th>9/12/12</th>
<th>10/12/12</th>
<th>11/12/12</th>
<th>12/12/12</th>
<th>Reference range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin</td>
<td>245</td>
<td>155</td>
<td>133</td>
<td>136</td>
<td>135-180 g/L</td>
</tr>
<tr>
<td>Red cell count</td>
<td>7.35</td>
<td>4.82</td>
<td>4.18</td>
<td>4.35</td>
<td>4.5 – 6.0 x 10^12/L</td>
</tr>
<tr>
<td>Haematocrit</td>
<td>0.68</td>
<td>0.45</td>
<td>0.40</td>
<td>0.41</td>
<td>0.39 – 0.52</td>
</tr>
<tr>
<td>Platelet count</td>
<td>*</td>
<td>179</td>
<td>148</td>
<td>157</td>
<td>150-400 x 10^9/L</td>
</tr>
<tr>
<td>White blood cell count</td>
<td>18.1</td>
<td>12.1</td>
<td>6.6</td>
<td>5.6</td>
<td>4.0-11.0 x 10^9/L</td>
</tr>
</tbody>
</table>

* platelet count not available due to platelet clumping

Table 8. Venous blood gases (at room air)

<table>
<thead>
<tr>
<th>9/12/12</th>
<th>Reference range</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.25 – 7.45</td>
</tr>
<tr>
<td>PCO2</td>
<td>39</td>
</tr>
<tr>
<td>PO2</td>
<td>50</td>
</tr>
<tr>
<td>O2 satur</td>
<td>77</td>
</tr>
<tr>
<td>P50</td>
<td>32.5</td>
</tr>
<tr>
<td>HCO3</td>
<td>16</td>
</tr>
<tr>
<td>ABE</td>
<td>-10.9</td>
</tr>
</tbody>
</table>

Table 9. Full blood counts showing relapse and correction post-treatment

<table>
<thead>
<tr>
<th>Date</th>
<th>9/12/12</th>
<th>10/12/12</th>
<th>11/12/12</th>
<th>12/12/12</th>
<th>Reference range</th>
</tr>
</thead>
<tbody>
<tr>
<td>07:50</td>
<td>169</td>
<td>236</td>
<td>258</td>
<td>210</td>
<td>151</td>
</tr>
<tr>
<td>Haemoglobin</td>
<td>169</td>
<td>236</td>
<td>258</td>
<td>210</td>
<td>135-180 g/L</td>
</tr>
<tr>
<td>Red cell count</td>
<td>5.27</td>
<td>7.07</td>
<td>7.70</td>
<td>6.45</td>
<td>4.72</td>
</tr>
<tr>
<td>Haematocrit</td>
<td>0.49</td>
<td>0.65</td>
<td>0.73</td>
<td>0.60</td>
<td>0.44</td>
</tr>
<tr>
<td>Platelet count</td>
<td>183</td>
<td>282</td>
<td>*</td>
<td>209</td>
<td>172</td>
</tr>
<tr>
<td>White blood cell count</td>
<td>6.6</td>
<td>18.2</td>
<td>33.6</td>
<td>36.3</td>
<td>19.5</td>
</tr>
</tbody>
</table>

* platelet count not available due to platelet clumping

He then had a bone marrow aspirate and trephine and some further testing as it was still unclear as to the cause of his results in these critical episodes.

The bone marrow report summary was: “Normocellular marrow with no morphologic evidence of a primary myeloproliferative process”. The culture for spontaneous erythroid colonies on the bone marrow was negative also, but there was a monoclonal protein detected in a serum electrophoresis screen (kappa IgG 3 g/L).

These bone marrow findings and previous tests did not fit the criteria for PV as outlined in Table 10.

After discussion of the case at a clinical review the conclusion was that this was a case of ISCLS, which is a diagnosis made by excluding all of the other possibilities, the rapid response to treatment of intensive rehydration and the presence of a monoclonal gammopathy (Doubek et al 2005).

Table 10. WHO diagnostic criteria for Polycythemia Vera (Swerdlow 2008)

- Diagnosis requires both major criteria, or the first non-maj or criterion plus two minor criteria
- Major criteria
  - Hemoglobin >18.5 g/dL in men, >16.5 g/dL in women or other evidence of increased red cell volume (see note below)
  - Presence of JAK2V617F or other functionally similar mutation
- Minor criteria
  - Bone marrow biopsy showing hypercellularity for age with red lineage growth (panmyelosis) with prominent erythroid, granulocytic and megakaryocytic proliferation
  - Serum erythropoietin level below the reference range for normal
  - Endogenous erythroid colony formation in vitro

Discussion

ISCLS is due to the dysfunction of the vascular endothelium which controls the passage of fluid and macromolecules between the intravascular and interstitial spaces. When there is severe leakage, and resulting depletion of intravascular fluid and proteins, hypotension and haemoconcentration occurs which can lead to shock and may be fatal (Clarkson et al 1960, Marks and Shuster 1973). Capillary leak can have many causes including increased hydrostatic pressure within the capillaries, increased capillary permeability and decreased capillary oncotic pressure.

The increased hydrostatic pressure within the capillaries and increased capillary permeability can force fluid and protein through the endothelial barrier and into the interstitium. The fluids tend to accumulate in the trunk and extremities. The increased permeability could be due to increased inflammatory mediators such as leukotrienes and tumour necrosis factor alpha (TNFα). The decreased capillary oncotic pressure also contributes by failing to retain fluid within the vascular space. The blood cells are usually retained in the vasculature and this causes the high counts of all the cell lineages (Clarkson et al 1960, Marks and Shuster 1973, Druey and Greipp 2010, Rondeau et al 1987).

The pathophysiology of ISCLS remains unclear, with several hypotheses proposed. These include increased levels of paraproteins during the acute phase, elevated levels of vascular endothelial growth factor (VEGF), endothelial cell apoptosis, involvement of endogenous interleukin-2, and the effect of inflammatory mediators.

Increased levels of paraprotein (monoclonal gammopathy) are present in approximately 80% of cases but it is unclear if the paraprotein itself is pathogenic or merely reflects underlying B-cell or plasma cell dysfunction which in itself is pathogenic (Clarkson et al 1960; Goussoff and Armoura 2009; Atkinson et al 1977). The levels have not been found to fluctuate substantially between attacks.
and there has been no clear link between the levels and the severity of the symptoms. There has also been no evidence of increased progression to multiple myeloma in these patients (Druy and Greipp 2010).

Elevated levels of VEGF have been found at baseline by Druy and Greipp (2010) and high levels were found during an acute severe episode by Lesterhuis et al (2009) in two patients which decreased with symptom resolution. VEGF has been implicated in endothelial permeability in several disorders including sepsis and the ovarian hyperstimulation syndrome, but the source of VEGF and its function in ISCLS is unknown (Druy and Greipp 2010).

Endothelial cell apoptosis leading to increased contraction has been proposed as another mechanism for increased capillary permeability by Johansson and Löfdahl (1979). They obtained muscle biopsies during attacks of ISCLS and demonstrated histological changes consistent with endothelial cell apoptosis.

Endogenous interleukin-2 (IL-2) has been implicated because patients who receive high dose recombinant IL-2 therapy can develop a capillary leakage syndrome (Schwartz et al 2002). Increased IL-2 expression was also found on perivascular blood mononuclear cells of symptomatic patients with ISCLS (Rosenberg et al 1985).

As previously mentioned, the inflammatory mediators leukotrienes and TNFα, have been implicated in ISCLS. Leukotrienes are produced from arachidonic acid metabolism within the leukocytes and may increase capillary permeability. A study by Rondeau et al 1987 found abnormalities in the in vitro leukotriene production from patients with ISCLS compared to normal controls. Another small study by Dowden et al 2009 reported elevations of TNFα during ISCLS episodes and this inflammatory mediator can increase vascular permeability.

The optimal management of ISCLS is unclear but requires careful fluid resuscitation to reduce the risk of shock in an acute episode. Several case reports demonstrating benefit of high doses of intravenous immunoglobulin (IVIG) have been published, and these patients also received prophylactic monthly IVIG. IVIG seems to consistently reduce frequency of episodes and it is approved for use in Australia for this indication (Lambert et al 2008).

Theophylline and terbutaline may prevent episodes of ISCLS as they increase intracellular cyclic adenosine monophosphate (cAMP) content which inhibits capillary leakage. Terbutaline increases the production of cAMP while theophylline blocks its degradation (Dowden et al 2009).

The mortality rate ranges from 30% to 76% with a five year survival of approximately 70% (Tahirkhel and Greipp 1999; Dhir et al 2007). Fatalities are predominantly due to initial hypoperfusion or subsequent remobilisation of fluid in the setting of large volume resuscitation causing pulmonary oedema. Druy and Greipp (2010) have found that the median survival for patients followed over 30 years was approximately 15 years.

Patient progress

He had four episodes in 2013 with his latest in September when his haemoglobin (Hb) on admission was 236 g/L and Hct was 0.66. After 48 h of treatment his Hb dropped to 128 g/L and Hct was 0.38.

He was commenced on theophylline and terbutaline and a trial of monthly IVIG in September last year.

He has not presented at any Brisbane hospital since that time.

References


Australian Institute of Medical Scientists
Immunohaematology Quality Assurance Program

RUNS BI-MONTHLY STARTING IN JUNE AT THE BEGINNING OF EACH FINANCIAL YEAR

LEVEL OF DIFFICULTY TO SUIT BOTH SMALL & LARGE LABORATORIES

INCLUDES BLOOD GROUPING, ANTIBODY SCREENING / IDENTIFICATION & COMPATIBILITY TESTING

ABILITY TO SEND MULTIPLE RETURNS ON THE ONE SUBSCRIPTION

THE REPORTS PROVIDE PARTICIPANTS’ OWN RESULTS ALONG WITH GRAPHICAL REPRESENTATION OF THE RESULTS OF THEIR PEERS ALLOWING FOR EASY COMPARISON AND ANALYSIS BY SUPERVISING STAFF

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STEVE MACKAY E-mail: aismsqap@dspl.com.au

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Redesigning workflow and staff competencies to deal with staff shortages in a regional laboratory

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³ Faculty of Health Sciences and Medicine, Bond University, Robina, Queensland

Introduction

The effect of the pathology workforce crisis on the pathology industry has been widely discussed (Legg 2008). However pathology testing is becoming more critical in the diagnosis and monitoring of disease in an ageing population (Australian Medical Association 2011). There are currently staff shortages in specific regions and areas of practice (Legg 2008). These include remote and rural regions and with multi-disciplinary staff. Providing an out of hours service can be expensive in terms of the cost of the call out or shifts as well as having sufficient well trained staff to provide the service. This begs the question as to whether there is a need to provide the service or a need to have the current staff provide that service. There is no doubt that the technology to provide and monitor the testing has changed and as the costs of service provision increase there is a need to analytically review the totality of the service.

Sullivan Nicolaides Pathology (SNP), a comprehensive laboratory service, provides a 24 hr urgent laboratory service via peripheral laboratories and point of care testing (PoCT) to metropolitan and regional private hospitals throughout Queensland and northern New South Wales. Typically, the regional laboratories have different requirements for the range and urgency of testing that needs to be provided. The size of the laboratory and thus the number of staff employed and their levels of qualifications differ between regional laboratories, which in turn can put pressure on the pathology service in meeting these demands. It can be difficult to attract and retain suitably qualified and experienced staff who are prepared to work the required number of hours. These staff must usually be skilled in multiple pathology departments and thus be able to remain competent in a broad range of testing. The challenge is to maintain the quality of pathology service in the face of a change in the skill base of the workforce. In this paper we will describe how SNP have approached the difficult problem of providing a sustainable, high quality service in different situations.

Background

Laboratory networks are asked to provide a broad range of testing throughout Australia. That range can depend on many local variables that can be historical, financial or dictated by workforce issues, either within the local community or the supporting network. These issues can change relatively suddenly because of a change in the number, expectations and type of referer, changes in laboratory staffing or changes in technology or logistics, either in the laboratory or the community. Initially we will discuss the factors that can influence what, how, when and if a laboratory will choose to do particular testing in a region, and then we will describe how this testing can be provided using different staff and equipment resources.

We can classify the type of testing that may be required in a number of different ways each of which provides some information useful in deciding how to provide a local pathology service.

What is the major type of referer?

The range of tests offered by each regional laboratory depends upon the requirements of the local medical community, such as whether there is an after- hours medical centre or private hospital. The presence of Accident and Emergency, obstetric and cardiac wards and the level of surgical procedures employed at a hospital will determine the range of tests required. General practitioners generally require different tests with different turnaround times to specialist referrers.

What is urgent?

A semi-quantitative pregnancy test can be urgent in the investigation of acute abdomen while Obstetrics & Gynaecology (O&G) will require quantitative βhCG to assist in the diagnosis of ectopic or threatened miscarriage.

It should be noted that the same test will have different urgency requirements in different situations. For example a test to aid in diagnosis will generally be more urgent than one to monitor the effects of treatment. Some results will
be required as soon as possible whereas others may only be needed within a 24 hr period depending on the severity of the patient’s condition or possible diagnosis.

In some areas specialised support testing may include hormones if there is an IVF unit operating or glycated haemoglobin for specialised diabetic units, especially paediatric diabetic units.

Frozen sections comprise part of a local histopathology service, and are therefore dependant on the presence of a histopathologist.

Blood Bank Service to most hospitals will require blood bank facilities and coagulation tests. Depending on the surgery performed, it may not be necessary to stock products such as FFP and platelets, but to obtain these only as required.

Blood bank is traditionally a department where only fully qualified scientific and technical officers are allowed to release blood products. A misidentification event or clerical error can result in death within 15 mins through transfusion of incompatible blood products. However, many blood bank procedures are highly automated today. Little technical skill is now required to perform routine group and antibody screens and to assign units that have fulfilled the criteria for electronic crossmatch. Note that patients with a positive antibody screen, a previous history of an antibody being present or where manual testing is required will be excluded from these criteria. It then remains that what is required to prepare safe and competent group and antibody screens or electronic crossmatch, is a well trained and competent, responsible laboratory or technical aide. It is well documented that the majority of transfusion-related adverse events occur through human error (Krombach et al, 2002; Linden et al, 2000) i.e. misidentification of the patient or clerical error. Highly trained staff such as physicians and anaesthetists are not excluded from these figures. Patient misidentification at the collection stage is surely the most dangerous occurrence but is usually beyond the ability of laboratory staff to detect, yet this is the step usually performed by the least trained person involved, the collector. It is difficult to rationalise why trained laboratory technicians cannot take responsibility for checking specimen identification and processing blood bank specimens in fully automated systems when we trust collectors to take the specimens in the first place. In an automated blood banking system the requirements of the staff are accurate patient identification and specimen matching, previous history checking and the checking of specimen acceptance criteria which are all clerical functions, albeit critical ones.

What support is available for a local laboratory?

Varying degrees of support can be provided by a central laboratory in a network to a regional laboratory depending on the IT network and technical expertise available. Sullivan Nicolaides Pathology has been operating the Apollo Laboratory Information System (LIS) since May 2003. This LIS oversees all departments and operations within the Practice, from the Specimen Reception Area (SRA) to final result authorisation. It allows authorised staff from one site to view Quality Control (QC) and specimen result data from an analyser in another laboratory in exactly the same way as they can in their own laboratory. As well there is a central laboratory which operates 24 hrs a day staffed with scientists who can provide technical support in terms of specimen artefact and QC interpretation. Within SNP, the term remote authorisation refers to one location (authorising laboratory) verifying results for testing performed at a separate location (peripheral laboratory). There is in-house 24 hr telephone instrument technical support available to assist in the event of analyser problems and laboratories have access to basic spares. The peripheral laboratories have local contingency plans set up in the event of a complete instrument failure and an on-call specialist pathologist is available for clinical issues.

There are a number of possible scenarios for processing specimens and reporting results in peripheral laboratories. Where there are sufficiently trained scientists available then the regional laboratory functions semi-autonomously only using the central laboratory in a situation where there has been an unexpected instrument failure. This may involve all specimens usually tested on the failed instrument being forwarded to the central laboratory.

In a second scenario, if a regional laboratory has a shortage of experienced scientists then a suitably trained and deemed competent staff member is used to provide basic testing. This will usually be in an after-hours situation but is not restricted to that time. This is the area where we will further describe the strategy used by SNP.

After hours testing at the peripheral laboratory is performed by technical support staff or in the case of PoCT, by collection staff. Results either auto-verify or are verified by a qualified scientist at the authorising laboratory. The auto-verification is based on whether or not the result is within the acceptable intervals specified in the computer algorithm as determined by a specialist pathologist. Authorisation of results outside of these limits must be performed by a suitably qualified scientist, either on site or by logging in from the authorising laboratory. There is also backup provided by an oncall scientist at the peripheral laboratory. They are available to be called in for testing beyond the scope of the staff or on the advice of the qualified scientist at the authorising laboratory. Additionally,
remote authorisation may be employed to offer a continuous pathology service to a regional community with a single-scientist laboratory. It is important to note that the on-site laboratory aide is not authorising any results.

This remote verification has been successfully employed in five peripheral laboratories and the role of the remote verification coordinator created to manage the process.

**Risk Management**

Basics of risk management – a process can be designed with enough checks that people must perform to all but eliminate risk. That is, a process can be virtually risk free. It is the people who pose the greatest risk. Some people are risk takers and some are risk averse. This risk preference is generally not related to the educational status but the person’s behavioural preference. Identification of the staff member’s likely response in a difficult situation needs to be assessed before they are deemed competent.

In changing a potentially critical process it is wise to consider potential risks and ensure that the system has some design robustness to cope with the most likely and most significant risks. SNP assessed the major risks as follows:

**Pre-analytical**

- Misunderstanding the request
- Inadequate patient preparation
- Incorrect sample tube
- Poor quality sample collected – e.g. swab

**Analytical**

- Sample artefact–authorisation haemolysis, lipaemia, jaundice
- QC failure
- Equipment failure
- Sample mix-up
- Qualitative results misinterpreted

**Post-analytical**

- Result not returned in an appropriate time
- Not returned to appropriate requester
- Results inaccurately transcribed
- Knowledge of critical results

Each step of the laboratory testing process was identified with the risk above and a minimum standard of competency was defined for each. As a corollary, the point at which any test must be referred to a scientist was also defined, as were the after-hours tests for which a scientist must always be called in as they were excluded from remote authorisation, for example crossmatch.

Training programs were designed to instruct non-scientifically trained staff to perform all pre authorisation steps, including testing, in the analytical process – see Table 1. These were staff with several years experience in the laboratory in areas such as SRA who had expressed an interest in further education. In some cases, long term employees had previous experience in performing instrument start up and the running of QC and specimens on analysers under supervision of the local scientists.

Non-scientific staff were chosen to participate in remote authorisation and PoCT and completed in-house training programs. Some staff also completed the Certificate IV in Laboratory Techniques through South Bank Institute of Technology (SBIT). They were supported throughout this by mentoring from local scientists, and given paid study leave, travel and accommodation to attend training at SBIT and at the main SNP laboratory at Taringa.

<table>
<thead>
<tr>
<th>Table 1: Training Program for non-technical staff</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Course</strong></td>
</tr>
<tr>
<td>---------------------------------------</td>
</tr>
<tr>
<td>Basic Quality Control</td>
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<tr>
<td>Other</td>
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<td></td>
</tr>
</tbody>
</table>

Note that all of these steps are currently performed in many laboratories across Australia by collectors, laboratory aides and administration/data entry staff. To mitigate against these risks a competency based training program was initiated based on the document Competency-based Standards for Medical Scientists (Pathology Associations Council).
Performed by Collection staff

Performed by Laboratory staff

Hospital POCT Collector on shift

Pathology request

Not urgent

Assess urgency

Routine admission

Collect specimens

Leave routine specimens for Lab staff next morning

Complete testing

We should create two referrals and episode numbers to separate results
1 Critical referral
2 Routine referral

Collect POCT and routine specimens

Perform PoCT i-STAT HmX

Contact GPH for verification

If non scientist and verification required

Deliver reports to ward

Urgent

Critical

Only PoCT required urgently

More than PoCT required urgently

Call in on call staff

Perform testing

Figure 1: Testing protocol
Some different situations

Each peripheral laboratory in the SNP network differs somewhat to the others in its location and scope of testing.

Routine laboratory testing in each remote laboratory, including PoCT, was reviewed. Factors considered in determining which tests would be available for remote authorisation included:

- Requirements of medical facilities e.g. cardiac laboratory/A&E/theatre/after-hours service/renal/oncology/haematology
- Results by PoCT or routine analyser
- Results & QC must be accessible by authorising scientist
- Minimal requirement for manual tasks or calculation in analysis

Laboratories using analysers for testing by remote authorisation offer as a minimum full blood count, electrolytes/liver function test, INR, APTT, TCT, D-dimer, Troponin T and βhCG. Depending on local service requirements, additional biochemical analytes, hormones, therapeutic drugs, or blood gases may be offered. The common factor is fully automated analysis. The tests available on PoCT instruments such as the i-Stat are Hb/Hct, prothrombin time, electrolytes, blood glucose, Troponin I, blood gases & pH – see Table 2.

How it works in practice
(Figure 1)

The specially designed training programs were developed to up-skill non-scientific staff who performed laboratory testing duties routinely during normal working hours. The skills they acquired allow them to operate independently and are appropriate to the tasks required of them.

The networked LIS allows remote access to a laboratory’s test and quality control results within the network.

Testing at the peripheral laboratory is performed by a person who has completed their training and been assessed for competency. This may be a scientist, non-scientist or collector. Essentially, they are required to:

- Check specimen acceptance criteria
- Prepare specimen for analysis e.g. centrifugation
- Perform instrument start-up
- Check and/or change reagents
- Perform calibrations if required
- Run QC
- Assess specimen integrity (clotted/haemolysed/insufficient/too old)
- Run specimens
- Prepare and run dilutions and reruns where necessary
- Perform initial instrument fault trouble shooting to their training level

After testing, results which meet the criteria set by SNP pathologists auto-verify and reports are automatically printed or electronically downloaded. The corporate protocol for faxing or phoning of critical results is followed in all locations. The local remote authorisation protocol includes whether the authorising or the peripheral laboratory is to phone the referrer, as it may be more expedient for a staff member with local knowledge to locate a referrer if urgent or critical results require phoning.

Test results that do not auto-verify are verified remotely by scientists with appropriate verification privileges. PoCT results are available in the ward at the time of testing. For laboratories which offer services such as blood bank, there is always a scientist on call locally if required. Competency assessments are conducted 12 monthly for low use staff and 24 monthly for high use staff.

<table>
<thead>
<tr>
<th>Tests available via RA</th>
<th>Community</th>
<th>Community after hours service</th>
<th>Hospital</th>
<th>Patient demographics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Haematology</td>
</tr>
<tr>
<td>FBC</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Electrolytes/LFT</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>INR/APTT/TCT/D-dimer</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>βhCG</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>PoCT (i-Stat)</td>
<td>✓</td>
<td></td>
<td></td>
<td>✓</td>
</tr>
</tbody>
</table>
Scientific and technical staff have tertiary qualifications from recognised institutions. In addition, all qualified laboratory staff must complete internal training and assessment prior to being given authorisation rights for the tests they perform. SNP is a Registered Training Organisation and trains all collectors to Certificate III in Pathology Specimen Collection. Non-qualified laboratory staff have been trained to Certificate IV in Laboratory Techniques in partnership with South Bank Institute of Technology. In addition, SNP runs internal training courses that cover topics such as QC, Westgard rules, instrument operation and troubleshooting, and precision and accuracy. This ensures that both qualified and non-qualified staff are trained in analyser operation. Currently, competency of scientific and technical staff is assessed through participation in Quality Assurance Programs (QAP) such as the RCPA QAP. SNP also runs parallel internal QAP programs for all laboratory staff. However, both internal and external QAP programs are weighted towards scientist and technicians. There is a need for external QAP programs to assess the effectiveness of training and ongoing competency of all staff.

It must be emphasised that what the laboratory or technical aide is doing in the remote authorisation process is essentially checking specimen identity, checking paperwork, running QC, loading reagents and putting the specimen on the analyser. These are all tasks currently performed by collectors and laboratory aides all over Australia, many of them without formal qualifications. The QC results, the calibration, the test results, and any error or other messages, can all be viewed directly by the off-site scientist in the authorising laboratory. When necessary - and according to strict criteria – a local scientist can be called to perform more complex testing.

The LIS is critical to the successful implementation of remote authorisation. SNP’s system utilises an expert system, which runs behind the LIS, to review results and allow results within acceptable ranges to auto-authorise, whereas abnormal results must be reviewed and authorised by a scientist, or in some instances, only by a pathologist. Scientific staff can be allocated authorisation rights by department or by test, if their local laboratory performs only a few tests from any given department. Authorisation rights are allocated by the laboratory manager to each scientist upon completion of internal competency-based training programs. Detailed training files are maintained.

**Conclusion**

Substituting non-scientifically qualified staff for scientifically qualified staff and employing remote authorisation and PoCT allows SNP to continue to provide essential 24 hr 365 day/year service to metropolitan and regional hospitals despite the pathology workforce crisis. In addition, it allows regional laboratories with a single scientist that do not perform complex testing, such as group and antibody screens or cross matches, to continue to offer an uninterrupted service when the scientist is on leave and a locum is not obtainable. The tasks performed in these laboratories are not technically or academically challenging at any time, and can be safely and confidently performed by an appropriately trained laboratory aide under the remote supervision of a scientist with many years experience.

**References**


**Disclaimer**

This article is the opinion of the authors and is not necessarily the opinion of the editors of the Australian Journal of Medical Science or of the Australian Institute of Medical Scientists.
A case of necrotising fasciitis in a 56-year-old male

Gillian Rozenberg

South Eastern Sydney & Illawarra Area Health Service, Prince of Wales Hospital, New South Wales

A 56-year-old male was transferred from a regional hospital to the intensive care ward at the Prince of Wales Hospital. He had extensive necrosis extending from the scrotum to his flank, axilla and shoulder and spreading along his arm. He had necrotising fasciitis and was to have surgical debridement. He was too unwell for the hyperbaric chamber.

A full blood count was received in the laboratory. The results were as follows:

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb</td>
<td>89</td>
<td>130-180 g/L</td>
</tr>
<tr>
<td>HCT</td>
<td>0.262</td>
<td>0.40 - 0.54</td>
</tr>
<tr>
<td>MCV</td>
<td>87.9</td>
<td>80 - 100 fl</td>
</tr>
<tr>
<td>MCH</td>
<td>29.9</td>
<td>26.5 - 33.0 pg</td>
</tr>
<tr>
<td>WBC</td>
<td>39.9</td>
<td>3.5 - 11.0 x 10^3/L</td>
</tr>
<tr>
<td>PLT</td>
<td>80</td>
<td>150 - 400 x 10^3/L</td>
</tr>
</tbody>
</table>

The blood film showed an absolute neutrophilia with marked toxic granulation; moderate numbers of microspherocytes and thrombocytopenia. These features are classically found in *Clostridium perfringens* infection. This was a case of severe sepsicaemia and haemolysis secondary to necrotising fasciitis.

The term necrotising fasciitis describes a condition of rapidly spreading infection, usually located in fascial planes of connective tissue resulting in tissue necrosis. Fascial planes are bands of connective tissue that surround muscles, nerves and blood vessels. The speed with which necrotising fasciitis spreads is directly proportional to the thickness of the subcutaneous layer. Many types of bacteria can cause necrotising fasciitis (e.g. Group A streptococcus (*Streptococcus pyogenes*), *Staphylococcus aureus*, *Clostridium perfringens*, *Bacteroides fragilis*, *Aeromonas hydrophila*). The disease is classified as either Type I (polymicrobial) caused by a number of different organisms or Type II (monomicrobial) caused by a single organism. The causative organism may be aerobic or anaerobic.

The frequency of necrotising fasciitis has been on the rise due to an increase in immunocompromised patients with diabetes mellitus, cancer, alcoholism, vascular insufficiencies, organ transplants, HIV infection and also occurs in patients with neutropenia.

The mean age of a patient with necrotising fasciitis is 38-44 years. The disease rarely occurs in children. Paediatric cases have been reported from resource-poor nations where poor hygiene is prevalent.

The patient in this case study was diagnosed with *Clostridium perfringens* induced necrotising fasciitis. *Clostridium perfringens* is a saprophytic organism inhabiting the bowel and genital tract. It has no pathological significance in the absence of clinical infection. *Clostridium perfringens* produces at least 12 antigenic protein toxins, the most common of which is the alpha toxin. These toxins react with lipoprotein complexes on cell surfaces, liberating potent haemolytic substances known as lysolecithins which result in cell lysis, hence the presence of microspherocytes on the blood film. This process leads to a severe haemolytic anaemia. Acute renal and hepatic failure develops leading to death in as short a period as 12 hours if not treated immediately.

*Figure 1. Absolute neutrophilia with toxic granulation and microspherocytes*
The chemistry results on this case were as follows:

<table>
<thead>
<tr>
<th>Test</th>
<th>Result (units)</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urea</td>
<td>10.1 mmol/L</td>
<td>RR 2.9 - 7.1</td>
</tr>
<tr>
<td>Creatinine</td>
<td>152 umol/L</td>
<td>RR 60 - 110</td>
</tr>
<tr>
<td>Bilirubin total</td>
<td>47 umol/L</td>
<td>RR 0 - 25</td>
</tr>
<tr>
<td>ALP</td>
<td>106 U/L</td>
<td>RR 38 - 126</td>
</tr>
<tr>
<td>GGT</td>
<td>71 U/L</td>
<td>RR 0 - 50</td>
</tr>
<tr>
<td>AST</td>
<td>89 U/L</td>
<td>RR &lt;45</td>
</tr>
<tr>
<td>ALT</td>
<td>72 U/L</td>
<td>RR &lt;45</td>
</tr>
</tbody>
</table>

The basis of treatment is surgical debridement of necrotic tissue and antibiotic therapy. In severe infections, hyperbaric oxygen is an important adjunct in the treatment of necrotising fasciitis. Massive doses of benzyl penicillin are administered intravenously. Should the patient be allergic to penicillin, metronidazole is effective in high doses.

The patient in this case study died within 24 hours of having been admitted into the ICU ward.

AIMS NSM 2013 SCHOLARSHIPS REPORTS

The 2013 AIMS National Scientific Meeting was held at the Grand Hyatt Melbourne on the 2nd - 4th September 2013. The AIMS scholarship award winners were:

**First Time Presenter Scholarship**

- Pranav Dorwal

**Remote Attendee Scholarship**

- Kathryn Eckersley

**Student Scholarships**

- Eleanor Tait (QUT)
- Kirsty Vigors (Curtin University)
- Sarah Henn (Curtin University)
- Nicola McDonald (University of Tasmania)
- Alice Baxter (James Cook University)
- Ana Maluenda (RMIT University)
- Felicia Chin (RMIT University)
- Nader Mankarious (RMIT University)

To view the scholarship reports please visit:
AIMS/RCPAQAP
Malarial Parasite/Morphology Workshop
AIMS Scholarship

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

In 2014 there will be a scholarship available for all financial members of the Institute for the second workshop held on the 7th, 8th and 9th August 2014, at the RCPA QAP Offices in Herbert Street, St Leonards (Sydney), NSW.

This workshop has been held at least twice a year for the last 23 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 three 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.

DEADLINE
Friday 30 March 2014

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

Application Form
AIMS/RCPA Blood Cell Morphology Workshop
AIMS Scholarship

Name: ___________________________________________ Membership No: ________

Address: __________________________________________

Telephone: __________________ Facsimile: ________________

Email: ____________________________________________

☐ My resume is enclosed which details my place of work, qualifications and employment history.

In 50 words or less, please explain why you believe you should receive the scholarship

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________
The APACE (Australasian Professional Acknowledgement of Continuing Education) scheme is a voluntary program that recognises continuing education, formal courses and a wide range of professional activities which contribute to your professional growth.

The NPAAC document “Requirements for Medical Pathology Services” states:

“C4.1(ii) All qualified staff involved in the provision of Medical Pathology Services must provide documented evidence of participation in continuing professional development to ensure maintenance and updating of the skills required to undertake their individual responsibilities.”

APACE is the perfect way to ensure compliance with this NPAAC requirement.

APACE offers an online user-friendly diary to record your professional activities. The APACE website features a step-by-step guide and our National Office staff are on hand to help. If you are an AIMS member, when you register for an AIMS event, your CPD points are automatically

APACE has been approved by the New Zealand Medical Laboratory Science Board as a recertification program for New Zealand Medical Laboratory Scientists and by the Royal College of Pathologists Australia (RCPA) as a continuing professional development recognition program for Fellows of the Faculty of Science.

APACE Accreditation is achievable by all. Credit where credit is due!
### Thursday 4 September 2014 “PAST”

**Focus - Long standing diseases**

<table>
<thead>
<tr>
<th>Time</th>
<th>Sessions</th>
</tr>
</thead>
<tbody>
<tr>
<td>8:00 AM - 9:00 AM</td>
<td>Arrival tea and coffee</td>
</tr>
<tr>
<td>9:00 AM - 9:30 AM</td>
<td>Official opening</td>
</tr>
</tbody>
</table>
| 9:30 AM - 10:30 AM | Keynote address  
Professor Matthew Brown  
Director  
The University of Queensland Diamantina Institute |
| 10:30 AM - 11:00 AM| Morning tea                                   |
| 11:00 AM - 11:40 AM| Longstanding infectious diseases  
Professor Eddie Holmes (ASM) |
| 11:40 AM - 12:05 PM| The history of haemophilia  
Dr Kevin Rickard          |
| 12:05 PM - 12:30 PM| Heart disease - old or new?  
David Sullivan            |
| 12:30 PM - 1:30 PM | Lunch                                        |
| 1:30 PM - 3:30 PM  | **Masterclass 1**  
Paediatric haematology  
Gillian Rozenberg       |
|                    | **Masterclass 2**  
VWD screening  
Dr Emmanuel Favaloro   |
|                    | **Masterclass 3**  
Quality assurance in haemostasis testing  
Dr Emmanuel Favaloro   |
| 3:30 PM - 4:00 PM  | Afternoon tea                                 |
| 4:00 PM - 5:30 PM  | **Masterclass 1 Cont.**                      |
|                    | **Masterclass 4**  
Biochemistry case studies  
Assoc Prof Tony Badrick |
| 6:30 PM - 8:30 PM  | Welcome reception                            |
# AIMS National Scientific Meeting Program

**Friday 5 September 2014 “PRESENT”**

**Focus - Obstetric and neonates, world pathology**

<table>
<thead>
<tr>
<th>Time</th>
<th>Sessions</th>
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</thead>
<tbody>
<tr>
<td>8:00 AM - 9:00 AM</td>
<td>Arrival tea and coffee</td>
</tr>
<tr>
<td>9:00 AM - 9:30 AM</td>
<td>The future of cervical screening</td>
</tr>
<tr>
<td></td>
<td>Jenny Ross (ASC)</td>
</tr>
<tr>
<td>9:30 AM - 10:00 AM</td>
<td>Fertility issues</td>
</tr>
<tr>
<td>10:00 AM - 10:30 AM</td>
<td>Haemoglobinopathy screening in the antenatal population</td>
</tr>
<tr>
<td></td>
<td>Dr Jill Finlayson</td>
</tr>
<tr>
<td>10:30 AM - 11:00 AM</td>
<td>Morning tea</td>
</tr>
<tr>
<td>11:00 AM - 11:40 AM</td>
<td>Delivery emergencies</td>
</tr>
<tr>
<td></td>
<td>Dr Claire McLintock (ASTH)</td>
</tr>
<tr>
<td>11:40 AM - 12:05 PM</td>
<td>Gestational diabetes</td>
</tr>
<tr>
<td>12:05 PM - 12:30 PM</td>
<td>Transfusion obstetric emergencies</td>
</tr>
<tr>
<td>12:30 PM - 1:30 PM</td>
<td>Lunch</td>
</tr>
<tr>
<td>1:30 PM - 2:00 PM</td>
<td>AIMS AGM</td>
</tr>
<tr>
<td>2:00 PM - 2:30 PM</td>
<td>Saal-Foley lecture</td>
</tr>
<tr>
<td>2:30 PM - 3:00 PM</td>
<td>Worldwide childhood mortality rates</td>
</tr>
<tr>
<td>3:00 PM - 3:30 PM</td>
<td>Paediatric tumours</td>
</tr>
<tr>
<td></td>
<td>Dr Ella Sugo</td>
</tr>
<tr>
<td>3:30 PM - 4:00 PM</td>
<td>Afternoon tea</td>
</tr>
<tr>
<td>4:00 PM - 4:30 PM</td>
<td>Paediatric metabolic disorders</td>
</tr>
<tr>
<td>4:30 PM - 5:00 PM</td>
<td>Current status of Alzheimers research</td>
</tr>
<tr>
<td>5:00 PM - 5:30 PM</td>
<td>SJOG pathology outreach program in East Timor</td>
</tr>
<tr>
<td></td>
<td>Kyle Jackson-Brown</td>
</tr>
<tr>
<td>7:00 PM - 11:00 PM</td>
<td>Conference Dinner</td>
</tr>
<tr>
<td>Time</td>
<td>Sessions</td>
</tr>
<tr>
<td>------------------</td>
<td>--------------------------------------------------------------------------</td>
</tr>
<tr>
<td>8:00 AM - 9:00 AM</td>
<td>Arrival tea and coffee</td>
</tr>
<tr>
<td>9:00 AM - 9:30 AM</td>
<td>New diagnostics for cancer</td>
</tr>
</tbody>
</table>
| 9:30 AM - 10:00 AM| Genomic sequencing  
                       Melody Caramins                               |
| 10:00 AM - 10:30 AM| The implementation of a large LIS network  
                       Shaun Grimmet, South Africa                          |
| 10:30 AM - 11:00 AM| Morning tea                                                             |
| 11:00 AM - 11:40 AM| Gene assay testing: What is being tested for,  
                       the applicability and the implications  
                       Prof Michael Buckley (HGBA)                        |
| 11:40 AM - 12:05 PM| The pathology laboratory of the future                                 |
| 12:05 PM - 12:30 PM| Confocal microscopy                                                     |
| 12:30 PM - 1:30 PM| Lunch                                                                   |
| 1:30 PM - 3:30 PM| Masterclass 5  
                       Molecular applications now and in the future  
                       Dr Sheryl Maher                                      |
| 3:30 PM - 4:00 PM| Afternoon tea                                                           |
| 4:00 PM - 5:00 PM| Masterclass 5 (continued)                                               |
AIMS NSM 2014 SCHOLARSHIPS & PRIZES

Up to four scholarships of $1000 each will be offered to financial members of AIMS in 2014 to support attendance at the AIMS Centenary National Scientific Meeting to be held at Rydges World Square, Sydney, 4th to 6th September 2014.

Up to $500 value towards an AIMS educational activity will be awarded to the best poster(s) presented at the AIMS Centenary conference.

**Eligibility**

Applicants must be members of AIMS at the time of the application, and must have held membership for at least six months at that time. Affiliate, retained, corporate or student members are not eligible to apply.

Other eligibility criteria may apply to each scholarship/award.

**Conditions of award**

The successful applicants must be available to take up the scholarship/award to attend the National Scientific Meeting in 2014. Successful applicants, except for first time presenter awards, will be advised by June 20th 2014.

Funds will be used for registration costs. Any remaining funds may be applied to travel, and/or accommodation costs. Payment of the scholarship will be made on receipt of documentary evidence of expenditure.

All recipients of AIMS scholarships are expected to write a short report (300-500) words on their experience at the NSM for possible publication in the Australian Journal of Medical Science

AIMS reserves the right not to make an award in any category.

**Early Career Scholarship**

Applicants must be Graduates or Full Members of the Institute, must have been in employment for no more than five years since graduation and must be under 30 years of age at 4th September 2014. Employment documentation must be provided.

Applicants must give examples of any special projects or initiatives of an investigative, scientific nature that is original work. These projects may be part of a team initiative but the applicant must demonstrate their involvement and commitment to the project. Examples may include the development of a new assay or being involved in commissioning a new laboratory instrument. Applicants must also demonstrate their reasons for wishing to attend the NSM and the relevance of the NSM to their professional practice. Total length of application must not exceed 500 words. This may be published in the Australian Journal of Medical Science.

**Poster Prize**

Posters will be judged at the conference and posters will only be considered if at least one author is registered for the conference.

**Application**

Applications must be on the appropriate application form, which is available on the AIMS website or from AIMS National Office.

Applications should be lodged electronically to: amsnat@aims.org.au

**APPLICATIONS CLOSE 4.00 PM QUEENSLAND TIME ON MONDAY 28th APRIL 2014.**

**LATE APPLICATIONS WILL NOT BE ACCEPTED**
Journal-based CPD No. 39
Page 1 of 2

Questions relating to 'Laboratory information systems in clinical biochemistry in Australia', page 2 of this issue.

1. The majority of respondents to the survey utilised a laboratory information system within the laboratory. True/False

2. Bi-directional interfaces predated unidirectional interfaces in most biochemistry laboratories. True/False

3. Without a laboratory information system it would not be possible to observe and simultaneously plot several levels of quality control data on a single graph. True/False

4. A major development in the utilisation of the LIS in the core laboratory was the introduction of rules governing the acceptance of patient results without further intervention by staff. True/False

5. This study looked at the implementation of decision support systems to enhance clinical outputs, the support of data analysis for audit, clinical risk management, disease surveillance and epidemiology (e.g. cancer registration, screening programmes, communicable disease reporting and external quality assessment data management). True/False

6. The response rate to the distributed survey was 82%. True/False

7. Laboratories were permitted to make multiple responses to cater for satellite laboratories in remote and regional areas. True/False

8. Unidirectional interfacing requires manual programming which has inherent problems including wrong laboratory identification numbers, incomplete requests being registered in the analyser and the necessity to check a print out of results against the primary tube. This wastes time and the intensive nature of manually registering patients' requests into analysers lengthens the turnaround time for patient results thereby reducing efficiency. True/False

9. The use of auto validated results requires that the laboratory has verified that the program is tested for limits required for the release of results and that auto-validation of results only occurs when both analytical and physiological checks of the result have been performed. True/False

10. The majority of laboratories utilise auto-validation of results with algorithms embedded in either middleware or the LIS. These algorithms are generally pre-formulated by the vendor companies to enable the maximum number of results to be accepted without further review. True/False

Name: ____________________________________________

Email: ________________________________

Please photocopy this page or print it from the electronic AJMS which is stored in the AIMS’ Member centre under the heading ‘Journal’ at www.aims.org.au. Circle your answers then post, fax or scan and email to us:

AJMS APACE Questions, AIMS National Office, PO Box 1911, Milton Qld 4064. Facsimile: 61 7 3876 2999

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## Journal-based CPD No. 39  
Page 2 of 2

Questions relating to 'Idiopathic systemic capillary leak (Clarkson) syndrome', page 10 of this issue.

1. In ISCLS fluid and protein are forced through the endothelial barrier and into the interstitium and tend to accumulate in the trunk and extremities.  
   - True/False

2. The erythropoietin (EPO) result for this patient was normal.  
   - True/False

3. WHO criteria for the diagnosis of PV requires both major criteria, or the first major criterion plus two minor criteria.  
   - True/False

4. The Hb and Hct took 48 hours to return to the reference range after the patient’s first admission.  
   - True/False

5. IVIG seems to consistently reduce frequency of episodes and it is approved for use in Australia for treatment of this syndrome.  
   - True/False

6. The patient had a history of 2 episodes of meningococcal sepsis with microbiological confirmation.  
   - True/False

7. ISCLS is a diagnosis made by excluding all of the other possibilities, the rapid response to treatment of intensive rehydration and the presence of a monoclonal gammopathy.  
   - True/False

8. The severe leakage in ISCLS, and resulting depletion of intravascular fluid and proteins, causes hypotension and haemoconcentration.  
   - True/False

9. The five year survival for patients with ISCLS is between 30% and 76%.  
   - True/False

10. The inflammatory mediators leukotrienes and TNFα, have not been implicated in ISCLS.  
    - True/False

Name: ____________________________  
Email: ____________________________

*Please photocopy this page or print it from the electronic AJMS which is stored in the AIMS Member centre under the heading 'Journal' at www.aims.org.au. Circle your answers then post, fax or scan and email to us:*  
AJMS APACE Questions, AIMS National Office, PO Box 1911, Milton Qld 4064. Facsimile: 61 7 3876 2999
YEAR 2014

APRIL 5 - 6
AIMS SA/NT Branch Conference
Paediatric & Geriatric Pathology
The Old Mill
Hahndorf Adelaide Hills SA AUSTRALIA
www.aims.org.au/events

APRIL 23 - 26
International Society of Cellular Therapy
Paris FRANCE
http://www.celltherapysociety.org/

MAY 10 - 12
International Society of Laboratory Hematology
The Haques NETHERLANDS
http://www.islh.org/2014/

MAY 29 - 31
AIMS/RCPA QAP Haematology Morphology Workshop (I)
29th: Malaria & Introduction to microscopy component
30th & 31st: Morphology component
Sydney NSW AUSTRALIA

JUNE 20 - 22
The XIII International Congress of Pediatric Laboratory Medicine
Istanbul TURKEY

AUGUST 7 - 9
AIMS/RCPA QAP Haematology Morphology Workshop (II)
7th: Malaria & Introduction to microscopy component
8th & 9th: Morphology component
Sydney NSW AUSTRALIA

3 - 6 OCTOBER
Australian Society of Cytology
44th Annual Scientific & Business Meeting
“Cytology on the Frontier”
Darwin Convention Centre
Darwin, NT, Australia
The Society will be holding the 2014 Tutorial after the Scientific Meeting on 7 -10 October.
http://www.cytology-asc.com/meetings/index.htm

OCTOBER 19 - 22
Haematology Society of Australia & New Zealand,
The Australian & New Zealand Society of Blood
Transfusion & The Australasian Society of Thrombosis
and Haemostasis
Perth Convention centre
Perth WA AUSTRALIA
http://www.haa2014.com/

OCTOBER 27 - 29
Australasian Association of Clinical Biochemists
52nd Annual Scientific Conference
Adelaide SA AUSTRALIA
http://www.aacb.asn.au/eventsinfo/aacb-52nd-annual-
scientific-conference

DECEMBER 6 - 9
American Society of Hematology
San Francisco USA
http://www.hematology.org/Meetings/Annual-Meet-
ing/11522.aspx

YEAR 2015

JUNE 20 - 25
International Society of Thrombosis and Hemostasis
Toronto CANADA
http://www.isth.org/?page=ISTHCongresses
BOOKS FOR REVIEW

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.

Unfortunately AIMS is unable to send books overseas.

Please send your request 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

Latest additions:
1. Pediatric and Adolescent Medicine Volume 17: Controversies in Pediatric and Adolescent Hematology
2. Burkholderia: From Genomes to Function
3. Applications of Molecular Microbiological Methods
4. Aspergillus: Molecular Biology & Genomics
5. Bacterial Gene Regulation and Transcriptional Networks
6. Bacterial Regulatory Networks
7. Bifidobacteria: Genomics & Molecular Aspects
9. Burkholderia: From Genomes to Function
10. Contributions to Nephrology Volume 157: IgA Nephropathy Today
11. Contributions to Nephrology Volume 180: Phosphate and Vitamin D in Chronic Kidney Disease
14. Cytokines, Growth Mediators & Physical Activity in Children during Puberty
15. Digestive Diseases The Keys to IBD 2010: Treatment, Diagnosis & Pathophysiology
16. Else Kröner-Fresenius Symposia Volume 1: Molecular Mechanisms of Adult Stem Cell Aging

Herweal & A.Egesten. Karger. x +162 pages


27. Knowing One's Medical Fate Challenges for Diagnosis and Treatment, Philosophy, Thics and Religion edited by G. Pfleiderer, M. Battegay & K. Lindpaintner. Karger. vi + 122 pages


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**Doctors Without Borders**

**MEDECINS SANS FRONTIERES**

**Doctors Without Borders**

**DOCTORS WITHOUT BORDERS**

**AID WITHOUT AGENDA**

**COMPASSION WITHOUT PREJUDICE**

**ACTION WITHOUT SILENCE**

Around the world Doctors Without Borders provides medical humanitarian aid regardless of our patients’ race, religion, gender or political affiliation. This year 167 Australian and New Zealanders are part of our global mission - saving lives and bearing witness to the true impact of violence, natural disasters and medical crises.

**NOT WITHOUT YOU**

**MSF.ORG.AU | MSF.TV**
Palliative Care for infants, Children and Adolescents – A practical handbook

Edited by Brian S. Carter, Marcia Levetown and Sarah E. Friedbert

The John Hopkins University Press

Soft cover 538 pages USD $66.50

This text is organized into three fairly equal parts: Part I is Societal and institutional issues, Part II The cycle of care and Part III covers special care environments and patient populations.

Part I gives background information and sets the scene. It asks more questions than it answers as it attempts to define Palliative care, who should receive it, how they should receive it and how it integrates with the rest if the healthcare system. There is a lot of data presented as statistics and previous studies are used in the search for answers. Barriers such as ethics, conflict and are funding are also discussed.

Part II walks us through the process of managing a life-limiting or life-threatening condition, and opens our eyes to the bigger picture. Palliative care is about so much more than pain relief and hospital care for the patient. We are provided with some guidance and instruction for how to effectively communicate a diagnosis, when to introduce the palliative care team, how social issues can be addressed etc. Each section is complemented by a real life example which puts the theory into context and helps the reader understand the application. At the conclusion of Part II the reader understands the topics of decision making, communication, social issues, religion/spiritual dimensions and bereavement with the final chapter focusing on caregiver suffering including strategies to address caregiver suffering.

Part III builds on topics discussed in Part II by zooming in on a few specific patient populations with one chapter each on Palliative care in: the neonatal period, in the intensive care setting, with genetic conditions, HIV patients and Haematology/Oncology. These chapters are easy to read as they primarily focus on the clinical scenario and patient examples.

There is USA specific information which is not applicable in Australia scattered throughout the text such as discussion of health care funding, Medicaid etc.

The most surprising thing is how broad the authors cover eg. The effects on schools of having pupils with life-threatening conditions and the involvement of the Sheriff’s office of patients spending their final time at home. These additional aspects really paint the overall picture and add to the readers understanding of the bigger picture.

At the end of the text the reader is left in no doubt of the importance of communication and the pivotal role it plays.

The use of patient examples enhance the text and each chapter is well referenced. Overall the text thoroughly examines what constitutes palliative care and outlines best practice and the latest research on how we can improve outcomes for patients and their families.

Ellouise Parsons MAIMS
Medical Scientist in Charge
ParkWest Nickol Bay

Hepatitis C: Antiviral drug discovery and Development

Seng-Lai Tan (Hoffman-La Roche Inc) and Yupeng He Abbott Laboratories

Caister Academic Press

Hard cover 389 pages

ISBN: 978-1-904455-78-3 USD $360.00

Hepatitis C virus (HCV) has infected over 170 million people worldwide. Transmitted by blood-borne and sexual routes, chronic HCV infection is a common cause of liver failure and liver cancer. While vaccines are available for Hepatitis A and B viruses, this is not the case for HCV, a problem compounded by the unavailability of an animal disease model that can replicate the complex pathogenesis of chronic Hepatitis C in humans.

While traditional antiviral drug discovery approaches have yielded significant successes, anti-HCV drug development has proven to be particularly problematical. This has led to several pharmaceutical companies dropping out of the race. Fortunately, those that have been resilient are finally witnessing promising progress in the race toward anti-HCV-specific drugs and treatments.

Hepatitis C: Antiviral drug discovery and development, is devoted to capturing information on recent advancements and challenges, advancements and emerging trends in the field. To this end, the editors have assembled 40 of the world’s highly regarded experts (mostly from USA, but some from UK, Japan and Australia, a veritable “Who’s who” in the field), who have collectively produced 19 highly readable chapters.
The first half of the book (Chapters 1-8) provides an updated view of the current understanding of the HCV lifecycle, a summary of commonly used assays, animal models, as well as an overview of the current HCV pipeline.

The second half of the book (Chapters 9-16) focuses on small molecule HCV inhibitors, viral resistance, and the ideal of combination therapy using different drugs acting on different targets to effectively inhibit HCV replication.

A major appeal of Hepatitis C: Antiviral drug discovery and development is the inclusion of scores of diagrams, illustrations and tables. The volume is comprehensively referenced and includes an extensive bibliography.

Hepatitis C: Antiviral drug discovery and development will appeal to and be a valuable resource to all healthcare workers in the field of hepatitis serology, particularly for medical scientists and researchers. It is highly recommended.

Dr Bevan Hokin MAIMS
Director of Pathology,
Sydney Adventist Hospital

The Vitamin A Story: Lifting the Shadow of Death
R.D.Semba, Baltimore, Md.
Karger
Hard cover xvi + 208 pages
ISBN 978-3-18-02188-2 USD $104.00

The author of this book provides a thorough and detailed account of the features of Vitamin A deficiency. The clinical signs were known long before the causative agent was identified.

The early chapters describe symptoms which appeared in the crews of nineteenth century naval vessels. Night blindness was a serious and common disorder associated with long periods at sea. Similar findings were noted in populations where malnutrition occurred especially in young children. Overtime other lesions were identified. These included corneal ulcers, xerophthalmia (dry cornea and conjunctiva) and Bitot's spots (conjunctival patches).

By 1871, the first suggestion that lack of an unidentified substance found in food may be the cause of many of the clinical signs seen in malnourished children.

At the end of the nineteenth century similar clinical findings were identified in soldiers of both sides in the American Civil War. Night blindness increased when Vitamin A rich foods became less available. Furthermore it became apparent that infectious diseases such as diarrhea were often associated with night blindness. Like the officers in the early naval ships, officers in the American Civil War were less affected by night blindness. This was because the diet in both cases included adequate amounts of the yet to be discovered Vitamin A.

The next step in the Vitamin A story was the identification of Vitamin A. It became clear that a good diet must include more than protein, fat, carbohydrates and minerals. Scientists using animal studies were instrumental in the recognition of vitamins. It is claimed that the full recognition of Vitamin A took more than one hundred and thirty years.

The next significant role to be determined was the anti-infective role of Vitamin A. It was shown that a deficiency of this vitamin was associated with an increased susceptibility to infection. Before the widespread use of antibiotics, Vitamin A was used in the treatment of puerperal sepsis.

These studies reinforced the view that Vitamin A was important in antenatal welfare. Furthermore, the role of Vitamin A as the anti-infective vitamin stimulated its use in the treatment of severe measles in children.

Finally, the author discusses the use of Vitamin A supplementation in children in poor countries such as the Philippines, India and Nepal. Although well-intentioned, studies in these countries were hindered by political interference and purists who wanted adequate Vitamin A levels to be achieved by dietary means and not by the use of supplements. Ultimately, governments removed supplement restrictions. However, there still remain large areas in Africa, India and Central America where Vitamin A deficiency continues to cause serious health problems.

This book follows the Vitamin A Story from the early clinical signs seen in sailors, soldiers, the poor and undernourished to the present day where the chemistry and nutritional importance of Vitamin A are known.

It is a story written primarily for students of nutritional history. However, because it is written in an "easy to read and understand" format, it is also recommended for those interested in the history of vitamins.

Neville Tingle
AIMS Life Member
The following instructions are based on the “Uniform Requirements for Manuscripts Submitted to Biomedical Journals”, also known as the Declaration of Vancouver, and on the Australian Government Style manual for authors, editors and printers, 6th edition, 2002. URLs were correct on September 29th, 2008.

Manuscripts that do not fully comply with the following ‘Instructions to Authors’ may be returned for revision before they are considered for publication.

The Australian Journal of Medical Science (AJMS) will consider for publication any paper relevant to the field of Medical Science. Disciplines include blood banking, clinical biochemistry, haematology, histopathology, immunology, microbiology and molecular biology. Areas of general interest to medical laboratory scientists, including toxicology, epidemiology, public and community health, and professional and management issues will also be considered.

Papers published in the AJMS are in the form of:
- Review Articles
- Original Articles
- Brief Communications
- Technical Notes
- Case Studies
- Letters to the Editor
- Book Reviews

Articles submitted for publication are understood to be offered only to the AJMS and those accepted become the property of the AJMS.

All individuals listed as authors must have made a substantial contribution to the conception and design of the study, the acquisition of data or the analysis and interpretation of data; the drafting of the article or revising it critically for important intellectual content; and final approval of the version to be published. The corresponding author must take responsibility for obtaining permission from all the authors for the submission of any version of the manuscript and for any changes in authorship.

When the manuscript is submitted the authors must disclose any potential conflict of interest and/or commercial support.

Requirements & preparation of manuscripts

General

Articles should be submitted in electronic format to ajms@aims.org.au. If an article is too large to be submitted by email, it should be submitted on a CD.

Number pages consecutively commencing with the title page.
Arrange the article in the following sequence:
- Title page
- Abstract and key words
- Main Text

- Acknowledgements
- References
- Tables - each table, complete with title and footnotes, on a separate page
- Legends for illustrations.

Authors should ensure that their manuscript communicates their ideas and concepts simply and clearly so that the article is easily read and understood. Authors are strongly recommended to refer to the recommendations on reporting standards as outlined in the statements and checklists of the CONSORT group (see: http://www.consort-statement.org/) and similar groups such as STARD (see: http://www.stard-statement.org/). The principles outlined in these standards may be used as general guidelines and not just as applied to clinical trials and diagnostic studies.

Title page

The title of the article should not exceed three lines (40 characters per line), including punctuation and spacing. All authors must be identified on the title page (e.g., William Smith, Susan Yeo, ...). Where applicable, the title page should also include the name of the institution with which each author is affiliated and to which the work should be attributed. In the case of multiple authors, the name, postal address, email address, telephone and facsimile number of the author responsible for correspondence relating to the manuscript should be indicated.

Abstract & keywords

The abstract should be approximately 150 words and should make sense when read alone or in conjunction with the article. The abstract should be a concise overview that describes the important details of the article including the purpose of the study/investigation, basic procedures (study subjects/experimental animals/observational and analytic methods) and the results and principal conclusions. New and important aspects of the work and its implications may also be included. References should not be included.

Three to ten keywords may be listed. Authors are advised to comply with the terms from the Medical Subject Headings (MeSH) list from Index Medicus (see http://www.nlm.nih.gov/mesh/). Keywords should be given below the Abstract.

Text

The style of writing should conform to acceptable English usage. Do not use slang, medical jargon or unnecessary abbreviations. Accepted spelling is the first choice given in the latest edition of the Macquarie Dictionary.

Wherever possible observational or experimental articles should be divided into sections headed:
- Introduction
- Materials and methods
- Results
Discussion
For other types of articles such as commentaries, reports and reviews, use an appropriate format or consult the Editors for guidance.

Introduction
Clearly state the purpose of the article leading the reader from the known to the unknown. Summarise the rationale for the study and state the question to be answered as appropriate. Give only strictly pertinent references, and do not review the subject extensively.

Materials & methods
Present the materials and methods in a logical sequence. Describe the selection of the observational or experimental subjects (patients or experimental animals, including controls) clearly. Notification of ethics approval must be given where relevant. Identify the methods, apparatus and procedures in sufficient detail to allow other workers to reproduce the results. Give references to established methods, including statistical methods. Adequately describe new or substantially modified methods. Identify precisely all drugs and chemicals used, including generic name(s), dosage(s), and route(s) of administration. Do not identify patients or hospitals without consent.

Results
Present the results in the same sequence as given in the Materials and methods; use tables and illustrations where these will help the reader understand the work being presented. Do not repeat in the text all the data in the tables or illustrations.

Discussion
Indicate the new and important aspects of the study and emphasise the conclusions that follow. Do not repeat in detail data given in the Results section and do not add new data. Include in the Discussion the implications of the findings and their limitations and compare the observations to other relevant studies. Recommendations may be included if appropriate. Link the conclusions with the goals of the study and answer the experimental question stated in the Introduction. However, avoid unqualified statements and conclusions not completely supported by your data. Avoid claiming priority and alluding to work that has not been completed. State new hypotheses when warranted, but clearly label them as such.

Acknowledgements
Acknowledge individuals who have made substantial contributions to the study including technical work and financial support. Authors are responsible for obtaining consent from all the individuals acknowledged by name as inclusion may be interpreted as an endorsement of the article’s contents.

References
The AJMS uses a modified Harvard System (author-date system).

Throughout the body of the manuscript cite the author/s name and the publication year in parentheses as in the following examples:

(i) Research in this area (Jones 1999) …
(ii) It has been successfully demonstrated that (Smith and Brown 1981; Auteur 1995; Sciienziato et al 2007).
(iii) Following further investigation, Wetenschapper (2002) highlighted the difficulties inherent in…

Where there are three or more authors, acknowledge only the first author, e.g., (Smith et al 2007). For two authors the following style should be used: (Smith and Brown 2007).

The reference list should be in the format described below. Journal titles should be abbreviated in Index Medicus format (see: ftp://nlmpubs.nlm.nih.gov/online/journals/jiweb.pdf) using standard abbreviations from the ISSN List of Title Word Abbreviations (see: http://www.isss.org/cn/node/344) All authors should be given in the reference list.

Do not use abstracts as references. “Unpublished observations” and “personal communications” may not be used as references, although references to written, not verbal, communications may be cited (in parentheses) in the text. Include in the references manuscripts accepted but not yet published, designate the journal followed by “in press” (in parentheses). Information from manuscripts submitted but not yet accepted should be cited in the text as “unpublished observations” (in parentheses).

Examples of the correct form for references are given below:

i) Journal Reference:

ii) Personal Author(s) of a book:

iii) Editor, Compiler, Chairman as Author:

iv) Chapter in Book:

v) Online documents:

Tables
Number tables consecutively with Arabic numerals and supply a brief title for each. Give each column a short or abbreviated heading. Place explanatory matter in footnotes, not in headings. Explain in footnotes all non-standard abbreviations used in each table.

For footnotes, use the following symbols in this sequence:

* † ‡ § ¶ ** ††
In preparing tables, consideration should be given to the page width of the Australian Journal of Medical Science. All tables should be prepared for publication vertically. In the text, cite each table in consecutive order, and mark in the margin of the text its approximate location.

If data from another published or unpublished source is used, written permission must be obtained and a copy must accompany the manuscript.

Illustrations
Colour illustrations may be submitted on a CD. Images should be scanned at a minimum of 300 dpi.

When plotting points, the following symbols are preferred:
- ○ • ▲ ▼ □ ▪

In most instances, figures will be reduced to one column in width. All letters and numbers should be drawn to be at least 1.5 mm high after reduction, symbols at least 1.0 mm. Titles for illustrations belong in the legends for illustrations and not on the illustrations themselves.

Photomicrographs must have internal scale markers and the magnification must be stated. Symbols, arrows, or letters used in the photomicrographs should contrast with the background.

Cite each figure in the text in consecutive order, e.g., “Figure 1 illustrates ...” or “... as shown (fig. 2)”. If a figure has been published, acknowledge the original source and submit with the manuscript written permission from the copyright holder to reproduce the material. Permission is required, regardless of authorship or publisher, except for documents in the public domain.

Legends for illustrations
When symbols, arrows, numbers, or letters are used to identify parts of illustrations, identify and explain each one in the legends. The figure legend must contain a boldface (a) name (“Figure” + arabic figure number) and (b) substantive title.

Abbreviations
Use only standard abbreviations (see list of commonly used abbreviations, below).

Avoid abbreviations in the title. The full term for which an abbreviation stands must precede its first use in the text unless it is a standard abbreviation for a unit of measurement.

Report measurements in the units in which the measurements were made. In most countries the International System of Units (SI) is standard.

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Additional information
The following are useful sources of information. The first two publications are used by the AJMS as standard references.
