ASCLS Vision Statement

The American Society for Clinical Laboratory Science, as the preeminent organization for clinical laboratory science practitioners, provides dynamic leadership and vigorously promotes all aspects of clinical laboratory science practice, education and management to ensure excellent, accessible, cost-effective laboratory services for the consumers of health care.

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Laboratories, along with many other healthcare providers, have been ‘squeezed’ for many years now by the payment policies of the outpatient Medicare program (Part B), and by those of managed care organizations. As has been stated frequently, this has converted the laboratory from the status it historically enjoyed of a ‘profit center’ to a ‘cost center’. An illustration of this dilemma is the fact that the Medicare Fee Schedule payments for outpatient laboratory tests have been frozen at the same level, without even a consumer price index (CPI) increase, for nine of the past 13 years. We all know that our employers’ costs have not remained stable during that time—we certainly hope that our salaries have not been frozen—so this is an issue of concern to all laboratorians, whether they are in management or not.

ASCLS has taken the lead for many years by including equitable payment for laboratory services in the issues presented at its Legislative Symposium. Nearly every year, one of the ‘leave-behind’ papers which we discuss with our Senators and members of Congress addresses Medicare payment for laboratory services. In addition, ASCLS is an active participant in the Clinical Laboratory Coalition, which has the slogan “Committed to Ensuring Access to Quality Laboratory Services”. Other groups which are members of the Coalition include: Advamed; American Association of Bioanalysts (AAB); American Association for Clinical Chemistry (AACC); American Clinical Laboratory Association (ACLA); American Medical Technologists (AMT); American Society of Clinical Pathologists (ASCP); American Society for Microbiology (ASM); and CLMA – Leadership in Clinical Systems Management.

Support for the position of the laboratory has been heard strongly from a report commissioned by Congress and published by the Institute of Medicine (IOM) in December 2000. (See details in the Washington Beat column in the Spring 2001 issue of Clinical Laboratory Science.) The IOM’s recommendations lend the support of an independent non-governmental commission to positions that ASCLS has taken over the years.

During the late summer of 2001, two companion bills were introduced in the Senate and the House of Representatives: S1066 sponsored by Senator Orrin Hatch (R-UT) and HR 1798 sponsored by Representative Jennifer Dunn (R-WA). ASCLS and the laboratory community were hopeful that the passage of a version of these bills would have lifted the five year freeze before the fifth year began in October 2001. There were also provisions that would address more expeditious and fair adoption of, and price setting for, new tests. This effort was put on hold by the events of September 11 and the change in focus for Congress. Ironically, ASCLS members and representatives of other Coalition organizations were in Washington the morning of September 11 to lobby on behalf of Dunn/Hatch.

Now that Congress has reconvened for the 2002 session, ASCLS is carefully watching legislation that will affect laboratory reimbursement, and also watching for provisions in the Bush administration budget that could affect laboratories. There is concern that the slowdown in the economy might cause the administration or Congress to propose extending the freeze. Or other strategies that ASCLS has opposed in the past could be raised again. Examples are the imposition of a co-pay for Medicare beneficiaries for laboratory tests, or perhaps a competitive bidding process among laboratories to provide services to Medicare. Fortunately, at the date of this writing, none of these three items is part of the administration’s budget proposal, nor have they been proposed in legislation introduced to date.

Dunn/Hatch itself has not been brought back to this Congress for consideration. However, there are some new pieces of legislation that address some of the reimbursement concerns that ASCLS and the Coalition are working to support. One of these is the Medicare Appeals, Regulatory, and Contracting Improvements Act, S1738 (MARcia). This is a broad Medicare reform bill. The Coalition has contacted Senators and members of Congress who sit on the committees that will review the bill to urge inclusion of language originally in the Dunn/Hatch bill about new tests in the MARCia bill. The portion in question addresses the IOM recommendation for “an open, timely, and accessible process” for incorporating new tests into the Medicare Laboratory Fee Schedule.

In addition, ASCLS supports the Medicare Laboratory Services Act of 2001 (HR 3388), introduced on November 30, 2001 by Representatives Phil English of PA and Peter Deutsch of FL. This bill focuses specifically on the reimbursement for specimen collection (venipuncture) which was set at $3.00 seventeen years ago and has never changed. It may never have completely covered the cost of a venipuncture, but with the increased costs of safer needles and other safety devices, as well as rising personnel costs, it is obviously quite inadequate now. The bill would raise the specimen collection fee to $5.25, which is the level it would have reached had CPI adjustments been applied for the last 17 years.

These are two very specific but important issues for the economic viability of the laboratories we all work in. The ASCLS Government Affairs Committee counts on its members to help contact their Senators and Representatives in support of these pieces of legislation and others that may come along. Our history of activism is a long and proud one!
Dyslipidemia Prevalence in a Laboratory Initiated Screening Program

JANE F EMERSON, MAHTAB JAFARI


DESIGN: 301 patients self-referred to the clinical laboratory for lipid testing in a two-year period. The patient population that participated was characterized in terms of insurance status, gender, age, and known cardiovascular risk factors. Lipid profiles were characterized as measured by total cholesterol, triglycerides (TGs), low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), and total cholesterol to HDL risk factor.

SETTING: Clinical laboratory in an academic medical center.

PATIENTS: Data from all patients that self-selected for screening were included.

INTERVENTIONS: Immediate laboratory results with both verbal and written interpretations and recommendations were provided to the patients.

MAIN OUTCOME MEASURES: Age, gender, insurance status, number of known risk factors, and lipid profiles in the subject group.

RESULTS: The mean age of participants was 57 years. Men (197) outnumbered women (104) by almost 2:1; most (94%) had health insurance. At presentation, 44% of the patients had more than one risk factor for coronary heart disease (CHD). 151 individuals (50%) had lipid findings that would require at least dietary intervention by NCEP guidelines.

CONCLUSION: A self-pay, self-referred screening program for lipid disorders is an effective means of improving screening and diagnosis rates. Patients with insurance were willing to pay for the convenience offered and men in particular were more likely to self-refer than women, independent of previous knowledge of risk factors or lipid disorders.

ABBREVIATIONS: CHD = coronary heart disease; HDL = high-density lipoprotein cholesterol; LDL = low-density lipoprotein cholesterol; NCEP = National Cholesterol Education Program; RF = risk factor; TG = triglyceride.
able in a small number of institutions and the practice has been controversial. Anecdotal and hypothetical situations arguing both for and against such programs have been presented; however formal evaluations have not been documented.

The purpose of this study was to assess a self-pay, self-referred screening program in which immediate results and consultations are provided to the patient. The intent was to determine the types and prevalence of dyslipidemias newly diagnosed by this program and to characterize the patient population for which this type of healthcare delivery holds promise. The hypothesis was that complementing conventional healthcare delivery pathways by promoting direct-access laboratory testing for dyslipidemias, along with review of other risk factors for coronary heart disease (CHD), will improve diagnosis rates and treatment outcomes for certain patient populations. Conventional medical care delivery, characterized by physician-ordered testing following an office visit, deters some individuals from seeking appropriate care. This study provides the preliminary data needed to formally evaluate outcomes from this type of healthcare delivery.

**METHODS**

A walk-in self-pay screening program for lipid profiles was made available to the general population. The clinical laboratory at the University of California, Irvine Medical Center was opened to patients, without appointment, two mornings a week. The service was minimally promoted; announcements were made through the medical center’s community newsletter on two occasions.

Upon presentation for testing, patients completed a questionnaire addressing family medical history, medical history, aspects of lifestyle including exercise habits, dietary fat estimates, tobacco use, and alcohol use. On the questionnaire, medical history was obtained by subjects’ selection of conditions phrased as high blood pressure, diabetes, heart attack, stroke, high cholesterol, and ‘other’ as a write-in. Family history was phrased similarly with a field to specify which relative(s) was (were) involved. Medical and family histories as reported by the patients were used to assess the number of CHD risk factors and were not confirmed by chart review or physical examination.

A capillary (fingerstick) sample of blood was analyzed on a Cholestech LDX System (Cholestech Corporation, Hayward CA) for total cholesterol, TGs, HDL, LDL, VLDL, and a cholesterol-to-HDL risk ratio was calculated. For cases in which the Cholestech system was unable to provide the complete profile because of analytes exceeding linearity ranges, a venipuncture was offered to the patients for subsequent testing on a Beckman LX20.

Patients were given printed results at completion of testing (approximately 5 minutes) and received a verbal consultation with either a clinical pharmacist experienced in lipid management or the medical director of the laboratory. Approximately 10 to 15 minutes were spent explaining results, addressing risk factors, answering questions about the availability and effects of lipid-lowering medications, and encouraging patients to seek medical care from their primary care provider or specialist. A letter was mailed to each patient re-stating their results and general recommendations; a referral service was offered for those patients without providers.

Laboratory results were interpreted according to National Cholesterol Education Program (NCEP) guidelines. For patients with less than two CHD risk factors, LDL values above 160 mg/dL were classified as undesirable and requiring intervention. For patients with two or more risk factors, the decision level for LDL was greater than or equal to 130 mg/dL; with a history of CHD the decision level was greater than or equal to 100 mg/dL. The decision level for HDL was less than or equal to 35 mg/dL. TGs above 200 mg/dL were classified as undesirable for all patients.

**RESULTS**

A total of 301 patients participated in this program over a two-year period (August 1998 through July 2000). Men (197, 65%) outnumbered women (104, 35%) by almost 2:1. Subjects ranged in age from 26 to 86 years (mean age 57 ± 13). 94% of the subjects had health insurance.

![Figure 1. Distribution of number of known risk factors at presentation for lipid screening](image-url)
Figure 1 charts the distribution of number of risk factors present in the participants. Forty-four percent of the subjects had more than one risk factor for CHD and 5% reported a history of CHD. Using NCEP guidelines, 87 (29%) were found to have LDL values above target, 69 (23%) had triglycerides above recommended levels, and 62 (21%) had HDL values below desirable. Overall, 151 patients (50%) had a condition that would require at least dietary intervention. Categories of lipid disorders found at screening are shown in Figure 2. Nine percent had combined LDL and TG elevations, 20% had elevated LDL only, 14% had elevated TG only, and 7% had low HDL only. Of the subjects for whom lipid findings warranted interventions, 34% were previously undiagnosed. Of the total number of participants, 17% were found to have a previously undiagnosed dyslipidemia for which intervention is recommended by NCEP guidelines. By gender, 49% of the women presenting had no knowledge of a previously diagnosed lipid disorder and 41% of the men were previously undiagnosed (Figure 3). Of the total number of participants, 33% had a previous diagnosis of lipid disorder but were not currently treated to target values.

**DISCUSSION**

No-appointment, self-pay screening as a method of accessing medical care was utilized by a population that in the majority was insured. The types of patient that self-selected for this program included both those with known risk factors for CHD and those without. During consultations, patients cited convenience and immediate consultation as factors inducing them to make use of the service. Patients in whom a lipid disorder had been previously diagnosed but who had ceased to comply with treatment recommendations reported that the availability of this program served to encourage them to return to their providers or seek new ones. Some patients made use of this service to monitor their treatment themselves, reporting that more frequent monitoring was an aid to compliance. However, previous knowledge of a lipid disorder did not seem to be a major factor in determining those patients that self-select for this screening for either men or women; in both groups, roughly half had no previous diagnosis.

Women are characterized as using more healthcare services than men. Of note is that men used this service at a rate of almost twice that of women. For men in particular, this entry point into medical care may effectively capture more patients than the con-
C L I N I C A L  P R A C T I C E :  C H E M I S T R Y

Conventional office-visit approach. Evidently, the rate of diagnosis of lipid disorders would be improved by making this type of program widely available. Whether this approach results in a higher rate of successfully treating dyslipidemia deserves formal study.

CONCLUSIONS
The prevalence of dyslipidemia in this patient group was over 50%. The majority of these, 60 subjects (20%), had an isolated increase in LDL. Elevated TGs accounted for 14%, 9% had combined elevated LDL and TGs, and 7% did not have elevated lipids but had HDL levels below desirable. Of the patients with dyslipidemia, 34% were previously undiagnosed.

A screening program, which increased convenience for patients and provided sufficient education was utilized and paid for by the patients, 94% of whom had health insurance and alternate means of obtaining medical care. The male to female ratio of patients that self-selected for this program indicates that this may be an effective means to increase diagnostic and treatment rates in men.

REFERENCES

Clinical Laboratory Science Announces 2001 Distinguished Author Award Recipients

Recipients of the Clinical Laboratory Science (CLS) Distinguished Author Awards are chosen by CLS readers and editorial board members. Nominations are based upon originality, quality of writing, and relevance and value to the clinical laboratory science profession. The Editorial Board of CLS is pleased to announce the following recipients of the 2001 Distinguished Author Awards:

Clinical Practice Section
Janice Matthews-Greer PhD, Kenneth L McRae MS, Ethylyn B LaHaye MS, and Richard M Jamison PhD for their article, Validation of the Roche COBAS Amplicon System for Chlamydia trachomatis, published in the Spring 2001 issue of CLS.

Reports and Reviews/Research Sections
Mary E Koenn MS, Beverly A Kirby MS, Linda L Cook MD FCAP FASCP, Julie L Hare, Sharon H Hall, Paula M Barry, Cheryl L Hissam, and Stephanie B Wojcicki for their article Comparison of Four Automated Hematology Analyzers in the Fall 2001 issue of CLS.

Focus Section
Teresa S Nadder PhD CLS(NCA) and Michael R Langley CLSp(MB) for their article The New Millennium Laboratory: Molecular Diagnostics Goes Clinical in the Fall 2001 issue of CLS.
Lessons Learned in Student Recruiting

J MICHÈLE STUART, JOANN P FENN

Nationally, clinical laboratory science programs are struggling for student applicants. Major challenges facing the laboratory profession include: 1) low salaries, 2) lack of public awareness, and 3) the myriad of career choices for new graduates. Increasing public awareness and actively recruiting students can overcome one of these challenges. This paper focuses on the successful student recruiting lessons learned at the University of Utah Medical Laboratory Science Program. Specific indicators show increased interest and activity for this program of study.

ABBREVIATIONS: CLS = clinical laboratory science; CLT = clinical laboratory technician; CLS/MT = medical technology/clinical laboratory science.

INDEX TERMS: academic advisor; clinical laboratory scientists; Internet; medical technology; NAACLS; recruiting.

In Laboratory Industry Report, medical technologist/clinical laboratory scientist (CLS/MT) salaries were published based on salary survey data from Salary.com. The report compares salaries for professionals with two to four years experience: medical technologists – $29,877; biotechnology chemist – $41,894; pharmacy clinical research assistant – $38,070; computer scientist – $45,000 to $55,000. Salaries represent a major challenge when attracting science-oriented students into CLS/MT instead of other areas of study.

Low student enrollment, fewer accredited programs, an aging workforce, and skills mobility add to the dilemma of the current national personnel shortage for CLS/MTs. The National Accrediting Agency for Clinical Laboratory Science (NAACLS) reports a significant decrease in graduates of CLS/MT programs - from 5318 graduates in 1983 to 2491 in 1999. Skills mobility makes it difficult to retain graduates in the profession. Biotechnology companies, computer firms, pharmaceutical companies, and research centers 'lure away' our well-trained and knowledgeable laboratory employees. NAACLS also reports a decrease in accredited CLS/MT programs—638 in 1983 to 271 in 1999—a closure of 367 programs. During the two-year period of 1997 to 1999, 40 CLS/MT programs closed. Recent information from NAACLS shows a decrease in 11 programs from 1999 to 2000. Considering that the average age of practicing CLS/MTs is 45 years, the current personnel shortage will worsen during the next 10 to 15 years. The U.S. Bureau of Labor Statistics projects that 5,300 new positions for CLS/MTs and clinical laboratory technicians (CLTs) will be created each year through 2008. In addition, another 4,000 positions will be vacated annually because of retiring CLS/MTs. These projections equate to a need for 9300 new CLS/MTs and CLTs each year, while in 1999 a total of approximately 5000 laboratorians graduated into the work force, including CLS/MTs, CLTs, cytotechnologists, histotechnologists, and histotechnicians.

Two years ago, the Medical Laboratory Science Program (MLS), Department of Pathology, University of Utah School of Medicine, created a 0.5 FTE position to oversee student recruitment and academic advising. With low numbers of applicants and difficulty by area laboratory facilities in hiring qualified CLS/MTs, it became clear that this program had to be more successful with recruitment. This article outlines the lessons learned and the successes of the recruitment process.

The peer-reviewed Clinical Practice section seeks to publish case studies, reports, and articles that are immediately useful, of practical nature, or demonstrate improvement in the quality of laboratory care. Direct inquiries to Bernadette Rodak M S CLS(NCA), Clinical Practice Editor, Clinical Laboratory Science Program, Indiana University, Fesler 409, 1120 South Avenue, Indianapolis, IN 46202-5113. brodak@iupui.edu
DESIGNATING A RECRUITER/Academic Advisor
Selecting the appropriate recruiter/academic advisor is critical. He or she will be the liaison between prospective clinical laboratory science (CLS) students and the program. The selected individual should possess strong multitasking abilities and people skills.

Adding a personal touch is imperative when assisting students during their pre-clinical laboratory educational experience. Students find added value in having a specific person to contact for support, advice, and general program information.

IDENTIFYING THE CURRENT PERCEPTIONS OF THE CLS PROGRAM
Defining, developing, and enhancing a recruitment program is an ongoing process. Success begins by developing a solid foundation. To assess how the program is promoted by the academic community, these focus questions should be asked: 1) How does the office of student recruitment and high school services, the critical liaison between prospective undergraduate students and the institution, present the CLS program information to students? 2) Is the program listed in the University's majors and degrees listing? 3) How accurately does the promotional material represent the program? 4) Is the material relevant? 5) Is the Web site address listed correctly? 6) Does the University General Catalog give up-to-date program information? 7) Are current recruiting documents accurate? The authors found several omissions and mistakes as they answered these questions about their program.

UPDATING AND REVISIONING EXISTING RECRUITMENT DOCUMENTS
One must update the available University information to accurately reflect current program status, and activities. For example, the updated CLS/MT program information should be shared with the office of student recruitment and high school services. Most universities and colleges have similar services that distribute valuable recruitment information not only to students but to parents and school administrators, as well.

If a program does not have a mission statement, it is time to develop one. A mission statement is critical to an organization or program and justifies its existence. When was the last time the mission statement was revised? Is it outdated? Does it reflect the organization's values, beliefs, and philosophy? Does the mission statement reflect the program's purpose? Since developing a mission statement for the University of Utah Medical Laboratory Science program, it has been used in a number of important documents and has been shared with other departments, faculty, laboratory managers, clinical site teaching specialists, and students. It is also displayed in the program's conference room.

RECRUITMENT STRATEGIES
Once the basic information materials have been refined, it is time to begin the recruitment strategies. A variety of approaches should be utilized to promote the educational program, rather than relying on only one marketing/recruiting technique. The following are recruitment strategies to consider:

Internet
A well designed Web site is a valuable recruitment tool. The Internet site conveys messages to large numbers of prospective students quickly and very inexpensively. The Internet puts information in the students' hands instantaneously. Think of the Internet as the program's business card. One can pass out thousands of business cards inexpensively 24 hours a day.

The Internet presence should be open, honest, and direct. The Web page must convey a clear introduction of the program and essential information the searcher can access. Some 'tips' and approaches the authors find useful are:

- Make the site user-friendly and attractive.
- Provide for mobility between Web pages.
- Link to the home page at the bottom of each page.
- Update the site frequently, maintain it for accuracy, and make it easy to access information.
- Register with powerful search engines, e.g., AltaVista, Yahoo, and SearchEd.
- Create a short Web address making the site easily accessible. Allow simple navigation of the site.
- Use hyperlinks to connect to additional academic departments, e.g., biology, pre-medicine, chemistry, other colleges, clinical laboratory sites, and professional organizations, e.g., American Society for Clinical Laboratory Science, American Society of Clinical Pathologists, and American Society of Microbiology.
- Provide an e-mail address on each page, making it effortless for the searcher to request information or ask questions.

After the Web site has established a history, one can gather statistics to determine the number of user sessions, length of user sessions, and dates of high usage (Table 1). This information can be correlated with recruiting plans. For example, an open house or information meeting can be planned around high user dates when students are thinking about the program. At the University of Utah we combine 'high tech with high touch' by holding open house events during mid-March and mid-November which relates to our high student user dates.

Personal student contact
Building personal relationships with prospective students and projecting a welcoming and friendly atmosphere are critical for recruitment. As a recruiter/advisor one should be available for students' questions. We recommend at least one hour per student as adequate advising time. Immediate follow up (within one week) with letters, phone calls, and e-mail should be provided. Staying in touch with students, and selling the program on a 'one on one level' is vital. Students value attention and promptness, and they want to know that the advisor cares about them and their academic progress.
To allow for ease of student follow-up we developed a Recruitment Contact Form (Figure 1). By using the Recruitment Contact Form prospective student databases can be created. With a good database more students receive general information and invitations to attend program activities.

Our experience indicates that prospective students seek and appreciate advice on career-related issues. Individual comments reaffirm the importance of personal student contact. Four examples follow:

“Thank you so much for meeting with Andy and your very nice follow-up letter. Andy was feeling a little lost and overwhelmed with college, but your gracious response and interest in him have really given him new focus and enthusiasm to go on and become a success in CLS!” (Parent of prospective CLS student)

“Thank you for the follow-up letter. Your efforts continue to inspire me to pursue this degree.” (Prospective CLS student)

“Thank you so much for the nice and encouraging letter and thanks so much for your help and care.” (Prospective CLS student)

“Thank you so much. You got back to me so quickly. I appreciate the information.” (Prospective CLS student)

**Personal professional contact**

While the Internet and published materials may initiate interest, personal contact with prospective students and organizations is still one of most productive ways to enhance program awareness. There are a number of ways to make and develop personal contacts.

Developing and maintaining relationships with high school counselors can be as simple as giving lectures or demonstrations at biology or career search courses, attending career fairs, becoming involved in science organizations, e.g., Health Occupations Students of America, arranging for student clinical laboratory visits, and sponsoring weekend workshops for junior and senior high school teachers.

Several recruitment opportunities are usually available on the college/university campus. We have had success by sponsoring open house information sessions in the biology department. This department is a ‘gold mine’ for potential students. Faculty can speak at undergraduate clubs, e.g., a science club, or pre-medicine society, attend freshmen orientation activities, and serve on college/university committees. The focus is to identify and recruit science professionals who are interested in the CLS field.

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**Table 1.** University of Utah MLS Web site statistics

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</tbody>
</table>

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**Figure 1.** University of Utah - MLS Recruitment Contact Form

School of Medicine
Department of Pathology
University of Utah

**MLS Recruitment Contact Form**

Date: _____________________________

Name: _____________________________

Address: _____________________________ Apt. No. ______

City: _____________ State: ______ Zip: _____________

Telephone Number: _____________________________

E-mail: _____________________________

Grade: __ Present School/College: _____________

MT ______ Cytology _____ Master’s Degree ______

How Did You Hear About The MLS Program? _____________________________

Date and Follow-up: _____________________________

Comments: _____________________________

_______________________________

_______________________________

_______________________________

_______________________________
minded students who are not passionately pursuing another major and to let other academic departments know the program exists. The recruiter should regularly meet with college counselors and advisors, and keep them updated on program curriculum and informed about employment opportunities.

Program accessibility
In this age of instant information and communication it is even more important to be accessible. The easier it is for someone to find out about a program the more contacts one will have. To accomplish this important goal of being accessible, it is crucial to use a variety of recruitment approaches. Pre-professional courses can be expanded to overlap other science majors’ requirements, e.g., pre-medical, pharmacy. The program should allow for ease of the application and admission process, offer a flexible admission date, and correlate admission dates with other disciplines. There should be a smooth transition from community or junior colleges through course articulation. Also, when meeting with potential transfer students a prepared articulation course guide for that college is useful.

Public awareness
More exposure brings more contacts. Most programs utilize one or more of the following strategies:
• Advertise in the local city newspapers’ career section.
• Submit articles to local newspapers focusing on careers and the current CLS/MT shortage.
• Advertise your program in high school newspapers.
• Participate in school health fairs at all academic levels.
• Speak at local civic organizations.
• Celebrate National Medical Laboratory Week activities.
• Provide information about your CLS/MT program using post- ers, flyers, brochures, videotapes, and computer presentations.
• Invite former students to promote the program at recruiting activities.
• Consider reminder items such as pens, bookmarks, calendars, brochures, or key chains.
• Include Web address on program envelopes and letterheads.

Employers
There are many benefits when program faculty maintain working relationships with potential employers, and participate in joint recruiting events. By staying current on employment opportunities to present to prospective and current students, the program becomes a valuable resource. More directly, students are informed about employer tuition reimbursement benefits and employment opportunities during and following CLS/MT education.

Students from other disciplines
Students often do not know their exact career track, which is why the successful recruiter will maintain a presence through other programs. To help students make that important career choice, the recruiter can talk with other closely related college programs, e.g., pharmacy, nursing, and biology, to obtain student application lists. Then every student on the list is invited to explore the world of CLS that may seem more attractive to them.

Word-of-mouth
Word-of-mouth is the least expensive way to advertise. Clinical laboratory professionals, students, and other college program advisors can successfully ‘spread the word’ about the CLS/MT program. Our experience indicates that personal student contacts are the most successful form of recruiting and ‘sparking an interest’ in prospective students.

Measurable effects
Our creative recruiting methods resulted in a diverse group of 2001 applicants. The entering 2001 CLS class welcomed two students from pharmacy, one transfer student from a local four-year college, and four transfer students from three Utah community/junior colleges. Student applications increased from 15 in the year 2000 to 26 in 2001. We have not had more than 20 applicants since 1996.

Current Web statistics have increased to over 500 user sessions/week, with an average user session time of 5 minutes 35 seconds (Table 1). The number of students seeking personal advising increased from 15 in 1999 to 79 students in the year 2000 (Figure 2).
CLINICAL PRACTICE: EDUCATION

Over a five-month period the number of students who were declared ‘Pre-MLS Majors’ increased from 15 in April 1999 to 40 students in September 1999 (Figure 2). The number of students requesting program applications for the 2001–2002 school year was 44, an increase of 29 over the 2000–2001 year applications.

CONCLUSIONS

For a program to succeed, students need to know it exists. CLS programs have to work harder at marketing than most health profession programs. A recruiting program should formulate strategies to wisely combine a variety of recruiting tools and marketing approaches. Each recruiting tool contributes to the success of the others. It is important to maintain accurate, up-to-date lists of interested students and to advertise current program activities. Professional contacts, word-of-mouth, and Internet recruiting activities may not work on their own, but together they will make a difference.9

It is our experience that personal student contact has the greatest impact on successful recruiting. As program stakeholders, all faculty members are encouraged to develop and improve recruiting strategies. These strategies are working and generating renewed interest in our CLS program.

REFERENCES

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NIAID Unveils Bioterrorism Research Agenda

The National Institute of Allergy and Infectious Diseases (NIAID) recently released the NIAID Counter-Bioterrorism Research Agenda for CDC Category A Agents, a document describing the Institute’s accelerated research plan for the most threatening agents of bioterrorism. The agenda outlines the research NIAID will undertake to help protect civilian populations from diseases such as smallpox, anthrax, and plague should they be unleashed intentionally by those who wish to do harm. The comprehensive plan includes short-, intermediate- and long-term research goals and describes specifically how bioterrorism countermeasures will be developed for each microbe. The document also contains a copy of the Strategic Plan for Counter-Bioterrorism Research of the NIAID, which provides a general overview of the Institute’s broad plans for attacking the full range of potential bioterrorism pathogens.


NIAID is a component of the National Institutes of Health (NIH). NIAID supports basic and applied research to prevent, diagnose, and treat infectious and immune-mediated illnesses, including HIV/AIDS and other sexually transmitted diseases, illness from potential agents of bioterrorism, tuberculosis, malaria, autoimmune disorders, asthma, and allergies.

An Ethnographic Report of Laboratory Practitioners

Kory Ward-Cook PhD FACB, Laura Culver Edgar MBA, Pamela Frommett MS. American Society of Clinical Pathologists–Board of Registry, Chicago IL

As the initial step in a multi-method approach to conducting a practice analysis of medical technologists (MTs), medical laboratory technicians (MLTs), and phlebotomy technicians (PBTs), these practitioners were observed and interviewed in their practice settings. This ethnographic, i.e., describing the characteristics of a group, report provided the qualitative data for a survey instrument that will be used to validate the performance domains of MTs, MLTs, and PBTs. The method of gathering this data was direct observation (n = 160). Certified medical technologists observed and conducted structured interviews in three geographically diverse regions of the U.S.—California, Florida, and Illinois. Practitioners in these states represented those with and without licensure requirements. California was also chosen because there is licensure of MTs, but not MLTs. The areas observed in 22 different facilities included, but were not limited to the traditional areas of a clinical laboratory, research, industry, and educational institutions. As expected, the tasks performed by these professionals did vary depending on location and type of facility. Although task analyses for these laboratory professionals have been performed in the past, a practice analysis has not. This ethnographic report shows that although MTs perform routine tasks as well as high complexity testing and research, there was still a clear distinction of duties between them and the MLTs. In most cases the PBTs did more than specimen collection. Type of tasks performed differed by region of the country, type of practice setting, and under what conditions the practitioner worked.

A CLT Program’s Assessment of Regional Laboratory Shortages and Salary Comparisons of Allied Health Professionals

Stacey Rohrbaugh MEd, Molly Saunders MEd, Allegany College of Maryland, Cumberland MD

A regional survey was conducted by Allegany College of Maryland, the last public institution in Maryland offering the clinical laboratory technician (CLT) curriculum. The purpose of the survey was to accurately document regional employment and salary data. The response rate to the survey was 60%. The survey data is being used to establish the future workforce needs in our area as well as to compile accurate salary information for recruitment publications. The data are essential for the development of future survival strategies. The survey asked respondents to provide salary data on laboratory professionals as well as other healthcare professionals. The regional survey included personnel categories that were based on the National Occupational Employment and Wage Estimates. This national data shows the CLT to be the lowest paid healthcare employee with an associate degree credential. Many of our local clinical laboratory employees have felt underpaid compared to other regional allied health professionals as well as to the national laboratory salary averages. In regard to the average salary data for the laboratory categories, the survey revealed strong parallels to the 1999 National Occupational Employment and Wage Estimate data as well as to the 2000 ASCP Wage and Vacancy Survey. In regard to the average salary data for the other healthcare salaries, the regional survey revealed the nursing scale to be the highest and the CLT salary to be the lowest as the national data had suggested. The regional survey showed that some institutions have the same salary scale for ancillary services like respiratory, radiology, and the laboratory. In other institutions, the laboratory has fallen behind the scales of similar ancillary service areas. The salary survey also revealed that the regional CLS average is below the national average. In addition to salary information, the respondents were also asked to identify the number of laboratory employees in each category according to age. The regional data confirmed suspicions that the regional laboratory workforce is older. Therefore, a recruitment plan to attract future laboratory personnel is necessary. The information collected in the survey was disseminated to regional laboratories.
Designing Web-based Courses in CLS: A Team Approach

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The concept of offering courses via the Web has become more acceptable as people are challenged with the difficulty of taking time away from work to complete a degree. The World Wide Web, a desirable educational resource that can enhance and augment student learning, is increasingly being used to deliver courses in clinical laboratory sciences (CLS). However, designing and teaching a Web-based course is a new endeavor for most faculty. Faculty need to consider issues such as instructional design, faculty-student interactions, technology skills, and student learning outcomes. To address these issues, the faculty at the UTHSCSA developed Web-based advanced level CLS courses using a team approach. The team consisted of CLS faculty, an instructional development specialist, an instructional program designer, a Web designer, a graphic artist, and an audio-TV staff. This team collaboratively worked out strategies in designing and delivering a template course. Student focus groups helped the team design the template. The first course completed is a case-based course in medical microbiology that incorporates multimedia technology and a Web-based discussion software program for on-line discussion. Pre-implementation student evaluation surveys indicated approval of the course content organization and design, ease of navigation, and appropriate incorporation of images. In conclusion, implementing Web-based instruction in CLS requires shared efforts of a multidisciplinary team. Strategies developed by the team helped address and minimize faculty anxieties regarding telecommunication, faculty-student relation, and student performance in the course.

Developing a Biotechnology Option within a CLT Program

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The clinical laboratory technician (CLT) program at Allegany College of Maryland developed a truly integrated biotechnology option within an existing CLT curriculum. Biotechnology is usually an expensive stand-alone curriculum that competes with CLT programs for students interested in science fields. The biotechnology and CLT skills and knowledge base are similar; therefore, a biotechnology option was designed that shares CLT courses. This combination track allows career flexibility between both curriculums. Graduates of the CLT curriculum can add a biotechnology certificate or degree within one year. The biotechnology graduate can also finish the few missing CLT courses in one year; therefore, a student could finish an associate in applied science degree in both options in three years. The benefits of developing the biotechnology curriculum in this integrated fashion include: cost savings to the college, increased enrollment in clinical laboratory technology courses, infusion of biotechnology techniques into the CLT courses, a mechanism for existing CLT practitioners to complete a biotechnology certificate, and decreased start-up time when biotechnology is started as a program option rather than a new stand-alone program.

Development and Implementation of a Course for Medical Students Focused on Bedside Procedures and Related Clinical Laboratory Testing

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Medical students and residents are required to perform specific bedside procedures involving the collection of specimens for laboratory analysis. Unfortunately, they rarely receive any formal education on the proper technique involved in specimen collection and handling and in the interpretation of laboratory results. Through a collaborative effort between clinical laboratory science and medical school faculty we have developed and implemented a course designed to provide second year medical students the opportunity to perform specific medical procedures and examine and discuss the role the laboratory plays in analyzing patient specimens. A patient case study approach is used to introduce each topic. After reviewing the patient history and physical findings, students learn the appropriate way to prepare the patient for the procedure. The use of universal precautions and aseptic technique is emphasized along with proper collection and transport of specimens such as CSF, blood, urine, and other body fluids. The laboratory analysis of specimens collected by each student from models and cadavers is discussed to ensure that students develop an understanding of what occurs in the clinical laboratory and the impact the quality of the specimen has on patient results. Students have the opportunity to learn to interact with laboratory personnel who can assist them in the interpretation of results and in ordering additional tests. It is anticipated that this course will better prepare future physicians to provide appropriate specimens for laboratory testing and establish a rapport with the clinical laboratory with the ultimate goal of improving patient care.
Development and Implementation of a Model On-Campus Blood Bank Rotation in Response to Declining Clinical Practicum Sites

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In an attempt to address the decreasing opportunities for clinical practicum sites, the 2+2 medical technology/clinical laboratory science program at Old Dominion University modified an existing blood bank practicum course with the goal of providing some of the clinical training on campus. This pilot course was initiated in the fall of 2000 and repeated in the summer of 2001. The on-campus practicum course is structured to offer six weekends of simulated clinical work followed by a two-week rotation at clinical sites. The curriculum plan, evaluation issues, costs, mechanisms for ensuring student competence, and the assessment of the effectiveness of this non-traditional approach to clinical education are addressed. The shortened clinical time resulted in an increase of clinical sites willing to take program students because of the reduced time commitment on their part. The preliminary feedback from both instructors and students has been very positive. Students have indicated that they are very satisfied and instructors have found the students to be “well prepared” and the “program effective”. This on-campus practicum course serves as a model for MT/CLS program faculty to address the decline in clinical practicum sites.

Development of a Survey to Assess the Need for a Baccalaureate-Level Program in Molecular Diagnostics

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Since the late 1980s, the field of molecular diagnostics has evolved into a multitude of sophisticated testing strategies to diagnose inherited, acquired, and infectious diseases. Programs currently available for training individuals competent in molecular diagnostics are limited to post-baccalaureate certificate programs and existing medical technology or cytogenetics programs that have integrated molecular diagnostics into the curriculum. In July 2001, the National Accrediting Agency for Clinical Laboratory Sciences (NAACLS) published the Molecular Essentials as a guideline “for the development and evaluation of molecular diagnostic science and molecular biotechnology programs”. As the first step to program development, the present study aimed to determine the need for a baccalaureate level program in molecular diagnostics in the northeast United States. A 24-item survey was developed to assess: 1) the need for individuals specifically trained in molecular diagnostics; 2) the requirements for training on molecular procedures based on current and future laboratory utilization; and 3) the impact of trends, e.g., insurance coverage, automation, medical advances, and ethical issues, that will impact the future of molecular diagnostics. The survey underwent content validation by three experts in the field of molecular diagnostics and clinical laboratory education, as well as pilot testing. Survey results from a mailing to directors of 247 molecular and cytogenetic laboratories in the United States and Canada (listed in the Association of Genetic Technologists’ Laboratory Directory) will provide direction on the development of a comprehensive educational program in molecular diagnostics.

Diversification of a CLS Program: Meeting Student and Institutional Needs

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During the years 1994 to 2001, 149 CLS/MT programs have closed their doors, with many pointing to the lack of student numbers and the cost-effectiveness ratio. Florida Gulf Coast University’s clinical laboratory science program was designed from its conception with diversification in mind, diversification that fulfilled both student and institutional needs. Student needs are fulfilled by offering a baccalaureate degree in clinical laboratory science, with a choice of three concentrations: clinical laboratory technology, biotechnology/pre-professional and forensic science. The department currently also offers two post-baccalaureate certificate programs in molecular biology and clinical laboratory technology. This year additional certificates in forensic science, pre-medical/pre-professional education, infection control, occupational health and safety, and public health microbiology will be offered. Institutional needs of increasing student enrollment are also fulfilled by giving the department flexibility and stability when there are fluctuations in demand for traditional clinical laboratory science majors. By having diverse choices for students, the department taps into varied student populations including traditional baccalaureate seeking students, articulating associate degree students, and post-baccalaureate students seeking certification and licensure to practice or continued education for entry into professional schools of medicine, veterinary medicine, dentistry, or physical therapy. Other educational opportunities await the criminal justice student desiring coursework in crime scene evidence analysis, and the professional community seeking continuing education and career advancement.
Educating Pre-Medicine Students about the CLS Curriculum and Profession

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The gap between clinical laboratory science practitioners, and their effective use as part of the healthcare team, exists primarily due to inadequate education of the healthcare team members. Primary care providers such as physicians, nurse practitioners, physician assistants, and nurses are unaware of the clinical laboratory scientist’s expertise and ability to contribute to the quality and efficiency of healthcare. This work was done to address and find solutions to this problem by reaching the pre-medicine students enrolled at Indiana State University. Several approaches were taken to this problem including faculty participation in freshman biology laboratories, encouraging use of the Clinical Laboratory Science Special Topics course as a pre-medicine elective, and clinical laboratory science alumni addressing the pre-medicine advisement group within the University. Participation in the freshman biology laboratories resulted in establishing a connection with the pre-medicine majors as well as an increase in undecided majors committing to a clinical laboratory science major. Working with pre-medicine students through the Clinical Laboratory Science Special Topics course was very beneficial to the student and the faculty member with positive results beyond this single course experience. Addressing the pre-medicine advisement group was similar to high school recruitment and yielded no known positive effect. The most effective avenue for educating the pre-medicine students was through the use of the Clinical Laboratory Science Special Topics course as a pre-medicine science elective. Small strides in education, such as this, can result in increased clinical laboratory practitioner involvement with the primary care provider.

Effective CLS Education—Facilitation via Use of International Student Exchange Programs

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The specific problem addressed is that there are virtually no educational experiences that train biomedical/clinical laboratory scientists for the workforce of the future, which will be transnational in nature. Knowledge and work are no longer reserved within national boundaries. Although presently we do not educate biomedical/clinical laboratory scientists internationally, health issues are international in scope. American health science education has suffered from isolation. European health science practitioners have had limited opportunities to learn about the unique American experience. Since knowledge is universal and learning does not recognize international boundaries, students as well as faculty can gain from international exchanges. There have been limited opportunities in the health sciences to engage in exchanges because of the very structured nature of the academic curricula with ultimate control exerted by government ministries; academic accrediting agencies; and licensure boards. Because of these conditions, very few educators have tried to form such linkages. We have established a student exchange program with several European institutions in England and Norway. Here we present our on-going results on these exchanges in terms of the students’ experiences. To date we have hosted more than fifty British and four Norwegian students in this program with a similar number of University of Kentucky allied health students sent in exchange. Students rotated through clinical facilities, attended didactic lectures for academic credit as well as conducted independent research under faculty supervision. These research projects have produced student presentations done locally, nationally, and internationally. We are encouraged with the progress made to date with this program and are actively recruiting more students and institutions to participate in this international initiative.

Entry-Level Skills for CLSs in Arkansas

Martha J Lake EdD, Ruth M Allen PhD, University of Arkansas for Medical Sciences, Little Rock AR

Many forces drive curriculum changes, including new accreditation standards, improvements in technology, changes in student preparation, and shifts in employer expectations. Our profession is one that is under continual pressure to change—now perhaps more than ever before. As our program seeks to adapt our curriculum to present and future needs, we sought to match the entry-level skills to the expectations of our graduates’ future employers. To accomplish this task clinical laboratory managers in Arkansas completed a questionnaire on expected entry-level skills for clinical laboratory scientists. The entry-level skills on the survey were based upon the July 2001 draft of the National Accrediting Association for Clinical Laboratory Sciences’ Essentials for CLS/MT programs. The survey instrument was designed for data tabulation using Remark® software. Descriptive statistics were used to analyze the data generated. Of the 125 surveys returned, 122 were usable for a 22.5% return rate with 95% from either hospitals (34%) or POLs (61%). Small laboratories predominated with 74% of the respondents performing less than 250,000 tests/year. Over 80% of the respondents rated entry-level skills in test performance and interpretation; decision making; quality assurance; application of regulations, and demonstration of ethics and professionalism as important or very important. However, less than half of the respondents rated entry-level skills in new instrument research, development, evaluation, and implementation; financial management; marketing; personnel management; and career planning as either important or very important. Information collected will be...
used to help with planning changes and/or additions to the curriculum in our CLS-level program.

**Integrating Point of Care Testing with Multiple Management Activities**

Patsy C Jarreau MHS CLS(NCA), Louann W Lawrence DrPH CLS(NCA), Louisiana State University Health Sciences Center, New Orleans LA

In response to increased emphasis on management in CLS programs, we recognized the need to develop creative methods to teach management principles. At the same time, an opportunity to perform cholesterol testing at health fairs arose. Strategies to integrate the health fair clinical experience with management projects in a realistic patient care setting were investigated. Point of care testing (POCT) instruments for cholesterol assay were purchased for use at two health fairs. Health fair participation allowed students to interact with patients, gain more experience performing finger sticks, work with classmates as a team, and educate patients about laboratory test results. Prior to the health fair, method evaluation was performed to compare the POCT method with traditional cholesterol testing and cost analysis was used to estimate revenue potential. Students performed workload time studies while setting up workstations and performing tests at the health fairs. Revenue generated was used to help defray costs of reagents and pay students’ expenses for the state professional society meeting. Students learned by realistic application of management techniques through the health fair experience rather than passive classroom lectures. This community outreach project allowed development of confidence in working with actual patients and enhanced professionalism. POCT can be used for multiple management as well as clinical learning experiences and also to generate revenue for student projects. Instrument costs are minimal and easily justified by the benefits achieved. In addition, correlation of multiple management activities with real life clinical experiences exposes students to practical uses of management techniques.

**Investigation of the Application of Learned Generic Skills by CLS/MT Graduates and Practitioners Working in Non-Traditional Jobs**

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During the past decade, the economic climate of corporate mergers and position freezes changed job opportunities for CLS/MT graduates and practitioners. Consequently, individuals were driven from laboratory bench work to alternate jobs within healthcare and other industries. A cohort of CLSs/MTs who considered themselves working in non-traditional jobs (NTJ) were differentiated from a larger sample group of technologists whose career paths were being studied by the ASCP–BOR Research and Development Committee. Individuals were asked whether they applied the following generic skills: problem solving, decision making, troubleshooting, analytical reasoning, data correlation, precision studies, research, quality assessment, communication, teaching, technical writing, computer use, utilization review and supervision to their current NTJ; and whether they learned these skills as CLS/MT students and/or practitioners. Comparisons for both learning and applying the skills were made between graduates of NAACLGS approved CLS/MT programs, and individuals holding other baccalaureate degrees. The response rate was 48% (50/103). Chi square analyses indicated a statistically significant difference ($p < 0.05$) between CLS/MT majors and Non-CLS/MT majors for learning problem solving, correlation, precision, research, analytical reasoning, and troubleshooting. Frequencies for CLS/MT majors learning was higher for all skills except teaching and utilization studies. There were no significant differences between doing the skills in the NTJ and being a CLS/MT major. The results indicate that generic skills learned as CLS/MT students and/or practitioners are applied to a variety of NTJ. Furthermore, CLS/MT majors learned these generic skills at least as well, if not better, than laboratory practitioners with baccalaureate degrees in other areas.

**Involving CLS Students in Establishing and Monitoring Quality Compliance of Point of Care Testing**

Marvin D Bærend MA, Linda A Smith PhD CLS (N CA). Shirlyn B McKenzie PhD CLS (N CA), The University of Texas Health Science Center at San Antonio, San Antonio TX

For many years, point of care testing (POCT) was performed outside the clinical laboratory without oversight. Now, the Joint Commission on Accreditation of Health Care Organizations has focused on control of POCT performed in all areas of the healthcare organization. During their clinical rotations, CLS students have little or no exposure to POCT competency assessment activities. One of our affiliate clinical laboratories had no extra personnel for a scheduled POCT competency assessment activity. Since the senior CLS students at UTHSCSA needed the experience, they participated in the “POCT Competency Assessment Fair”. Student preparation involved lectures, assignments, and audio conferences. They evaluated a rapid group A strep kit and wrote a procedure and competency checklist for the test. During the “Fair”, nursing personnel rotated through various competency assessment stations and teams of students were responsible for verifying competency of the staff in glucose testing, group A strep testing, spun hemocrits, pregnancy testing, and chemical urinalysis. Students also posed questions concerning the procedures, specimen collection, and trouble-shooting. Students indicated it was a worthwhile project and they came to appreciate that not all healthcare work-
Employers, and a certificate program. In 1998, with program re-
double due to connections made with the program, 
enter the program has increased retention. One-third to one-half of 
become employable as phlebotomists and processors while earning 
early and continued contact keeps them con-
provide motivation for coursework. These student employees ac-
table benefits, including tuition reimbursement. One large hospital 
and a rural hospital offer substantial scholarships in exchange for two-
two- to three-year work commitments after graduation. Even 
with financial assistance, some students are unable to enroll full-
time, but are anxious to enroll in clinical laboratory classes. The 
1998 introduction of a clinical assistant certificate that parallels the 
the associate degree has enabled students to get started in the field, and 
become employable as phlebotomists and processors while earning 
an associate degree over a three-year period. The certificate is re-
ponsible for 20% of retained students.

Making Critical Connections to Increase Enrollment

A Janelle Gohn MA CLS (NCA), Cincinnati State Technical and Community College, Cincinnati OH

This session presents innovations that have led to enrollment growth in a clinical laboratory technician (CLT) program during a period of increasing competition for qualified students in health programs and well-documented shortages of laboratory practitioners. Since 1997, the enrollment in this mid-western urban community college program has doubled due to connections made with the program, employers, and a certificate program. In 1998, with program re-
renchment a possibility, the advising of CLT students who needed 
remediation became the responsibility of the Program Chair. Direct 
personal contact is the most effective means to attract and retain 
students. Three-quarters of incoming students need remedial coursework, but the early and continued contact keeps them con-
ected to the program. Connecting students with employers as they 
for two- to three-year work commitments after graduation. Even 
with financial assistance, some students are unable to enroll full-
time, but are anxious to enroll in clinical laboratory classes. The 
1998 introduction of a clinical assistant certificate that parallels the 
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ponsible for 20% of retained students.

Management Competencies Expected of CLSs at Entry Level and Beyond

Susan Beck PhD CLS (NCA), University of North Carolina at Chapel Hill, Chapel Hill NC

This study was undertaken to evaluate the level of education re-
quired to perform tasks related to laboratory management. The 560 
respondents to the national survey included educators, managers, 
and practitioners who reviewed a list of 44 tasks and indicated 
whether the task would be expected of a CLS at entry level, in the 
first three to five years of practice with no additional education, or 
in the first three to five years of practice with additional education. 
The percent of respondents classifying a task in each educational 
category was tabulated. Tasks were further grouped into one of four 
major management functions: laboratory operations, human resource 
management, financial operations, and communications and con-
sultation. All tasks classified as expected at entry-level were labora-
tory operations functions, e.g., routine testing and explaining test 
principles. With three to five years of experience but no additional 
education, expectations in laboratory operations included tasks that 
grew beyond testing and encompassed the total testing process, e.g., 
turn around time studies. In this educational category, graduates 
were also expected to have a high level of communication and con-
sultation skills. The laboratory operations tasks classified as expected 
with three to five years of practice plus additional education in-
cluded specialized testing and tasks that require an understanding of 
the healthcare system, e.g., developing compliance programs. Most 
of the tasks in human resource management and financial manage-
ment areas were in this educational category. Educators can use this 
information to select the appropriate level of instruction for compet-
tencies in the CLS curriculum.
Multiple Site Clinical Experiences for Students in a CLS Program

Carol A Golyski MS CLS(NCA), University at Buffalo, The State University of New York, Buffalo NY

The merging of laboratory services, downsizing of healthcare facilities, introduction of core laboratories, and laboratory personnel shortages have forced clinical education coordinators to seek various clinical sites for placement of students. The medical technology program in the Department of Biotechnical and Clinical Laboratory Sciences at the University at Buffalo assigns students to multiple sites for clinical training. In this program, students rotate at the clinical sites during the second semester of the senior year. The rotation schedule is divided into five blocks of a three-week duration. Students experience one block each of clinical chemistry, microbiology, hematology, and blood banking at different facilities. The fifth block is an elective, and students are placed in a variety of settings based on individual interests. Examples of elective rotations include: a police department laboratory, public health nuclear medicine laboratory, milk cooperative testing laboratory, student health laboratory, and experience in departments of virology, flow cytometry, cytogenetics, or histopathology. During the elective rotation, students also have a phlebotomy experience. Clinical sites affiliated with the University at Buffalo include hospital laboratories, a health maintenance organization laboratory, and a physician group laboratory within the greater Buffalo area. Hospital laboratory sites include government and community hospitals. Students are exposed to a variety of methodologies and automation, and also interact with many laboratorians. This approach is advantageous to both the students and the clinical affiliations. The students have the opportunity to experience different clinical settings and observe differences in organizational structures among the various government and community facilities. Students work on many different laboratory instruments that provide them with a vast technical background that they may not have received if placed in one clinical setting for their entire clinical experience. Students make more contacts for employment opportunities and job references when placed in multiple clinical settings than the student placed in only one setting. Satisfaction with clinical rotations was highly rated by the students upon their exit questionnaire. The clinical laboratories benefit by having students placed in multi-patient settings. During times of personnel shortage, laboratory remodeling, or equipment installation a student will not be placed in a particular clinical setting. This relieves the clinical faculty of teaching duties and allows time to take care of other priorities. Any given clinical faculty has the opportunity to observe the performance of most students in the program. This enables the sites with a large pool of applicants for employment.

Partnering with Industry to Provide a State-of-the-Art, Cost-Effective, CLS Molecular Diagnostics Course

Sharon S Ehrmeyer PhD, Sue Beglinger M S, University of Wisconsin, Madison WI; Rick Salatino M S, Karin Borgh PhD, Promega Corporation, Madison WI

Clinical laboratory science (CLS) programs must provide an up-to-date curriculum to prepare graduates for an ever-changing healthcare environment. To that end, the University of Wisconsin’s CLS program undertook an extensive curriculum revision; part of the revision included a new course in molecular diagnostics. Because of budgetary constraints, we sought industry support. Madison WI is fortunate to be the home of Promega Corporation, a nationally and internationally recognized biotechnology company. As part of its educational mission, Promega was interested in partnering with the University to provide an introductory course in the principles and practices of molecular diagnostics. Discussions were undertaken with the intent to design a model partnership. The CLS program faculty and Promega collaborated to plan appropriate course content and materials, laboratory experiences, exams, and evaluation procedures. The entire 40-hour course is conducted in Promega’s facilities and taught by their MS and PhD scientists. The CLS program pays Promega $250 for each student to offset the cost of reagents used in the laboratory sessions. To date, over 50 CLS students have completed the course. Students benefit from the knowledge and expertise of highly qualified instructors and the opportunity to view an industrial setting first hand. Promega is able to fulfill its educational mission, including its desire to partner with the University. The CLS curriculum includes a state-of-the-art molecular diagnostics course at a cost far less than would be incurred on the University campus. Consequently, this arrangement has proven to be a synergistic "town and gown" collaboration.

Program Recruitment in CLS Programs

Janelle M Chiasera MS, The Ohio State University, Columbus OH

There is a current shortage of our professionals available for employment. Our accredited CLS programs have steadily decreased to almost half over the past ten years resulting in a substantial decrease in the number of our students graduating from our programs and entering the profession. Concurrently, the bureau of labor statistics anticipates the need for 93,000 more CLS professionals by the year 2008, which is 57,000 (17%) more jobs than in 1998. This renders program recruitment a necessity to assure the survival of our programs and the growth of our profession. Surveys were sent electronically (55%) or by mail (45%) to program directors of NAACLS- and CAAHEP-accredited CLS programs across the country to gather information about program recruitment at their institutions. We sent a total of 265 surveys...
and received 152 that yielded a response rate of 57%. Of the re-
sponses, 47% were from university-based programs and 50% were
from hospital-based programs. Ninety-seven percent of respon-
dents stated that they needed to recruit with 84% of them actively
recruiting. Twenty-five percent of those that did recruit had a mean
allotted budget figure of $2000. Of those that do not recruit, over
half reported that they lack funds and personnel to support pro-
gram recruitment. From the data we collected, it will be possible
to identify recruitment efforts that worked best at programs across
the country so that time and money can be focused on only a few
efforts that have proved to be successful at other institutions.

Recruitment Strategies and their Effect on Program
Recruitment in a University-Based CLS Program

Janelle M. Chiaera MS, The Ohio State University, Columbus OH

In general, clinical laboratory science (CLS) programs are under
tough scrutiny by academic administrators because of low enroll-
ment and high cost per student. Many programs over the years
have been closed, and those that remain are at an increased risk for
closure. In an effort to remain viable, our university-based CLS
program has been involved in active aggressive student recruit-
ment for the past year. Our recruitment efforts over the past year
included: campus career days, dormitory presentations, letters to
recent college graduates, campus-wide fliers, mailbox stuffers, e-
mail messages to undecided undergraduates, counselor informa-
tion days, updated website, campus advertisement, and the de-
velopment of a CLS club. In addition, we created a database to moni-
tor the effectiveness of each recruitment effort so we can focus our
energy in the future on those activities that generated the best
return on investment. We found that flyers, word of mouth, and
pre-allied medical profession student letters generated the most
amount of inquiries (24%, 25%, and 17% respectively). Career/
job fairs, undergraduate letters, and table tents generated the least
amount of inquiries (2%, 2%, and 1% respectively). Therefore,
our program will focus primarily on a combination of flyers, word
of mouth, and pre-allied medical profession student letters as our
source of recruitment activities.

Report on the State of Washington Laboratory Per-
sonnel Shortage Workgroup

Dave Abbott, Linda Briewick, Cynthia Hamby, Ann O’Neill, Claudia
Steen, Mary Lampe, University of Washington, Seattle WA

A laboratory personnel shortage workgroup (WLPSW), composed
of representatives of laboratory professional organizations, train-
ing program directors, and members of the Department of Health
Advisory Council, was formed in September 1999. The goal of
the workgroup was to determine if a shortage of clinical labora-
tory personnel exists, the extent of the shortage, and the actions to
address any shortage. A survey of laboratory managers found an
average vacancy rate of 3.7% for CLS/MTs and 8.9% for CLT/
MLTs. The six training programs reported declining numbers of
applicants. A targeted mailing was sent to all high school coun-
seors and science teachers describing the clinical laboratory profes-
sions and a questionnaire assessing their knowledge of the profes-
sions. Counselors and teachers were invited to an educational ses-
sion at the Northwest Medical Laboratory Symposium. A website
for the clinical laboratory profession was established,
www.labcareers.org. A statewide salary survey was conducted to
obtain current salary information. Recruitment materials includ-
ing posters and flyers were updated. An article was written for the
state professional society newsletter describing how laboratories
can become a training site for an educational program. To follow
up on these activities, a new survey of training programs showed
that enrollments increased by approximately 65%. There were also
more facilities interested in becoming clinical sites for the training
programs. In summary, the WLPSW has successfully increased
knowledge about the clinical laboratory profession and is begin-
ing to reverse the laboratory personnel shortage.

The Sensitivity and Specificity of the Allied Health
Professions Admissions Test

Nancy Goodyear PhD, Mary F Lampe PhD, University of Wash-
ington, Seattle WA

The purpose of this study was to set criteria for the Allied Health
Professions Admissions Test (AHPAT) (The Psychological Cor-
poration, San Antonio TX) to be used as predictors of success in
the University of Washington Medical Technology Program
(MTP). The sensitivity and specificity of several cutoff schemes
were calculated for 183 students admitted to the MTP between
1990 and 2000. Failure was defined as first-try failure on the BOR
or dismissal from the MTP for low scholarship. The cutoff schemes
consisted of combinations of the following limits: AHPAT total:
100 or 150; Verbal subsection: no cutoff or 5; Biology subsection:
no cutoff or 10. True negative was defined as a failure that fell
below the cutoff, false negative as a success below the cutoff, true
positive as a success above the cutoff, and false positive as a failure
above the cutoff. The scheme that primarily eliminated the fewest
successes (sensitivity) while secondarily identifying the most fail-
ures (specificity) was a requirement where the applicant must ex-
cede two of the following three criteria: AHPAT total: 150; Biol-
ogy: 10; and Verbal: 5. Sensitivity for this cutoff was 100%, and
specificity was 26.7%. When applied to the database, no students
who succeeded would have been eliminated, while five of 13 fail-
ures would have been admitted. While other criteria would have
eliminated more of the failures (higher specificity), they would
have also eliminated some of the successes. These new criteria were
applied for the first time for applicants for Autumn Quarter, 2002.
Statewide Management Symposium for CLS Students

Elaine M Keohane PhD CLS(NCA), H Jesse Guiles EdD CLS(NCA), Bernadette Bekken CLS(NCA), University of Medicine and Dentistry of Newark NJ; Janet Hiler Bowman MEd, Augusta Medical Center, Fishersville VA

Knowledge of laboratory management, laboratory utilization, the healthcare environment, and professionalism is essential for today's clinical laboratory science (CLS) graduates. Typically, this content is delivered in individual programs at various levels of quantity and quality due to the difficulty in identifying content experts who are available to teach relatively small groups of students in each program. In an effort to present up-to-date and relevant content in these areas in an efficient, cost-effective, and high quality manner, CLS educators in New Jersey and in Virginia developed two to three day management symposia that were conducted for all the CLS students in each state. The topics were approved by the faculty of the various programs and included human resource management; laboratory finance including costs, budgets and reimbursement; laboratory accreditation, laws and regulations; and trends in healthcare and laboratory practice including managed care. Experienced faculty, highly recognized at the state and national level, were identified to serve as presenters as well as role models. Participation among the CLS Programs in each state was high, and the feedback from students and faculty was excellent. An added benefit was the input of faculty from various programs into the content and the opportunity for student interaction and networking across programs. Plans are to continue this activity into the future.

TECHNOLOGY DEMONSTRATION

Course Management Computer Programs: Comparison of WebCT with Prometheus

Joyce A Bulgrin MSA, Susan L Raab EdD, University of Wisconsin/Stevens Point, Stevens Point WI

CLS instructors are continuously challenged to provide additional educational experiences with minimal increases in funding for faculty positions. The search for innovative resources is essential. Course management programs represent a means to improve instructor efficiency while enhancing student-learning. A variety of Web-based course management computer programs exists. Most of the programs provide components that allow students to access course materials on a 24/7 basis, communication opportunities among students and faculty, links to other Web sites, student assessment with immediate feedback, and grade book management. A problem arises in deciding which of the programs may be most appropriate to meet the needs of instructors and students. Two computer management programs currently available to educators include WebCT and Prometheus. The integration of these programs into the laboratory course curriculum will be demonstrated. Interaction with each of these two programs will allow participants the opportunity to compare functional components of the programs and to identify advantages and disadvantages of each program. Individuals will gain a foundation upon which to make more informed decisions concerning course management programs.

Reaching the Rural Frontier and Beyond... MED Net: Connecting Outside the Box

Mary Banman CLS (NCA), Susan Kuntz MS, University of North Dakota, Grand Forks ND

The CLS program at the University of North Dakota School of Medicine and Health Sciences encompasses four states, eight higher education institutions, and over 40 medical centers. Continuing education opportunities currently provided span a global spectrum, reaching across North America to as far as the Middle East. Opportunities exist for undergraduate and graduate students and also the adult learner. MED Net (Medical Education and Distance Learning via the Internet) was created primarily to offer continuing education opportunities to the rural professional. However, additional benefits include enhanced quality of instruction, improved communications, and increased program efficiency. MED Net is a complete Internet access system in a box. It consists of a metal carrying case, a high-speed laptop, and a video conferencing camera. Connectivity options allow the user to connect via telephone, DSL, Ethernet, or wireless router. An internal firewall provides facility protection. The system is completely mobile and weighs less than 35 pounds. CLS program faculty in conjunction with the UND SMHS Medical Instructional Technology faculty have developed a curriculum designed to meet the needs of the
distant learner. MED Net allows for asynchronous learning yet provides face-to-face communication opportunities, which further enhances the learning process.

**Web-Enhanced Instruction for Laboratory Sciences**

**Cheryl Jackson-Harris MS CLS**, California State University, Dominguez Hills CA; Carol Moeller MS CLS, David Dietzel CLS, Cedars-Sinai Medical Center, Los Angeles CA

Our purpose in demonstrating this technology is to exemplify the advantages of integrating laboratory instruction via computer utilization. Web-enhanced instruction is incorporated into the clinical component of the CLS student program. This direction is achieved by posting objectives on our internal Web site (http://www.cedars-sinai.edu/pathology/MTCourseDescription.htm), with relevant Web pages and images linked to specific learning task objectives. Students are directed to Internet sites that offer both image (photos and graphics) and explanatory (primarily text) information. These Web pages may be authored inside and outside of our respective institutions (the latter widening our scope of instruction). In the laboratory, students can access voluminous material directly related to the bench procedure at hand, using already-in-place bench top computers without having to concern themselves about amassing a large library of contaminated texts and other learning materials. Students and instructors also may interact at any time in a dedicated computer discussion room, enabling students and licensed technologists alike to learn from each other's questions and answers. Likewise, students can be outside of the hospital or classroom, and can greatly expand their information by accessing computer-based material. The goal of this type of enhanced instruction is to enable a closer, more comprehensive connection between the practical and the didactic aspects of laboratory learning. Exercises are dispersed throughout allowing the instructor to assess learning by the students' ability to demonstrate specific performance skills, evaluate data, and apply cognitive knowledge relevant to the skill.

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**ASCLS ANNUAL MEETINGS INFORMATION**

Forms for submitting program proposals and abstracts for future ASCLS Annual Meetings will be available on the ASCLS Web site under meeting information. The Web site address is: http://www.ascls.org/
<table>
<thead>
<tr>
<th>Time</th>
<th>Workshops</th>
<th>Governance</th>
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<tbody>
<tr>
<td>8:30 am – 10:00 am</td>
<td><strong>W01</strong> Intestinal Protozoa: What’s New, What’s Different, What’s Possible with Collection, Ordering &amp; Identification Options MIC</td>
<td>IAMLT Council (Continued from Monday) ASCLS Board of Directors</td>
</tr>
<tr>
<td>10:00 am – 10:30 am</td>
<td><strong>W02</strong> Una Vista global y actualizada de la Parasitologia MIC</td>
<td><strong>W03</strong> Hematology Instrumentation: Technology &amp; Interpretation ADM, GEN, HEM</td>
</tr>
<tr>
<td>10:30 am – 12:00 pm</td>
<td><strong>W04</strong> Risk Management 2002 ADM, CON, GEN</td>
<td><strong>W05</strong> Abnormal Morphologic Manifestations Encountered in the Hematology Laboratory HEM</td>
</tr>
<tr>
<td>12:00 pm – 1:00 pm</td>
<td>Break</td>
<td>IAMLT Council ASCLS Board of Directors</td>
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<tr>
<td>1:00 pm – 2:30 pm</td>
<td><strong>W01</strong> (Continued)</td>
<td><strong>W04</strong> (Continued) ASCLS Committee Chairs Orientation IAMLT GAD-Open Forum (1:00 pm – 4:00 pm)</td>
</tr>
<tr>
<td>2:30 pm – 3:00 pm</td>
<td>Break</td>
<td><strong>W05</strong> (Continued) ASCLS CLS Consulting Editors ASCLS CEAC ASCLS PA.C.E.® Committee ASCLS PAC Board ASCLS Presidents’ Seminar ASCLS Student Orientation</td>
</tr>
<tr>
<td>3:00 pm – 4:30 pm</td>
<td><strong>W01</strong> (Continued)</td>
<td>ASCLS Abstract Review Committee ASCLS Awards Committee ASCLS Educational Affairs Committee ASCLS Govt. Affairs Committee ASCLS Nominations Committee ASCLS Scientific Assembly Chairs</td>
</tr>
<tr>
<td>4:30 pm – 6:00 pm</td>
<td><strong>W01</strong> (Continued)</td>
<td>ASCLS Bylaws Committee ASCLS Judicial Committee ASCLS Professional Affairs Committee ASCLS Publications Committee</td>
</tr>
<tr>
<td>6:00 pm – 7:30 pm</td>
<td><strong>W01</strong> (Continued)</td>
<td>Alpha Mu Tau Board</td>
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<tr>
<td>7:00 pm – 8:30 pm</td>
<td><strong>W01</strong> (Continued)</td>
<td><strong>W03</strong> Hematology Instrumentation: Technology &amp; Interpretation ADM, GEN, HEM</td>
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<tr>
<td>7:00 pm – 9:30 pm</td>
<td><strong>W01</strong> (Continued)</td>
<td><strong>W03</strong> Hematology Instrumentation: Technology &amp; Interpretation ADM, GEN, HEM</td>
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<td>Time</td>
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<tr>
<td>8:00 am – 10:30 am</td>
<td>Opening Ceremony, Awards and Keynote Presentation:</td>
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<tr>
<td>11:00 am – 1:45 pm</td>
<td>Shuttles to Convention Center</td>
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<tr>
<td>1:45 pm – 3:15 pm</td>
<td>Synthetic Oxygen Carriers I/H</td>
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<tr>
<td>3:15 pm – 5:00 pm</td>
<td>The Global Movement Toward Quality Systems ADM, EDU</td>
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<tr>
<td>3:30 pm – 5:00 pm</td>
<td>Clonar o no Clonar - Esta no es la única interrogante GEN, VIH</td>
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<td>5:00 pm – 5:30 pm</td>
<td>Return shuttles to Sheraton World</td>
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<tr>
<td>5:30 pm – 7:30 pm</td>
<td>U.S. State Legislative &amp; Licensure Issues GEN, PSD</td>
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<tr>
<td>7:00 pm – 8:00 pm</td>
<td>ASCLS Presidents’ Council &amp; Issues Update</td>
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<tr>
<td>8:00 pm – 11:00 pm</td>
<td>Presidents’ Reception and Welcome Mixer</td>
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# THURSDAY

**Thurs., August 1, 2002**

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
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<tbody>
<tr>
<td>7:00 am - 8:00 am</td>
<td>Governance ASCLS 2003 CLEC Planning Committee</td>
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<tr>
<td>7:00 am - 9:00 am</td>
<td>ASCLS Forum for Concerns of Minorities Business Meeting and Breakfast</td>
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<tr>
<td>8:00 am</td>
<td>Shuttles to Convention Center</td>
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<tr>
<td>8:30 am - 10:00 am</td>
<td>#14 Editing &amp; Publishing Your Organization's Newsletter PSD</td>
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<tr>
<td>8:30 am - 10:00 am</td>
<td>#15 CLT to CLS: On-line Articulation EDU</td>
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<tr>
<td>8:30 am - 10:00 am</td>
<td>#16 Cell-Dyn Hematology Users Group HEM</td>
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<tr>
<td>8:30 am - 10:00 am</td>
<td>#17 (8:45 - 10:00) The Clinical Laboratory: Abettor of or Defender Against Bioterrorism ADM, BUL, GEN, MIC</td>
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<tr>
<td>10:00 am - 1:30 pm</td>
<td>Dedicated Time for Exhibits</td>
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<tr>
<td>12:00 pm - 1:00 pm</td>
<td>Administrators/Industry/Consultants Lunch Men's Lunch</td>
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<tr>
<td>1:45 pm - 3:15 pm</td>
<td>#18 Routine Genital Cultures: A Test of the Past MIC</td>
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<tr>
<td>1:45 pm - 3:15 pm</td>
<td>#19 Implementation of a Coagulation Instrument/Reagent System in a Multiple Hospital Network HEM</td>
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<tr>
<td>1:45 pm - 3:15 pm</td>
<td>#20 Human Genome Project Issues &amp; Implications GEN</td>
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<tr>
<td>1:45 pm - 3:15 pm</td>
<td>#21 Disaster Preparedness: The 2002 G8 Summit Experience ADM, GEN, VIH</td>
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<tr>
<td>3:15 pm - 3:30 pm</td>
<td>Break</td>
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<tr>
<td>3:30 pm - 5:00 pm</td>
<td>#22 La comunicación involucra algo más que un proceso de dos direcciones ADM, GEN</td>
</tr>
<tr>
<td>3:30 pm - 5:00 pm</td>
<td>#23 Products &amp; Practices for Needlestick Safety ADM, GEN</td>
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<tr>
<td>3:30 pm - 5:00 pm</td>
<td>#24 Common College of American Pathologists (CAP) Laboratory Deficiencies ADM, CON, GEN</td>
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<tr>
<td>3:30 pm - 5:00 pm</td>
<td>#25 Mycology: From Bench to Bedside MIC</td>
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<tr>
<td>5:00 pm - 5:30 pm</td>
<td>Return shuttles to Sheraton World</td>
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<tr>
<td>5:30 pm - 6:30 pm</td>
<td>ASCLS Scientific Assembly Meetings:</td>
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<tr>
<td>6:30 pm - 7:30 pm</td>
<td>T'nT Boot Scootin' Boogie Bash</td>
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<tr>
<td>7:30 am - 8:45 am</td>
<td>#26 Using Outcomes Measurement to Reduce Medical Errors and Improve Patient Safety - Part I</td>
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<td>#27 Dade Behring Chemistry Users Group BUL</td>
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<tr>
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<td>#28 Building, Enhancing and Marketing Your Organization’s Web Site ADM, EDU, GEN, PSD</td>
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<tr>
<td>9:00 am - 10:00 am</td>
<td>#29 Using Outcomes Measurement to Reduce Medical Errors and Improve Patient Safety - Part II</td>
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<td>#30 Nutritional Assessment: What the Dietitian Needs From the Laboratory BUL, HEM, GEN</td>
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<td>10:00 am - 10:15 am</td>
<td>Break</td>
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<tr>
<td>10:15 am - 11:45 am</td>
<td>#31 DNA Fingerprinting GEN, I/IH</td>
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<td>#32 Membership Development - Integrated Marketing: The Profession is the Message PSD</td>
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<tr>
<td>11:45 am - 12:30 pm</td>
<td>Roundtables</td>
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<tr>
<td>12:30 pm - 2:00 pm</td>
<td>R01 Continuing Education Provider: An Opportunity for Clinical Laboratory Scientists ADM, EDU</td>
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<td>R02 Interdisciplinary Clinical Professional Development Seminar EDU</td>
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<td>R03 Emergence of Clinical Research in the Clinical Laboratory Sciences EDU, GEN</td>
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<td>R04 Web-Assisted Clinical Chemistry BUL, EDU</td>
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<td>R05 Development of a Master’s Program in Diagnostic Molecular Pathology ADM, EDU, GEN</td>
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<td>R06 CLIA 88 y Politicia de Pago de Medicare en Puerto Rico y su Impacto en la Practica del Tecnologo Medicico ADM, GEN</td>
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<td>R07 How to Prepare Scientific Materials for Publication in CLS EDU, GEN</td>
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<td>R08 Genetic Based Testing in the Traditional Clinical Laboratory Science Fields EDU, GEN</td>
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<td>R09 Anthrax Outbreak: The Florida Department of Health’s Response MIC</td>
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<td>R06 Development of a Master’s Program in Diagnostic Molecular Pathology ADM, EDU, GEN</td>
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<td>R07 Leadership Development: Preparing &amp; Mentoring Future Leaders PSD</td>
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<td>2:00 pm - 2:15 pm</td>
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<td>2:15 pm - 3:45 pm</td>
<td>R03 Emergence of Clinical Research in the Clinical Laboratory Sciences EDU, GEN</td>
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<td>R07 Leadership Development: Preparing &amp; Mentoring Future Leaders PSD</td>
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<td>IAMLT Farewell Banquet and Alpha Mu Tau Fraternity Dinner</td>
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<tr>
<td>8:30 am - 10:00 am</td>
<td>#44 Moving To Competency-Based Certification ADM, GEN</td>
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<td>#45 Defining ISO Standards ADM, GEN, I/H</td>
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<tr>
<td>10:00 am - 10:30 am</td>
<td>Break</td>
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<tr>
<td>10:30 am - 12:00 pm</td>
<td>#46 Comparisons and Contrasts in Exotic Animal Hematology GEN, HEM</td>
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<tr>
<td>12:00 pm - 2:00 pm</td>
<td>Break</td>
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<tr>
<td>2:00 pm - 5:00 pm</td>
<td>Break</td>
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<tr>
<td></td>
<td>IAML General Assembly of Delegates ASCLS House of Delegates</td>
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</table>
CONCLUSION: Those tested for several other combinations.

RESULTS: For these two systems, local on-site calibration was performed using photo-optic and mechanical ISI manufacturer values were used for these two systems. Local on-site calibration was performed using frozen plasma calibrators to determine ISI values for each thromboplastin. Post-calibration, 95 patient samples were assayed for each reagent/instrument system combination using the manufacturer ISI and the local calibrated ISI to determine the INR result.

PATIENTS: Patients from whom samples were obtained included five with a lupus anticoagulant, 30 on heparin therapy, and 60 on coumadin therapy.

OBJECTIVE: This study reports the feasibility of a new method to locally calibrate ISI of thromboplastin using the mechanical STA automated coagulation analyzer (Diagnostica-Stago Inc.) and two photo-optic coagulation analyzers, the BCS (Dade-Behring) and CA-540 (Sysmex).

Design: Neoplastine Cl+ (Cl+) (Diagnostica-Stago Inc); Thromboplastin C+ (TC+); Thromborel S (TRS); and Innovin (I) (Dade-Behring) were used in this study. A mean normal PT (MNPT) was determined for each reagent/instrument combination using samples from 25 normal individuals. Manufacturer instrument specific ISI values were not available for the STA with TC+, TRS and I. The CA540 had no ISI value for Cl+ and the BCS system had no manufacturer assigned ISI values for TC+ and I; generic photo-optic and mechanical ISI manufacturer values were used for these two systems. Local on-site calibration was performed using frozen plasma calibrators to determine ISI values for each thromboplastin. Post-calibration, 95 patient samples were assayed for each reagent/instrument system combination using the manufacturer ISI and the local calibrated ISI to determine the INR result.

RESULTS: Differences between manufacturer versus local calibrated ISI ranged from 0.9% to 18.9% for normal sample INRs and from 0.8% to 16.4% for patient sample INRs. The number proportion of patient specimens with clinically significantly different INR values (>10.0% difference) ranged from zero for (or proportion) of patient specimens with clinically significantly different INR values (>10.0% difference) ranged from zero for several reagent combinations to more than half (or >50.0%) of those tested for several other combinations.

CONCLUSION: Our results indicated that by locally calibrating ISI values, each laboratory may eliminate variability and guesswork between different reagent/instrument systems for ISI values when performing PT/INR assays and potentially improve the clinical accuracy of their patients’ PT/INR results.

ABBREVIATIONS: CI+ = Neoplastine Cl+; INR = international normalized ratio; IRP = international reference preparation; ISI = international sensitivity index; MNPT = mean normal prothrombin time; OAT = oral anticoagulant therapy; PIVKAS = proteins induced by Vitamin K antagonists; PT = prothrombin time; TC+ = Thromboplastin C+; TRS = Thromborel S; WHO = World Health Organization.

INDEX TERMS: international normalized ratios; international sensitivity index; local calibration; prothrombin time; reagent/instrument combinations.

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Although the PT is the principal assay for monitoring patients undergoing oral anticoagulant therapy, there are many variables such as proper sampling and testing techniques that can have an effect on the accuracy of the assay. Probably the most important of these variables is the thromboplastin reagent selected for the assay. Commercial thromboplastins vary widely in their sensitivities to warfarin. Instrument choice can also play a significant role in the performance of the PT assay. With so many variables, clinicians can be easily confused when having to compare patient results from a variety of laboratories using different thromboplastin reagent/instrument combinations. High sensitivity thromboplastin reagents lead to greater prolongation of the PT time results than assays performed with a lower sensitivity. Thus, a patient may have a PT of 14 seconds with a low sensitive thromboplastin and a PT of 18 seconds with a more sensitive thromboplastin. Therefore, a patient monitored with insensitive thromboplastins would require a higher dosage of warfarin to result in an appropriate prothrombin time ratio.1,2,3

In 1977, the World Health Organization (WHO) recognized the difficulty of comparing PT times performed with different thromboplastins and introduced a thromboplastin that was to serve as an international reference preparation. Then in 1983, the WHO described a model for PT standardization based on a method in which the PT value is reported as an international normalized ratio (INR). Theoretically, the INR is the PT that one would obtain if the assay were performed using a WHO primary reference with
an ISI value of 1.0. The ISI compares the sensitivity of a given thromboplastin to an international reference plasma that has been calibrated using the WHO reference plasma. The INR is calculated using the formula:

\[
\text{INR} = \frac{\text{Patient PT} \times \text{ISI}}{\text{Mean Normal PT}}
\]

The advantage of the INR method of reporting is that the patient’s result is compensated for between differing thromboplastins or instruments. While thromboplastins now have ISI values that may range from 0.9 to 3.0, as assigned by the manufacturer, the patient values can be compared using the calculated INR. The INR allows for a better regulation of the dosage of oral anticoagulation.2

Concerns regarding the INR system have concentrated primarily on the assignment of ISI values, method or instrument variations, and calculation errors. ISI values appear to be instrument-dependent. The ISI is used exponentially in calculating the INR and, therefore, any error in this number may result in significantly inaccurate values. INR variability, which may occur when there exists significant differences in ISI values from reagents with low ISI values versus reagents with high ISI values, has been reported.4-10 These differences could result in inappropriate management of patients on oral anticoagulant therapy (OAT) with possible dire consequences of thrombotic or bleeding episodes.

The individual variability between reagent/instrument test systems suggests that each laboratory may need to calibrate its own PT/INR test systems. One method that has been somewhat reliable is the WHO protocol. The method uses an International Reference Preparation (IRP) of thromboplastin with the manual (tilt-tube) method with 20 fresh samples from normal subjects and 60 fresh samples from normal subjects on OAT, performed in quadruplicate. Obviously this is not a practical method for many clinical laboratories due to lack of practice with the manual procedure or the unavailability of so many patient samples.11,12

Local system calibration using well characterized plasma calibrants may be a practical alternative to the WHO protocol. However, until recently there have been no FDA clearedibrator plasmas commercially available. Controversy exists regarding the use of artificially depleted vitamin-K plasmas or actual OAT plasmas. Results with these plasmas in various investigations have given disparate results, presumably due to the influence of proteins induced by Vitamin K antagonists (PIVKAS).13-15 Lyophilization may also cause changes in plasma and affect results in coagulation assays.16,17 This effect may vary for different reagent/instrument systems. In addition, there are many investigators who recommend using large plasma pools instead of individual patient plasmas.12 One manufacturer uses 20 artificially depleted plasma calibrators prepared from normal donors that cover the OAT therapeutic range.

This is a one-day protocol that uses the local reagent/instrument combination with the PT assays being performed in quadruplicate and analyzed with orthogonal regression analysis.18 This protocol may not take into account the day to day variability seen in a laboratory setting.

Recently, the idea of frozen calibration plasmas for local calibration of ISI values has been introduced. Precision BioLogic (Dartmouth NS Canada) has produced an ISI calibration set consisting of five frozen OAT frozen plasmas and one frozen normal plasma that have been assayed against a standard WHO IRP of human recombinant thromboplastin (RTF/95).11,19 In a study with 122 participating laboratories the normal frozen reference plasma gave an INR of 1.06. The frozen OAT calibrators had a range of 1.72 to 4.62. The INR results of the normal plasma and the OAT calibrator plasmas encompassed the four therapeutic categories used in OAT (<2.0; 2.0 to 3.0; 3.1 to 4.5; and >4.5).

In a study sponsored in part by Dade-Behring Inc (Deerfield IL), we evaluated the frozen plasma calibrants to determine if local calibration of ISIs for a variety of thromboplastins could be simplified to improve correlation of INR results between different reagent/instrument combinations.

**MATERIALS AND METHODS**

**Instrumentation:** electro-mechanical STA automated coagulation analyzer (Diagnostica-Stago Inc, Parsippany NJ) and two photometric coagulation analyzers, the BCS (Dade-Behring, Deerfield IL) and CA-540 (Sysmex, Kobe Japan).

**Thromboplastins:** Neoplastine CI+ (CI+) (Diagnostica-Stago Inc), Thromboplastin C+ (TC+) (Deerfield IL), Thromborel S (TRS) (Deerfield IL), and Innovin (I) (Dade-Behring, Deerfield IL). Thromboplastin CI+ is a rabbit-brain source thromboplastin as is TC+. TRS is a human placenta source. I is human recombinant thromboplastin.

All of the specimens for this study were obtained after informed consent was obtained from each subject. All of the patient samples for this study were obtained previously and stored in the following manner. An atrumatic venipuncture was performed using a Vacutainer collection system with 3.2% sodium citrate in a 9:1 blood to anticoagulant ratio on each test subject. Platelet-poor plasma was obtained by centrifuging each specimen at 2500g for 15 minutes. The specimens were aliquoted into cryovials and stored at approximately −70 °C until ready for testing. Just prior to testing, the samples were thawed rapidly at approximately 37 °C. A mean normal PT (MNPT) was determined for each reagent/instrument combination by assaying 25 normal individuals with no known coagulation abnormalities and who were not on any medication that could influence their coagulation system. The samples from normal donors were assayed three separate times, with each
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reagent/instrument system using three different sets of reagents for each combination, over a three-day period. Manufacturer instrument specific ISI values were not available for the STA with TC+, TRS, and I. The CA540 had no ISI value for CI+. The BCS system had no manufacturer assigned ISI values for TC+ and I. Generic photo-optic and mechanical ISI manufacturer values were used for these two systems. The MNPT was determined using a geometric mean. Currently Dade-Behring Inc can now furnish instrument specific ISI values for all of their own reagent/instrument combinations.

A local on-site calibration to determine international sensitivity index (ISI) values for each thromboplastin was performed using a protocol for frozen ISI calibration plasma sets from Precision BioLogic (Dartmouth NS Canada). Calibrators were run in duplicate for five individual runs, with freshly diluted reagents on each reagent/instrument system. A total of 60 PT data points (10 normal and 50 abnormal) for each reagent/instrument combination were derived. The results were sent to Precision BioLogic, which used orthogonal regression analysis to determine the local calibrated ISI of each system.

After the local ISI results had been determined, we assayed 95 patient samples on each reagent/instrument system using the manufacturer ISI and the local calibrated ISI to determine the INR result. The patient samples included five from subjects with a lupus anticoagulant, 30 from heparinized subjects, and 60 from coumadin patients. We then compared the PT/INR results using the manufacturer ISI to the INR results achieved using the locally generated ISI values.

RESULTS
Table 1 shows the geometric mean results of each reagent/instrument combination MNPT. The times ranged from 8.9 to 13.9 seconds. In Table 2 it is interesting that the percent difference in the ISI did not directly correlate to the sensitivity of the thromboplastin with each reagent/instrument combination. The differences in INR means ranged from 0.9% to 18.9%. We note that some of the reagents were made for mechanical systems while others are directed towards photo-optic instruments. The local ISI calibration is designed to correct the reagent/instrument generated bias that the INR calculation is supposed to correct. Table 3 shows that there can be clinically significant mean differences (>10.0%) between INR results using manufacturer ISI values versus locally calibrated ISI results. The last column (Results >10.0% difference) expresses the number of patient samples (n = 95) that had INR values of >10.0% difference between the different ISI generated values. It was noted that the TRS thromboplastin gave no values that had a >10.0% difference in the subject values with any instrument. Some other reagent/instrument combinations had 64.9% of the patient samples with a >10.0% difference between the vendor assigned ISI and a locally calibrated ISI.

DISCUSSION
The accuracy and precision of the INR is dependent on the PT assay and the ISI of thromboplastin. Other researchers have noted that, since the ISI is the exponent of the INR equation, the higher the ISI assigned to thromboplastin the greater the imprecision of the INR as a result of the mathematical outcome. The large difference in assigned ISI values is one variable that influences the poor correlation seen in reagent/instrument combinations. Thromboplastins with an ISI less than 1.20 produce a wider range of values in the PT and PT ratio. Consequently, the precision of the INR is improved. Since the calculation of the INR requires using the ISI exponentially, the farther the ISI value is above 1.0, the greater any system inaccuracies will be magnified in terms of INR. Manufacturer assigned ISI not specific to the local reagent/instrument set-up may introduce even more inaccuracy. Instrumentation can also greatly influence the INR values. In our institution we saw serious clinically significant differences in INR results between photo-optic and mechanical reagent/instrument systems using manufacturer generated ISI values particularly at the upper limits of the OAT INR range (>3.0). This could lead to serious errors in OAT treatment decisions. Table 4 demonstrates the large INR differences that resulted for selected patient samples between different reagent/instrument combinations. Because manufacturers provide limited guidelines for all instruments assigned ISI values, the laboratory should be able to validate INR results by performing local on-site ISI calibration. Early researchers in INR studies used the tilt tube method making today’s studies comparing photo-optic and mechanical clotting endpoint values suspect, at best. For mechanical endpoint clot detection systems most manufacturers still use the Fibrometer to assign ISI values. With today’s

Table 1. Summary of MNPT according to reagent/instrument test system

<table>
<thead>
<tr>
<th>Instrument</th>
<th>Reagent</th>
<th>MNPT (sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnostica</td>
<td>Neoplastine CI+</td>
<td>13.9</td>
</tr>
<tr>
<td></td>
<td>Thromborel S</td>
<td>12.9</td>
</tr>
<tr>
<td></td>
<td>Thromboplastin CI+</td>
<td>13.9</td>
</tr>
<tr>
<td></td>
<td>Innovin</td>
<td>9.9</td>
</tr>
<tr>
<td>Sysmex 540</td>
<td>Neoplastine CI+</td>
<td>12.7</td>
</tr>
<tr>
<td></td>
<td>Thromborel S</td>
<td>11.9</td>
</tr>
<tr>
<td></td>
<td>Thromboplastin CI+</td>
<td>11.7</td>
</tr>
<tr>
<td></td>
<td>Innovin</td>
<td>10.6</td>
</tr>
<tr>
<td>Dade Behring BCS</td>
<td>Neoplastine CI+</td>
<td>13.8</td>
</tr>
<tr>
<td></td>
<td>Thromborel S</td>
<td>12.6</td>
</tr>
<tr>
<td></td>
<td>Thromboplastin CI+</td>
<td>11.0</td>
</tr>
<tr>
<td></td>
<td>Innovin</td>
<td>8.9</td>
</tr>
</tbody>
</table>
highly automated mechanical clot-detection systems, this appears to be a less than optimal instrument method for assigning ISI values. Photo-optical coagulation systems use many diverse methods for determining a clot formation that may also greatly influence the ISI of different reagents.

Table 2. Summary of mean INR results on 25 normal patient samples before and after local ISI calibration with each reagent/instrument test system

<table>
<thead>
<tr>
<th>Instrument</th>
<th>Reagent</th>
<th>Mean INR using vendor assigned ISI</th>
<th>Mean INR using locally calibrated ISI</th>
<th>Difference in INR means (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnostica</td>
<td>Neoplastine CI+</td>
<td>1.24</td>
<td>1.29</td>
<td>-3.9</td>
</tr>
<tr>
<td>Stago/STA</td>
<td>Thromborel S</td>
<td>1.12</td>
<td>1.13</td>
<td>-0.9</td>
</tr>
<tr>
<td></td>
<td>Thromboplastin C+</td>
<td>1.96</td>
<td>1.76</td>
<td>10.1</td>
</tr>
<tr>
<td></td>
<td>Innovin</td>
<td>0.92</td>
<td>1.00</td>
<td>-8.5</td>
</tr>
<tr>
<td>Sysmex CA</td>
<td>Neoplastine CI+</td>
<td>1.24</td>
<td>1.09</td>
<td>11.9</td>
</tr>
<tr>
<td>540</td>
<td>Thromborel S</td>
<td>1.06</td>
<td>1.02</td>
<td>3.4</td>
</tr>
<tr>
<td></td>
<td>Thromboplastin C+</td>
<td>1.95</td>
<td>1.81</td>
<td>7.4</td>
</tr>
<tr>
<td></td>
<td>Innovin</td>
<td>1.02</td>
<td>0.92</td>
<td>10.3</td>
</tr>
<tr>
<td>Dade Behring</td>
<td>Neoplastine CI+</td>
<td>1.24</td>
<td>1.16</td>
<td>6.9</td>
</tr>
<tr>
<td>BCS</td>
<td>Thromborel S</td>
<td>1.06</td>
<td>1.02</td>
<td>3.5</td>
</tr>
<tr>
<td></td>
<td>Thromboplastin C+</td>
<td>1.77</td>
<td>1.57</td>
<td>11.1</td>
</tr>
<tr>
<td></td>
<td>Innovin</td>
<td>0.90</td>
<td>1.07</td>
<td>-18.9a</td>
</tr>
</tbody>
</table>

Table 3. Summary of mean INR results on 95 patient samples before and after local ISI calibration according to test system

<table>
<thead>
<tr>
<th>Instrument</th>
<th>Reagent</th>
<th>Mean INR using vendor assigned ISI</th>
<th>Mean INR using locally calibrated ISI</th>
<th>Difference in INR means (%)</th>
<th>Results &gt;10% difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnostica</td>
<td>Neoplastine CI+</td>
<td>2.58</td>
<td>2.69</td>
<td>4.1</td>
<td>0.0</td>
</tr>
<tr>
<td>Stago/STA</td>
<td>Thromborel S</td>
<td>2.56</td>
<td>2.58</td>
<td>0.8</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>Thromboplastin C+</td>
<td>2.39</td>
<td>2.15</td>
<td>10.0</td>
<td>37.1</td>
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<td>Innovin</td>
<td>2.45</td>
<td>2.67</td>
<td>7.9</td>
<td>22.1</td>
</tr>
<tr>
<td>Sysmex CA</td>
<td>Neoplastine CI+</td>
<td>3.46</td>
<td>2.90</td>
<td>16.1</td>
<td>63.9</td>
</tr>
<tr>
<td>540</td>
<td>Thromborel S</td>
<td>2.69</td>
<td>2.58</td>
<td>4.1</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>Thromboplastin C+</td>
<td>2.82</td>
<td>2.60</td>
<td>7.8</td>
<td>27.8</td>
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<tr>
<td></td>
<td>Innovin</td>
<td>2.49</td>
<td>2.25</td>
<td>9.6</td>
<td>39.2</td>
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<tr>
<td>Dade-Behring</td>
<td>Neoplastine CI+</td>
<td>2.81</td>
<td>2.60</td>
<td>7.5</td>
<td>20.6</td>
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<td>BCS</td>
<td>Thromborel S</td>
<td>2.67</td>
<td>2.57</td>
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<td></td>
<td>Thromboplastin C+</td>
<td>2.86</td>
<td>2.51</td>
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<tr>
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<td>Innovin</td>
<td>2.66</td>
<td>3.29</td>
<td>16.4</td>
<td>64.9</td>
</tr>
</tbody>
</table>

CONCLUSION
In our protocol we used 12 different reagent/instrument combinations and determined the local ISI by calibration for each coagulation system. We then compared the results using samples from normal subjects and specimens from variety of patients. Our results indicate that this local on-site calibration protocol may help eliminate variability and guesswork between any reagent/instrument sys-
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Table 4. Comparison of selected INR differences of OAT subjects plasma on the STA and MLA 900C with thromboplastins CI+, T-D, T-R, and the MLA 1600C with T-D only

<table>
<thead>
<tr>
<th>Human Sample</th>
<th>MLA 900C CI+</th>
<th>MLA 900C T-D</th>
<th>MLA 900C T-R</th>
<th>MLA 1600C T-D</th>
<th>STA CI+</th>
<th>STA T-D</th>
<th>STA T-R</th>
<th>Difference in INR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>167</td>
<td>2.77</td>
<td>3.41</td>
<td>3.72</td>
<td>3.62</td>
<td>2.68</td>
<td>3.24</td>
<td>3.41</td>
<td>38.8</td>
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<tr>
<td>1181</td>
<td>2.53</td>
<td>3.20</td>
<td>3.65</td>
<td>3.36</td>
<td>2.64</td>
<td>2.85</td>
<td>2.91</td>
<td>44.2</td>
</tr>
<tr>
<td>1180</td>
<td>3.95</td>
<td>5.98</td>
<td>5.83</td>
<td>7.16</td>
<td>4.02</td>
<td>4.93</td>
<td>5.05</td>
<td>81.2</td>
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<tr>
<td>1398</td>
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<td>3.94</td>
<td>3.44</td>
<td>4.14</td>
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<td>3.61</td>
<td>3.35</td>
<td>40.8</td>
</tr>
<tr>
<td>1393</td>
<td>3.57</td>
<td>4.98</td>
<td>4.48</td>
<td>5.00</td>
<td>3.57</td>
<td>4.39</td>
<td>4.18</td>
<td>40.1</td>
</tr>
<tr>
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<td>3.03</td>
<td>4.14</td>
<td>3.41</td>
<td>4.43</td>
<td>3.13</td>
<td>3.82</td>
<td>3.14</td>
<td>46.2</td>
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<td>3.72</td>
<td>5.82</td>
<td>4.99</td>
<td>6.29</td>
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<td>5.57</td>
<td>4.47</td>
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<td>3.94</td>
<td>3.93</td>
<td>4.44</td>
<td>3.12</td>
<td>3.70</td>
<td>3.79</td>
<td>50.5</td>
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<tr>
<td>1814</td>
<td>3.15</td>
<td>1.97</td>
<td>4.00</td>
<td>4.85</td>
<td>3.24</td>
<td>4.23</td>
<td>3.58</td>
<td>146.2</td>
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<tr>
<td>1669</td>
<td>3.25</td>
<td>2.41</td>
<td>3.66</td>
<td>3.93</td>
<td>3.24</td>
<td>4.29</td>
<td>3.28</td>
<td>78.0</td>
</tr>
</tbody>
</table>

Cl+ (Neoplastine CI+, Diagnostica-Stago Inc. Parsippany NJ); T-D (Thromboplastin-D, Pacific-Hemostasis, Huntersville NC); T-R (Recombiplastin, Hemoliance, Pleasantville NY).

tems for ISI values when performing PT/INR assays and potentially improve the clinical accuracy of PT/INR results for patients on OAT.

ACKNOWLEDGEMENTS

I would like to thank Dade-Behring Inc for their financial and technical assistance in support of this protocol. I would like to thank the following individuals for their personal support: Julie Carlucci, Diane Shafer, Ruben Siller, Tom Hogan, and Sherry Hagman from Dade-Behring Inc for technical and administrative support. Steve Duff from Precision Biologic was always available for support. Captain Eric Olsen and Rachel Montez gave outstanding editorial assistance.

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This article was presented in part at the ASCLS meeting 2000.

REFERENCES

**OBJECTIVES:** The objectives of this review paper are to: describe the fetal fibronectin assay, its purpose, and clinical significance; evaluate the sensitivity and specificity of the fetal fibronectin test; describe the specimen collection and measurement of the fetal fibronectin test; and present the advantages and disadvantages of incorporating fetal fibronectin testing in routine prenatal care.

**DATA SYNTHESIS:** Current literature.

**DATA SOURCES:** Current literature.

**RESULTS:**

Fetal fibronectin (fFN) is detected in the cervicovaginal fluid of pregnant women as a predictor of risk for preterm delivery (PTD). A recently developed qualitative solid-phase immunosorbent assay for fFN may significantly reduce hospital stay and costs for these women. Currently in the United States, PTD occurs in approximately 10% of births and is a leading cause of neonatal morbidity and mortality.1,2,3 This rate has not changed significantly in the past forty years despite advances in perinatal care.4 Early detection of PTD risk will hopefully allow clinicians delivering prenatal care to reduce its occurrence and resulting morbidity and mortality. At the same time, healthcare costs should be reduced by designating those with symptoms of PTD from those that are truly at risk and require intervention.

Fibronectin proteins are found in plasma and extracellular matrix and function as components of cell adhesion and migration. They also play a role in cell differentiation and growth.5 One of these fibronectins, fFN, is an oncofetal antigen present in some malignant cell lines. Similar to other oncofetal antigens, it is a normal protein in fetal life, present in amniotic fluid and placental tissue. In fetal life, it exists in the extracellular matrix where the implanted ovum and placental membranes come in contact with the uterine wall. It most likely functions as an adhesion protein, connecting the placenta to the uterus. When this extracellular matrix is broken down because of stress, infection, or hemorrhage, fFN leaks into cervicovaginal secretions.2,4,5,6,7

**ABSTRACT:**

Fetal fibronectin (fFN) is detected in the cervicovaginal fluid of pregnant women as a predictor of risk for preterm delivery (PTD). A recently developed qualitative solid-phase immunosorbent assay for fFN may significantly reduce hospital stay and costs for these women. Presently in the United States, PTD occurs in approximately 10% of births and is a leading cause of neonatal morbidity and mortality.1,2,3 This rate has not changed significantly in the past forty years despite advances in perinatal care.4 Early detection of PTD risk will hopefully allow clinicians delivering prenatal care to reduce its occurrence and resulting morbidity and mortality. At the same time, healthcare costs should be reduced by designating those with symptoms of PTD from those that are truly at risk and require intervention.

Fibronectin proteins are found in plasma and extracellular matrix and function as components of cell adhesion and migration. They also play a role in cell differentiation and growth.5 One of these fibronectins, fFN, is an oncofetal antigen present in some malignant cell lines. Similar to other oncofetal antigens, it is a normal protein in fetal life, present in amniotic fluid and placental tissue. In fetal life, it exists in the extracellular matrix where the implanted ovum and placental membranes come in contact with the uterine wall. It most likely functions as an adhesion protein, connecting the placenta to the uterus. When this extracellular matrix is broken down because of stress, infection, or hemorrhage, fFN leaks into cervicovaginal secretions.2,4,5,6,7

Fetal fibronectin concentrations in vaginal and cervical secretions in pregnancy follow a pattern that correlate with its role in implantation and adhesion. In the early weeks of pregnancy before 20 weeks gesta-
tion, fFN is measurable in significant concentrations. In a normal pregnancy, after 20 to 22 weeks gestation when the gestational sac would be attached to the endometrium, fFN decreases to <50 ng/mL, an undetectable level by routine assays. Therefore, its presence in detectable concentrations after 20 weeks should indicate some type of premature rupture in the attachment of fetal membranes in the uterus. A rupture of these membranes places a woman at high risk for premature delivery (delivery before 37 weeks).

Symptoms of premature delivery, most often uterine contractions before 37 weeks, do not always result in premature birth. Digital cervical examination and other procedures such as transvaginal ultrasound to evaluate the cervix, are performed to help determine risk of PTD. The patient may be treated with tocolytic agents to arrest contractions and/or antibiotics, if a bacterial infection places patient at risk for early delivery. Researchers have been seeking a biochemical marker or markers for PTD measurable in blood or secretions. Utilization of biochemical marker(s) in conjunction with tocolytic therapy and antibiotics may increase fetal survival rates. In 1995, the FDA approved the fFN enzymatic immunoassay as a biochemical marker for preterm labor. It has been approved for the diagnosis of PTD in symptomatic women and as a screening assay for premature labor in asymptomatic women who are at risk for PTD.

To perform a fFN assay, cervicovaginal secretions are collected with a Dacron swab and placed in a tube of buffer provided in manufacturer's specimen collection kit (Adeza Biomedical Corporation, Sunnyvale CA). The qualitative assay is performed on a solid-phase immunosorbent cassette containing a monoclonal anti-fetal fibronectin antibody. The specimen is extracted, filtered, and dispensed into a sample well and resulting color intensities are interpreted by the instrument in 20 minutes. Color intensity is compared to a reference calibrator of 50 ng/mL; a positive reaction indicates a concentration of fFN greater than or equal to the calibrator and a negative indicates a concentration of less than 50 ng/mL. A quantitative assay that uses antibody coated micro titer wells is also available.9,10

If a patient is to have a digital examination or vaginal cultures collected, the fFN sample should be collected first. These procedures are disruptive to the membranes and may cause leakage of fFN into vaginal secretions. Moderate and gross vaginal bleeding also interfere with result interpretation. Since fFN is normally present in amniotic fluid and fetal membranes, patients with advanced cervical dilatation and rupture of amniotic membranes are unsuitable for the test. The manufacturer also recommends not collecting samples on patients who have had sexual intercourse in the past 24 hours; test results on these patients are also difficult to interpret.9,10,11,12,13

There have been numerous studies evaluating fFN measurement and preterm delivery prediction. Several of these studies compared fFN to other biochemical markers of PTD and other researchers included cervical dilatation, transvaginal ultrasound, or presence of bacterial vaginosis. Most studies included symptomatic and asymptomatic patients. Some researchers have compiled the data and published meta-analysis of results, reporting fFN sensitivities and specificities overall, and for specific weeks’ gestation. In a meta-analysis published in May 1999, Leitich reviewed 27 studies published in English. Table 1 lists sensitivity and specificity for all patients for delivery at <37 and <34 weeks’ gestation. Table 2 depicts overall sensitivity and specificity rates for delivery within 7, 14, 21, and 28 days of sample collection for all patients and Table 3 for symptomatic patients. This data supports their conclusion that fFN is an effective predictor of PTD in asymptomatic women. Another earlier meta-analysis by Revah in 1998, reviewed 24 studies and found similar sensitivities and specificities. Their overall specificity was 80% for all outcomes, very close to 84% and 83% on Table 1. Their sensitivities and specificities were grouped differently than those on Table 2 and Table 3 but were also lower for asymptomatic women. For a patient with symptoms of PTD, a negative test for fFN is useful in ruling out delivery in the next seven to ten days. These authors concluded that testing for fFN is not as useful in asymptomatic women as in symptomatic individuals.22

### Table 1. Sensitivity and specificity by delivery for all patients

<table>
<thead>
<tr>
<th>Delivery</th>
<th>&lt;37 weeks</th>
<th>&lt;34 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>56%</td>
<td>61%</td>
</tr>
<tr>
<td>Specificity</td>
<td>84%</td>
<td>83%</td>
</tr>
</tbody>
</table>

### Table 2. Sensitivity and specificity by sample collection date for all patients

<table>
<thead>
<tr>
<th>Specimen collection within days of delivery</th>
<th>7 days</th>
<th>14 days</th>
<th>21 days</th>
<th>28 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>76%</td>
<td>68%</td>
<td>61%</td>
<td>43%</td>
</tr>
<tr>
<td>Specificity</td>
<td>88%</td>
<td>89%</td>
<td>91%</td>
<td>93%</td>
</tr>
</tbody>
</table>

### Table 3. Sensitivity and specificity by sample collection date for symptomatic patients

<table>
<thead>
<tr>
<th>Specimen collection within days of delivery</th>
<th>7 days</th>
<th>14 days</th>
<th>21 days</th>
<th>28 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>89%</td>
<td>78%</td>
<td>76%</td>
<td>71%</td>
</tr>
<tr>
<td>Specificity</td>
<td>86%</td>
<td>86%</td>
<td>88%</td>
<td>83%</td>
</tr>
</tbody>
</table>
Reductions in healthcare costs with the addition of fFN testing in preterm labor care and treatment have been evaluated. Decreased hospital admissions for preterm labor, reduced length of hospital stays, and fewer prescriptions administered without adverse consequences for these patients would justify routine addition of fFN assays on follow-up clinic visits. They compared their study group costs that included fFN assays to a baseline group before the addition of fFN in patient care. There were no changes in neonatal intensive care admissions, neonatal intensive care length of stays, or days of ventilator support per patient in the two patient groups. They calculated a savings of $416,120 for the study group; the two patient groups. They calculated a savings of $416,120 for the study group; this included the additional costs incurred for fFN assays on follow-up clinic visits.12 They compared their study group costs that included fFN assays to a baseline group before the addition of fFN in patient care. There were no changes in neonatal intensive care admissions, neonatal intensive care length of stays, or days of ventilator support per patient in the two patient groups. They calculated a savings of $416,120 for the study group; this included the additional costs incurred for fFN assays on follow-up clinic visits.12

Though the fFN test is a useful marker in evaluating PTD, some researchers and practitioners are still hesitant to advocate its use.19,23 The accurate prediction of PTD does not necessarily decrease its occurrence. Others are concerned that the test results may cause unnecessary anxiety for some patients. The successful use of tocolytic agents in preventing PTD needs further investigation. Also needed is documentation that antibiotic administration is effective when a patient has a positive fFN and follow-up cultures indicate a vaginal or cervical bacterial infection. More research is required to find interventions to prevent PTD when it is predicted to occur.21

Other biochemical markers of PTD are also being investigated.1,2,3,4-6 Table 4 lists those found in literature on PTD. Interleukin-6 (IL-6), other cytokines, and C-reactive protein (CRP) indicate the presence of an inflammatory process or infection. Proteases such as collagenase, granulocyte elastase, and matrix metalloproteinases, increase in breakdown in the placental uterine protein interface. Increased levels of the hormones listed on Table 4 indicate maternal or fetal stress.

**Table 4.** Other biochemical markers of preterm delivery

<table>
<thead>
<tr>
<th>Marker</th>
<th>Specimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytokines:</td>
<td></td>
</tr>
<tr>
<td>Interleukin-6 (IL-6)</td>
<td>Amniotic fluid, cervicovaginal fluid, and maternal plasma</td>
</tr>
<tr>
<td>Tumor necrosis factor (TNF)</td>
<td>Cervicovaginal fluid</td>
</tr>
<tr>
<td>Proteins:</td>
<td></td>
</tr>
<tr>
<td>C-reactive protein (CRP)</td>
<td>Maternal plasma</td>
</tr>
<tr>
<td>Proteases:</td>
<td></td>
</tr>
<tr>
<td>Collagenase</td>
<td>Maternal plasma</td>
</tr>
<tr>
<td>Granulocyte elastase</td>
<td>Cervicovaginal fluid and maternal plasma</td>
</tr>
<tr>
<td>Matrix metalloproteinases (MMPs):</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Maternal plasma</td>
</tr>
<tr>
<td>Hormones:</td>
<td></td>
</tr>
<tr>
<td>Human chorionic gonadotropin</td>
<td>Maternal plasma</td>
</tr>
<tr>
<td>Corticotropin releasing hormone</td>
<td>Maternal plasma</td>
</tr>
<tr>
<td>Estradiol-17β</td>
<td>Maternal plasma</td>
</tr>
<tr>
<td>Estriol</td>
<td>Maternal saliva, plasma, and amniotic fluid</td>
</tr>
<tr>
<td>Progesterone</td>
<td>Maternal plasma</td>
</tr>
</tbody>
</table>

**REFERENCES**


References continued on page 115.
It has been generally acknowledged that a number of obstacles, or barriers, exist in the articulation process. Based on literature review, student characteristics as well as institutional characteristics may act as barriers. This paper focuses on institutional characteristics. The changed mission of the community college and a lack of standardization of curricula between two-year and four-year institutions of higher education have been identified as barriers to articulation. Suggested reforms are described.

INDEX TERMS: articulation; barriers; junior college; transfer student

CONCLUSIONS: The reports and reviews section seeks to publish information on important clinical laboratory-related topics such as technological, clinical, and experimental advances and innovations. Case studies and literature reviews are also included. In addition, brief reviews of books, computer programs, audiovisual materials or other materials of interest to readers are appropriate for this section. Manuscripts and literature reviews published as a Report are peer-reviewed. Direct all inquiries to Isaac M. Montoya, PhD, Affiliated Systems Corporation, 3104 Edloe, Suite 330, Houston TX 77027-6022. (713) 439-0210, (713) 439-1924 (fax). imontoya@affiliatedsystems.com

Perceived Barriers to Articulation: Institutional Characteristics

JEANNE KRUMPELMANN

In the earlier days of the community college, during the 1950s, when they were still called “junior colleges”, the student transfer rates were approximately 50%. What might be the reason for a continual decline in transfer rates over the years? Researchers have addressed this question with another question: “What is the relative impact of initial attendance at community colleges versus initial attendance at senior institutions on baccalaureate attainment?”

Three different national longitudinal surveys, initiated in the early 1970s, “found that, on the average, 70% of four-year college entrants received a baccalaureate degree when followed up four to fourteen years later, whereas only 26% of public two-year college entrants reached the same destination.”

Kevin Dougherty, an educator in favor of collegiate reform, reiterates what other researchers have concluded: “There really is a baccalaureate gap, and it is only partially explained by the different characteristics of the two student bodies. Even when these differences are controlled, students entering community colleges with the hope of receiving a bachelor’s degree are 11% to 19% less likely to do so than comparable students entering four-year colleges.”

With over five million undergraduate students attending community colleges in the 1990s, it became more urgent to seek out the causes of this problem. The body of research is in agreement. Student characteristics such as academic skills, socioeconomic factors, social integration, and emotional strengths are often predictors of success (or failure) in persistence toward attaining the baccalaureate degree. However, characteristics due to the nature of the institution (institutional and curricular characteristics) also act as barriers to articulation.

INSTITUTIONAL CHARACTERISTICS

Institutional characteristics are defined as those characteristics rooted in the organization, governance, history, and mission of the higher education system. Both two-year institutions and four-year baccalaureate degree institutions present their own barriers to articulation. However, critics as well as advocates of the community colleges agree that the changed mission of the community college is largely responsible for the perceived barriers to articulation and the general decline in transfer rate and subsequent graduation. This situation is explored briefly prior to consideration of specific barriers.

COMMUNITY COLLEGES: CHANGE IN MISSION

An open-door policy in higher education had been well established by the time U.S. veterans returned home following the end of World War II. The G.I. Bill of Rights was passed, providing funding for their education. A sharp rise in enrollments in community colleges followed.
“In 1947, the philosophy of open access was further advanced by the Truman Commission on Higher Education, which strongly advocated education for all and established the basic functions of community colleges—providing proper education for all the people of the community without regard to race, sex, religion, color, geographical location, or financial status.”

Originally called junior colleges and intended to function primarily as two-year academic pre-transfer institutions, community colleges were considered a “point of entry into the hierarchy of U.S. higher education”. Junior colleges also offered postsecondary education up to a terminal associate degree.

Democratizing sentiments in society, such as those evidenced in the Truman Commission on Higher Education, demanded greater accessibility to education for all. As a result, throughout the 1950s and 1960s, two-year colleges took on a comprehensive focus, offering a variety of programs, including academic, general education, as well as vocational education. Their name was changed to ‘community college’, and the increased access to higher education that they offered became known as the ‘community college movement’. Between 1950 and 1970 enrollments increased by 750%.

As these colleges became increasingly comprehensive in nature, with an emphasis on vocational programs, their academically oriented pre-transfer curricula decreased. The needs of a diverse and unselected student population were diverting the two-year college from its original mission. Even community college advocates admit that during the late 1960s and 1970s, known as ‘transition years’ for the community college, these schools relaxed their pre-transfer function, leaving the setting of standards up to the post-transfer institution. A lack of good counseling left students, who had initially intended to transfer, to inform themselves of the criteria of the post-transfer institution and to plan accordingly. By the late 1970s the transfer rate was slightly less than 25%.

“While the removal of academic, economic, social, and geographical barriers serves to democratize higher education, it also poses a dilemma: the problem of providing open access with quality.” For the last two decades, many educators researching this issue have been critical of the community college, claiming that it actually hinders students from transferring to four-year colleges. They associate the change in mission from ‘academic’ to ‘comprehensive’ with a perceived decrease in quality of education.

INSTITUTIONAL BARRIERS AND SUGGESTED SOLUTIONS

A number of institutional barriers have been identified. Because they exist independently of student characteristics, and are attributable to the nature of the institution, they are responsible for what Dougherty refers to as the “negative institutional effect”. For brevity, a few selected barriers and suggested reforms are discussed.

Community colleges: barriers and suggested reforms

Lack of academic quality

“In many community colleges, programs ostensibly designed to prepare students for eventual transfer to four-year colleges have become essentially open-door programs with virtually no entry or exit requirements. Consequently, transfer courses are often not up to university standards of instruction.” Some researchers propose that faculty do not maintain high academic expectations for their students, that they grade relative to the class norm, and assign fewer difficult readings and essay exams than university faculty members.

Solutions include suggestions such as: improving pre-transfer academic preparation by familiarizing community college instructors of the university’s academic expectations, increasing academic expectations of students, and pre-testing students to determine if they are academically prepared to enroll in courses that will transfer to a four-year school.

Lack of transfer advising

Studies suggest that transfer aspirants receive minimal advice and encouragement, and that community college counselors are often uninformed about transfer courses.

Solutions include suggestions such as: establishing centers at the community college with specific transfer information, clearly labeling transfer courses, and establishing more interaction between student and advisor to assess the student’s progress in transfer courses. Gallego also suggests certain interventions, such as additional mentoring by counselors for remedial students who have transfer as a goal.

Four-year colleges/universities: barriers and suggested reforms

Loss of credits

Because of the selective admission policies of four-year colleges/universities, students who wish to transfer to baccalaureate degree programs often lose credits in the process. Lower division credits may not be recognized by four-year institutions. Dougherty cites a recent study in which 58% of community college students from nine urban universities across the country reported losing credits in transferring, with 29% losing ten credits or more. Four-year colleges often are reluctant to accept technical credits from an occupational or vocational program (Associate of Applied Science degree), essentially because there are no comparable courses in their own curricula.

The ‘capstone’ or ‘inverted’ program has been suggested as a solution for the technical school graduate who desires to articulate. The concept of the capstone initiative involves the acceptance of technical credits by the four-year institution, while allowing the student to complete general education credits in the last two years of upper-division education. It has also been suggested that four-year institutions increase their flexibility in acceptance of credits,
and, in fact, increase their overall receptiveness to the ever-growing numbers of nontraditional students.

Lack of established common course numbering or course equivalence Four-year institutions have been known to deny credit earned in a community college course, although the course content has been comparable to one of their courses. Claiming that the course belongs in their upper division curriculum and has been taken out of sequence, or that the content does not meet their criteria, they require that the course be repeated. This is a common situation, for example, with business courses.

The following anecdotal information gleaned from two interviews initiated during the course of personal research, confirms this barrier. In one case, a state legislator related the story of a student who had taken an accounting class at a community college. In the process of articulating, the post-transfer institution required that the course be repeated in its upper-division. The student agreed. However, when he entered the classroom, he found the same instructor teaching this class. The instructor, recognizing him, stated: “You don’t have to be here. You have already taken this course”.

A similar situation was described by the president of a local technical institute. He referred to these barriers as “turf issues”, indicating that faculty at different institutions are apprehensive of encroachment on what they consider to be their domain. Apparently, job security is a concern, because the technical college president remarked: “the perfect solution would be that everyone transfers and everyone keeps their jobs”.

A legislative mandate requiring common course numbering or the clear labeling of equivalent courses has been suggested as a means of ensuring that “transfer courses indeed parallel university courses in credit hours, course sequencing, and prerequisites”. This solution involves, not only four-year college administrators, but community and technical college administrators, as well as state policymakers (including Board of Higher Education administrators and state legislators) working together to meet the needs of students by facilitating articulation.

Recent initiatives, known as ‘dual admission’ or ‘joint admission’ programs have been implemented between two- and four-year colleges across the country. According to Cohen: “One of the most powerful aids to transfer is a set of inter-institutional agreements erected program-by-program so that students who want to obtain bachelor’s degrees in certain fields are encouraged to begin at the local community college, with the assurance that the curricula articulate and that a place in the university’s junior class will be available to them”. For the 30% to 40% baccalaureate aspirants attending community/technical colleges, these initiatives will provide an alternative and less expensive route to attaining the baccalaureate degree.2,3

CONCLUSIONS

Students entering higher education bring with them individual strengths and weaknesses. Student characteristics, such as academic skills, social integration, as well as emotional strengths, are often predictors of success, or failure when these strengths are found lacking. In addition, the socioeconomic background of a student may influence academic achievement.

Institutional and curricular characteristics, independent of student characteristics, may also present barriers to academic achievement. Referred to as a ‘negative institutional effect’, both two-year and four-year baccalaureate degree institutions present their own barriers, particularly for the articulating student.

The changed mission of the community college, from ‘academic’ to ‘comprehensive’, may be responsible for barriers encountered in the articulation process. At the community college level a perceived lack of academic quality and transfer advising has been cited as barriers. The consensus of research indicates that just as able and motivated students will not necessarily be hindered by the community college experience, neither will academically or socially disadvantaged students be likely to find the institutional assistance they may need in order to negotiate transfer and progress to the baccalaureate degree.

At the four-year baccalaureate degree post-transfer level, selectivity and lack of standardized curricula between the two- and four-year institutions are cited as perceived barriers. This has often resulted in a significant loss of credits for the articulating student.

Reforms include establishing course equivalence and common course numbering between the two systems of higher education. Initiatives, such as ‘dual or joint admission’ or ‘capstone’ programs have been either suggested or instituted in many states. However, all reforms involve the common thread of increased communication and cooperation among state legislatures, faculty at all levels of higher education, and students in order to facilitate the articulation process.

REFERENCES

OBJECTIVE: The purpose of the study was to clarify the knowledge base of clinical laboratory science (CLS). This research was motivated by questions concerning the knowledge base itself and its abilities to meet the demands of reality. The following questions were therefore asked to achieve the purposes of the study: • What are the knowledge fields and inner patterns in CLS? • Which research objects could CLS focus on in order to promote development in practice, education, and research?

DESIGN: The findings of the study were arrived at by means of hypothetical-deductive approach and inductive, content analytic strategy. The journal Clinical Laboratory Science of the American Society for Clinical Laboratory Science (ASCLS) provides the source material for the analysis.

SETTING: Åbo Akademi University. Faculty of Social and Caring Sciences.

RESULTS: The findings of the study are discussed in the light of starting points of the theory of science and lead to nine hypotheses concerning CLS.

CONCLUSION: The purpose of the present study was to create clarity in CLS as a science of its own. This has been achieved by capturing and describing facts and qualities, and thereafter presenting fundamental hypotheses in CLS. The results of this study give a thought structure for continued development and deepening within the theory and practice of CLS.

ABBREVIATIONS: ASCLS = American Society for Clinical Laboratory Science; CLS = clinical laboratory science; MT = medical technologist.

INDEX TERMS: Clinical laboratory science; epistemology; ontology; origins.


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Marcel Proust’s “The real voyage of discovery consists not in seeking new lands, but in seeing with new eyes” was the polestar in this research process. Representatives of the clinical laboratory have worked hand in hand with other fields of healthcare and nursing, to seek the knowledge base of their work. My interest in this inquiry has always been in providing the best for the patient, in developing a knowledge base from a holistic perspective and, thus, developing the content of education and training.

The central aim of clinical laboratory practice is—with good care as a guiding principle—to protect and safeguard the patient’s integrity and health. This goal leads to different types of activities within a clinical perspective, thus examining both a body of knowledge and an activity. In Finland, medical technologists (MTs) are trained at Polytechnics and the length of the education is three and a half years. Discussions concerning the body of knowledge (knowledge base) have been carried out among educators who represent today’s education of MTs in Finland. Discussions, however, have not been undertaken regarding an intrinsic description of the knowledge and skills at a fundamental ontological level; rather descriptions have often remained at scientific technological knowledge levels. To move forward toward a university degree, a separate body of knowledge and professional description that could reflect the unique knowledge for MTs in Finland, has been discussed, principally among technically engaged MTs and educators involved in the training of MTs. The aim of this study, thus, is to create clarity in CLS as it is seen as a science.

THE KNOWLEDGE BASE WITHIN CLINICAL LABORATORY PRACTICE

During the last several years, evaluation of the various areas of health services has come more and more to the fore in discussions concerning the content of science and possibilities for application. This is also the case in clinical laboratory work. The intent is to evaluate and develop the knowledge and sphere of activity. This involves asking whether laboratory work consists of its own unique knowledge and if it is founded on its own science. In international literature, and above all, in American literature, the concept of CLS is encountered. The stand taken for CLS in the United States appears primarily in the journal Clinical Laboratory Science, partly in the journal’s name, as well as in many articles. In a lead article from 1988 in Clinical Laboratory Science, Doig and others, pur-
port that it is CLS and not sciences; since CLS is something more than a collection of various disciplines such as clinical chemistry and hematology, etc. It is also pointed out that those carrying out their profession within CLS are in possession of knowledge that has been developed from a broad, general basis. The philosophic application of CLS is seen primarily in the Code of Ethics that was accepted by the ASCLS in June 1995. The International Association of Medical Laboratory Technologists (IAMLT) has stated in its Code of Ethics, point 1, that "medical laboratory technologists shall be dedicated to the use of clinical laboratory science to benefit mankind".

The distinctive criterion for a science, especially in northern Europe and Scandinavia, is autonomy. Autonomy can be examined as a synthesis of three levels, that is to say, theoretical, sociological, and psychological. The theoretical level defines the scientific knowledge, the ideology of the science, and the nature and function of research. The sociological level is represented by the social norms within that science: possession of a professor’s position, the right to present doctoral dissertations and to publish scientific journals. The psychological level sheds light on the identity, the researcher’s paradigm, and the occupational paradigm within the science. The three levels have a certain autonomy in relation to each other. At the same time they are dependent upon each other. The levels are related to the stage of development of the science. To be able to clearly define a science, a clear and explicit choice of approach is implied. If the aim is to reach the heart of the science and describe what is unique about it, the researcher should be open-minded and have a holistic approach. However if a researcher chooses to concern himself or herself with the traditional ‘doing level’ it can be difficult to find the ontology of the science.

The development of knowledge within science can occur on various levels. The metatheoretical level is concerned with issues that touch upon the formation of knowledge and in paradigm development. This takes place through fundamental research. The issues concerning science are clarified and established. This is where, among other things, the demand that method-theory-ontology form a coherent form for current science is established. The ontological starting-points become the foundation upon which science rests. At the theoretical level, the factual knowledge concerning current activities is developed. Science at this level is not identical with technology or practical activities. The data that are developed here constitute the starting point for the clinical laboratory theories. The activities at the technological level differ from the scientific level by having a different goal. The goal of technology is practical benefit.

Clinical laboratory theories are also developed at this level. These consist of a theoretical and a practical part. Although the utilitarian aspect here is very important, it is of the greatest importance to preserve the unique element in one’s own area. If science is directed too much by society’s demand for it to be useful, it runs the risk of losing its own profile. CLS’s technology, as a scientific sub-area, comprises knowledge about aims, methods, and conditions for clinical laboratory work. Technological knowledge is, by its very nature, interdisciplinary and consists of empirical and ethical knowledge. The interdisciplinary nature of technology leads to a body of concepts consisting of concepts from many different sciences. Technology’s field of knowledge spans theoretical, practical, social, communicative, innovative, and informative qualifications.

METHODS

CLS is still trying to find its form and position. Hence the goal of the study becomes to get a clear picture of CLS as a science using the journal Clinical Laboratory Science as its starting-point. By capturing and interpreting data and qualities in order to arrive at what is ‘really real’ in CLS, this researcher endeavors to offer a thought structure for a ‘deepening’ of understanding within the field. In order to achieve the aim of the study the following questions are posed:

• What are the knowledge fields and inner patterns in CLS?
• Which research objects could CLS focus on in order to promote development in practice, education, and research?

Design of the study

The routes to seeking knowledge can be described as “the way of discovery or the way of proof”. In qualitative research the way of discovery exists as a means for obtaining and developing knowledge. The way of discovery results in theories or hypotheses. According to Enever, the first foundation stone in a qualitative method is a holistic approach to the world and its various phenomena. With the help of a qualitative method, a researcher wishes to obtain information about what kinds of qualities a certain phenomenon contains.

Qualitative research methods take as their starting point ‘patterns’, meaning the phenomena that are being studied. An explorative approach can be applied when a new area of science is to be described. CLS is ‘still in the making’ and therefore the central phenomena and concepts within the science must be discovered and explained. With the help of an explorative descriptive design, fundamental information about the ‘what-why-when-how-where-and-in-which context’ may be arrived at and can be described.

The present research approach is hypothetical-deductive. Research according to the hypothetical-deductive method starts with a problem, which is clearly delineated. A hypothesis is put forward as an explanation to the problem. The hypothesis is then tested through observations or experiments until proven false, or assumed to be true if it cannot be proved to be false. The purpose of the hypothetical-deductive method is to obtain true hypotheses. However, the main aim of some research is the hypotheses themselves. Thus this study ends in the putting forward of hypotheses. The core content of the theory of science forms a foundation for reflection. Data processing is based upon an inductive strategy. With the help of various
RESEARCH

dialogues within the text, structures emerge. The structures in the categories are examined, where quality and meaning in the category are considered an aspect of reality. This appears in direct quotations from the data. In the same way, data in the text form aspects of each quality. The shape that emerges is then discussed in view of the theory of science and background of the study.

**DATA ACQUISITION AND SELECTION**
The journal, Clinical Laboratory Science, forms the source for the analysis for this study. The journal is American in origin and specific to the science from a conceptual point of view. Articles from the 1988 to 1997 volumes covering ten years, were chosen. Each volume contained six issues. The researcher had access to 55 issues out of a total of 60.

The background to the journal Clinical Laboratory Science is found in the striving for professionalization that has existed for many decades and especially during the latter part of the 1900s. Beginning in 1935 the journal was published under the name The American Journal of Medical Technology. In 1984 the name was changed to The Journal of Medical Technology. Since 1988 the journal has been published under the name Clinical Laboratory Science. ASCLS has published the journal on a bimonthly basis, six issues per year. Over the years this publication has given practitioners, researchers, administrators, educators, students, and representatives of industry the opportunity to influence the development of clinical laboratory work, both on a theoretical and a practical level.16 Space has been given for specialist articles, review focus articles, research findings from a theoretical and practical perspective, and discussions as well as room for students’ work and related articles.

With a view to giving a clear presentation of the journal together with doing justice to this publication, the researcher first read carefully all the articles and then chose to examine the contents more closely.1 The study excluded commercial texts and discussions on American healthcare policy as well as training issues related to clinical laboratory practice. The contents were pre-grouped into subject areas such as the clinical laboratory entity, education, management, and organization together with quality issues. Subject areas were specified with subheadings related to content, partly to facilitate a summary and also to be able to evaluate a primary emphasis concerning the journal’s contents.

To capture and describe qualities in CLS a selection of major articles for closer analysis was undertaken using articles concerning all the phases of the clinical laboratory process including: patient’s problem and need—clinical question; clinical question—test selected and ordered; guidance of the patient—preparation for the examination; examination; collection of the specimen (sample) for clinical testing; preparing the sample; analyzing the sample; recording the result; assessment of the result; and notification of the result to the caring department or directly to the patient. The selection of articles was made easier by the researcher familiarizing herself with the journal during the first reading and during a review of contents. Articles that concerned administration, health policy, and teaching methods were excluded.

**ANALYSIS AND SUMMARY OF DATA**
Content analysis can be applied to a study in which the purpose is to analyze documents: written, spoken, or symbolic materials. Methods can be quantitative, manifest, or qualitative latent. A quantitative content analysis means, among other things, that the researcher presents, numerically, the degree in which the analyzed material is represented in various categories. In a qualitative contents analysis the study is directed at certain properties in the content materials. To answer the question concerning the knowledge field and inner pattern of CLS, a ‘latent contents analysis’ was chosen. By means of this method, the researcher seeks to reach the underlying meaning and qualities in the material. The meaning emerges inductively in the material and cannot be forced onto the material in advance.6,14,16,22

In the examination of this material, analysis and synthesis are united. The material is differentiated into conceptual elements and brought together to a scientific conclusion.7 The data analysis process can occur on various abstract levels and levels of understanding that can be noticed in a concept formation. On a surface level, the linguistic structure and construction of the texts are examined; on the context level, the texts are examined in relation to their context; and on the existential level, the texts’ deeper meanings are studied. The researcher aims at studying the texts at the contextual and existential levels. Data are summed up finally in one or more essential forms. From the static perspective, the permanence of the material is sought.14

The process for data analysis and data processing can be described step-by-step as follows:
1. The researcher reads the materials and obtains an overall view of the contents of the journal.
2. The researcher reads the materials again and notes what could construe various categories in the material (semi-structured preceding).
3. Detailed data analysis is taken. The researcher separates the text in order to obtain similar categories. At this stage the researcher asks the following questions: What is the text about? What is its starting point? What are the contents? What is happening? What is the aim? Why does the activity described in the text exist?
4. The researcher codes the content of the text entity 1, for example, as A.
5. The researcher analyzes text entity 2 and if the contents are the same as in the text entity 1, designates it as A, otherwise it is designated as B and so on. The researcher continuously compares new coded data in one category with previous texts coded in the same category in order to be able to develop its characteristics.

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6. The analysis proceeds in this manner such that the contents in each text entity are compared and coded with previously analyzed material, and thus new contents are discovered and new categories emerge on the basis of the coded text entities. The work with coding continues until a theoretical saturation is reached, which happens when the analysis no longer contributes to discovering something new about the category.

**RESULTS**

The articles reviewed in *Clinical Laboratory Science* related to the clinical laboratory process were analyzed by means of the latent content analysis. After having read the articles in question, the researcher made an outline description of the field of knowledge and patterns of facts (semi-structured pre-coding) that appear in the text. Next, a more detailed analysis of the data was made; the researcher separated the original text into main categories and subcategories, and stated the contents of the categories. With the aim of illustrating the foundation for the categorization, typical examples from all the articles are presented in the form of direct quotations.

During the course of the analysis process, essential forms in CLS were developed. After presentation of results in each essential form, including main and subcategories, a summary of the figuration of facts in each main category as well as what is important in it is provided.

**The person/patient - the origin of CLS**

The person/patient is the origin in CLS and is therefore the first essential form. **The main category**—person/patient includes the subcategories of a person/patient as a unique, indivisible entity as well as a person/patient as an individual with various levels of existence, e.g., at the level of cells and molecules, the levels of tissue and substance, and the level of organs.

**Subcategory A**

Unique person/patient

**Content of the subcategory**

Indivisible entity, dignity, existence

**The subcategory is manifested by:**

“I want to let you know exactly who I am. I am a human being with all the emotions and needs of other human beings... I am still a person, a person with feelings who has a certain amount of pride. Please do not take this from me. Many times, pride is all I have left... I have lost my job and may lose my home and savings. Is that any legacy to leave a loving spouse and two young children? I need food, water, friendship, warmth, love, sex, and security, both physical and financial. I also need to be touched by another human being. This is called skin hunger.”

...viewing patients as a member of their family and the community, not as a tube of blood on an automatic sampler..."24

**The subcategory** is manifested by:

“Tetraiodothyronine (T4; thyroxine) is a low molecular weight (777 daltons), iodine containing hormone secreted by the thyroid gland. Derived peripherally from conversion of T4 to T3 at sites of tissue action, triiodothyronine (T3) is the more biologically potent hormone. Important physiologic functions, including carbohydrate, protein, and lipid metabolism, T4 overproduction (hyperthyroidism) or underproduction (hypothyroidism) result in clinically important consequences.”

In summary, it can be noted that the person/patient as an origin in CLS is perceived both from a holistic perspective and from a biological perspective. The person/patient is seen, on the one hand, as a unique individual with his/her own thoughts, feelings, experiences, suffering, and vulnerability that must be understood in relation to his/her total life situation, and as a biological individual with specific biological qualities. These specific qualities relate to levels of cells and molecules, levels of tissues and substance, and levels for which organs are manifested, e.g., in the form of molecular weight, cell morphology; color, shape, size, degree of maturity, number of cells, cell division; concentrations; or as normal physiologic-pathophysiological properties. Equally important, humans are unique individuals, as described above. The core of meaning in this category is respect for a person’s/patient’s integrity from a holistic and a biological perspective.

**Encounter and relationship - a unifying force in CLS**

A unifying force - encounter with the patient as well as the relationship to what the patient submits to the professional, e.g., a specimen constitutes essential form number two in CLS. The patient’s wish to relate to the professional, the encounter between the patient and the professional, including technology, as well as the relationship between the patient’s specimen and the professional appear as subcategories in the main category of encounter/relationship.

**Subcategory A**

Patient’s wish to relate to the professional

**Content of the subcategory**

To relate to the whole individual. Reciprocity

**The subcategory is manifested by:**

“I also need to be touched by another human being. Will you stay near as I leave this life and enter another? ...see me as a human being and not a number or a disease. Please help me to under-
stand.... Give me a little of your precious time. Not a lot of time but quality time. Time enough to remind me that I am a worthy human being.... Please forgive me if I am less than courteous to you.... If you can dry but one tear, do it.”23

“Patients who wish to take control of their healthcare want to skip the middle man, and deal directly with the laboratories.”26

Subcategory B
Encounter between the patient and the professional, including an encounter with technology.

Content of the subcategory
Unique human/patient, unique patient specimen, unique human patient test/examination. Specific problem solving—harmony between the unique patient and valid quality requirements

The subcategory is manifested by:
“...as we participate in office and home testing, where our contact and expertise with patients is maximized... to assist seniors in dealing with medical terminology.”27

“At the time of original venipuncture, the technologist had noted that the patient’s blood had a bright red, arterial-like color, even though it was a venous sample.”28

“Patient identification: The blood collection process can be monitored and tracked by using a closed system once the patient and specimen have been positively identified.”29

Subcategory C
Relationship between the patient’s specimen and the professional.

Content of the subcategory
A unique fragile, vulnerable patient and his/her specimen. Qualitative adjustment of methods and equipment to the unique patient specimen

The subcategory is manifested by:
“...observed lower reticulocyte counts on patient smears prepared outside the routine laboratory hours....the problem of EDTA specimen stability for reticulocyte counting.”30

“A complete patient history including exercise habits is an essential part of patient information in all circumstances and should be available when interpreting laboratory data.”31

In summary, it can be noted that the figuration of facts in the essential form encounter and relationship confirm a unifying force in CLS. Closeness, commitment, respect, security, relief, reciprocity, trust, and trustworthiness are qualities that originate from the encounter between the patient and professional as well as from a relationship to the patient’s specimen—something that the patient submits to the professional, to take care of in the best possible way. Awareness of the vulnerability of the unique patient motivates an ethical point of view, including respect for a unique patient by means of listening, discussing, attempting to understand each patient and his/her situation, and by helping him/her in accordance with his/her needs. The figuration of facts concerning the unique, fragile, and vulnerable patient’s specimen/test is permeated by precision, a use of systems, scientifically verified knowledge, and a qualitative adjustment of methods and equipment when the professional is entrusted with the unique patient specimen or when the test is conducted in the patient’s presence. The core of meaning in this category is reverence for and care of the patient.

The patient’s health— the goal-orienting force in CLS
The patient’s health as the committing and goal-orienting force appears as essential form number three in CLS. The main category of a patient’s health includes the subcategories of: patient’s health pattern from a holistic perspective, patient’s biological health pattern from a general perspective, and a patient’s specific biological health pattern form the basis of the data gathered.

Subcategory A
Patient’s health pattern from a holistic perspective

Content of the subcategory
Health as a part of life
Health, suffering, reconciliation
Health resources, obstacles to health

The subcategory is manifested by:
“I want to let you know exactly who I am. I am a human being with all the emotions and needs of other human beings. Because of my medical condition my emotions and needs may be somewhat exaggerated... Because of my medical condition I have lost my job and may lose my home and my savings, I may even lose my life. I have many fears. A fear of death... Do you know what it feels like to have your body fail you when you need it so badly? I do not know what to expect on the other side of life. I fear financial ruin... I fear loss of control... I fear loss of family and friends... I fear dying alone... I fear the unknown... I am afraid... I fear pain... I want to tell you how much you mean to me. You are often my only link to life. I need you. I also need you to respect me as a person.”24

“...complaining of exhaustion, headaches, dizziness, blurring of vision, nausea and lack of appetite.”28

“Patients who wish to take control of their healthcare...”26
Clarification of the patient’s biological health pattern— a motivating force in CLS

A motivating force in CLS is to clarify the patient’s biological health pattern and this constitutes essential form number four. This essential form is characterized by the process, including technology, that a patient’s specimen/test is submitted to in order to achieve a laboratory test result. The main category of bioanalysis as well as the subcategories of biological materials include the objects of analysis, reference materials of analysis, methods and instruments of analysis, procedures of analysis, and quality of analysis that are formed on the basis of articles in the journal Clinical Laboratory Science.

Subcategory A
Biological materials as the object of analysis

Content of the subcategory
Goal-oriented, specific

Subcategory B
Reference material of analysis

Content of the subcategory
Comparability, exactness

Subcategory C
Methods and instruments of analysis

Content of the subcategory
Analytical performance; physical and biochemical qualities; analytical capacity and purposefulness

Subcategory B
Patient’s biological health pattern from a general perspective

Content of the subcategory
Comparability, generalizability

The subcategory is manifested by:
“It should be noted that the literature divides reference ranges for newborns and infants into several categories, e.g., at birth, 12 hours, one day, and one week. The reference range for white blood cell (WBC) counts is actually quite large. Newborns can have leukocyte counts from 9.0 to 30.0 x 10^9/L, with a mean of 15.0 to 20.0 x 10^9/L.”

“All results from the 20 healthy individuals tested were between 5.9 and 11.2 µg/dL, confirming the validity of the suggested range of 4.5 to 12.0 µg/dL.”

Subcategory C
Patient’s specific biological health pattern

Content of the subcategory
Relativity, individuality, exactness

The subcategory is manifested by:
“Initially, the patient’s hemoglobin (HGB) and hematocrit (HCT) were evaluated... On the third hospital day, however, the HGB and HCT began to drop and continued to decline for the next six days... Laboratory results reflect a variety of influences: direct tissue damage, expected compensatory mechanisms, treatment effects, and postburn complications.”

“For most analytes, the patient condition is a relatively minor consideration, but blood gas data can vary from minute to minute.”

In summary, it must be noted that the patient and his/her experienced, total, and objectively biological health is the goal-orienting force in CLS. Health is to be seen as more than a part of life and not only as a result of biological analysis. A laboratory test that explores the biological health pattern is to be seen in relation to the patient’s total health situation, to the agreed reference ranges and to the patient’s own biological reference values. ‘Health is relative’, and the biological health pattern may vary from one individual to another, from day to day, depending on age, gender, and the like. CLS may be able to provide patient a choice, because of increased awareness of health hazards and biological health patterns. The core of meaning in this main category comprises care of the patient’s total and biological health.
The category is manifested by:

“We can look forward to more specific and sensitive diagnostic techniques, ...which use monoclonal antibodies coupled with various methodologies such as enzyme-linked immunosorbent assay (ELISA) and immunofluorescent assay (IFA)....Electron microscopy is presently the most sensitive method for examining intestinal tissue.”35

“This method uses dry-reagent technology in the form of test cards (Keto-Site) to determine exclusively B-OHB levels in blood, serum or plasma based on the enzymatic reaction....Optical density measurements were obtained using a Gilford Spectrophotometer Model 250 for both specimens and GDS B-OHB controls at a wavelength of 505 nm.”36

“Differential information would be entered directly through a differential pad. The results would be generated by the instrument and transmitted directly from the instrument to the computer. The answers would be checked for accuracy on a word sheet that would become part of the chart copy when the patient report was printed.”37

Subcategory D
Procedure of analysis

Content of the subcategory
Analytical flow including well-defined sequences

The subcategory is manifested by:

“Four drops of blood were added to a commercially available reticulocyte staining system utilizing dry brilliant cresyl blue stain....mixed and incubated between 10 to 20 minutes. Wedge smears were prepared and allowed to air dry. Reticulocytes was counted under a 100X oil objective over five fields of approximately 200 RBCs/field.”38

Subcategory E
Quality of analysis

Content of the subcategory
Exactness, regularities related to the method of analysis; exactness, regularities related to biomedical diagnosis

The subcategory is manifested by:

“A stepwise multiple regression analysis was performed using sex, age, body mass index (BMI), previous cholesterol value, and smoking as independent variables and cholesterol as the dependent variable... to predict cholesterol levels.”39

“Linearity-defined as the percent difference between observed versus expected T4 concentration calibrator solutions containing...Precision of the T4 method in the AxSYM immunoassay analyzer was good (<10%) to excellent (<5%) at T4 concentrations ranging from low (3.4 µg/dL) to high (18.4 µg/dL)....Although the value we obtained for the analytical sensitivity...”35

In summary, it can be noted that the motivating force to clarify a patient's biological health pattern by means of scientific methods comprises a responsibility to protect the patient's biological integrity, including exactness in relation to the method, equipment and procedure in achieving a laboratory test result. Each subcategory includes specific qualities. The biological material as an object of analysis is well defined. Methods, instruments, and reagents are essential to analyze the ‘object’. They must be specific for the purpose, have certain biochemical and physical qualities, reference capacity, and an advanced control system. The procedure of analysis is described clearly step by step with specific quality requirements. The quality of analysis is examined from a method-of-analysis-related and biomedicine-related point of view, including such qualities as analytic and diagnostic specificity and sensitivity, precision, correlation, interference, etc.

CONFIGURATION OF FACTS IN CLS

The reason for defining CLS has been born from the need to develop the work, and the need to define the knowledge base for a specific professional body, that is to say MTs. An aim of this study thus became to create clarity in CLS as a science. In order to be able to capture that ‘something’, the ‘really real’ configuration of facts, that could lead to the adoption of the science and its origin, the study has been characterized by an open view on knowledge and reality.

The configuration of facts that has emerged by means of a latent content analysis of certain selected articles from the journal Clinical Laboratory Science expresses the essence and inner patterns of CLS. The person/the patient is the origin within CLS and he/she is seen from a holistic point of view and from a biological point of view. The unifying force is the encounter and the contact with the patient, as well as the relationship to which the patient submits to the professional, often the specimen. The goal-orientating force is the patient and his experienced, total and objective biological health. Elucidating the patient’s biological health pattern is what constitutes a primary motivating force. Other forces that emerge set in motion activities and processes in order to help the patient in the best way. What is essential in CLS is one’s regard for a human’s integrity from a holistic and a biological point of view, reverence for and care of the patient, and his/her health including a responsibility for safeguarding the biological integrity of a patient.

The statement that the idea of a human within CLS is synonymous with that to be found in caring science is not in total agreement with the configuration of facts that have appeared in the journal Clinical Laboratory Science. Knowledge about the biological human is predominant. It can be noted that knowledge about a human from a holistic perspective and about the encounter with the human/the patient in a clinical laboratory context is imperfect. This appears clearly in the subcategory ‘the patient’s desire to meet the professional’. Does this indicate that researchers, educators, and all persons involved in a clinical laboratory context have not opened their eyes to the whole task?
Health should be seen as a part of life and not merely as the result of biological analysis. The laboratory examination and information that ensues and that charts the biological health pattern, is to be seen in relation to the patient’s health viewed as a whole. Knowledge from CLS can serve patients and facilitate freedom of choice for the patient, starting from an increased awareness about the relation of health hazards to his/her biological health pattern. The need for laboratory professionals to safeguard each patient’s biological health and biological integrity, by reliable laboratory examination performance is seen in the demands for quality, which characterize the entire bioanalytical processes.

Whether CLS is based on an interdisciplinary or a multidisciplinary foundation, has not been thoroughly discussed. Doig states in the Clinical Laboratory Science lead article in 1988 that the science is CLS and not sciences since CLS is more than a collection of various sciences. She does not take a position concerning multi-disciplinary or interdisciplinary science but, instead, gives a viewpoint for a science of its own. Hentinen points out that training in the option CLS should be multidisciplinary. My interpretation in the study of the paradigm of Medical Laboratory Technologists (MT) 1988 is that professionals put into practice interdisciplinary knowledge in the exercise of their profession.

Representatives of CLS endeavor to find an autonomous science of their own as a basis for the practical work. This is seen in the possibility to study this science, in the scientific journal, and in the effort to carry out basic research and development models. The scientific paradigm is weak in that disagreement exists concerning the knowledge base. An autonomous science contains a unique theoretical core, based upon its own basic motive and can never constitute a series of reduced scientific theories or realities, but it is a unique reality where a unique pattern emerges. Basic research, which is not directly connected to economic activity and vocational training, is needed in order to discover the unique knowledge pattern in a science without being influenced by the complexity and the multi-disciplinary application of knowledge in practice. By developing knowledge within the fundamental research and establishing it through applied research and development work, the new knowledge reaches an acceptance among the people involved in the practical work. The issue of whether CLS is an autonomous science or whether it is founded on an inter-disciplinary or a multi-disciplinary basis is not answered in this study.

According to Fawcett and Downs certain issues have to be borne in mind in the development of the science. Is the phenomenon of interest? Does it have a relevance in a practical task? Is it possible to implement the innovations that may possibly be developed? Are the innovations equal in all respects with the ‘clients’ expectations? Do the innovations result in favorable results, etc.? In the studies of clinical laboratory work it can be noted that there are phenomena and problem situations, which no one deals with because they do not ‘belong to their area of competence’. An example is the phenomenon related to collecting of specimens/examination from the patient’s point of view.

As for the development of methods in the bioanalytical process, research regarding the specificity and sensitivity of laboratory diagnostics in relation to various states of ill-health falls within the scope of clinical laboratory medicine. Proposals for research objects within CLS and clinical laboratory work are shown in Table 1. Knowledge is given its significance by means of the context. Research and knowledge development are absolutely necessary within the metatheoretical, theoretical, and technological levels of CLS in order to arrive at a body of knowledge, which will be able to serve the whole of clinical laboratory work.

Without genuine interest and care for the patient the researcher, educator, or practitioner cannot develop qualitatively good clinical laboratory activities. In order to be able to keep the wording of one’s promise; “I promise to put into practice my knowledge of CLS for the welfare of mankind and also to work for the development of clinical laboratory work”, research and development work for the whole field of activities should be encouraged. The findings of the study are discussed in the light of the starting points of the theory of science and lead into the following nine hypotheses about CLS:

- The person/patient is the origin in CLS.
- The encounter and the relationship is a unifying force in CLS.
- The patient’s health is the goal-orienting force in CLS.

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<th>Table 1. Clinical laboratory science divided into systematic and applied science</th>
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<td><strong>Clinical Laboratory Science</strong></td>
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<td><strong>Systematic</strong></td>
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<td>Motives and basic values</td>
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• Clarification of a patient’s biological health pattern is the motivating force in CLS.
• The core of meaning in CLS comprises respect for a person’s/patient’s integrity from the holistic and biological perspectives, reverence for and care of the patient and his/her total, experienced, and biological health including responsibility to protect the patient’s biological integrity.
• CLS studies interdisciplinary motives, develops concepts, models and theories.
• CLS studies specific qualities in a person’s/patient’s biological health pattern in his/her prenatal development stage, during his/her whole lifetime and even post mortem.
• CLS studies qualities concerning the encounter between the patient and the professional and qualities concerning the relationship to a patient’s specimen.
• CLS studies goals, methods, and conditions in the context of a specific caring process, caring technology, and bioanalysis.

The formal requirements that are placed on research and its findings are that they shall be able to be considered valid and agree with generally accepted requirements for scientific objectivity. In natural science and quantitative studies the results are judged among other things, on the basis of criteria such as probability, reliability, and validity.37 The appropriateness of qualitative research methods should be examined from other aspects than the ones just cited.38,41,43 Eneroth says further that while qualitative research methods strive to find a concept (a connected whole of qualities) on the basis of observations, quantitative research methods try to find certain observations in relation to a given concept to measure the degree/extent of its appropriateness for the phenomenon.38 Burns points out that a qualitative study should be examined in relation to its descriptive clarity and vividness, its methodological congruity, its analytical precision, its theoretical connection, and heuristic relevance.42 Larsson has proposed the criteria awareness of perspective, internal logic, and ethical value, wealth of meaning, structure and theoretical growth, discourse, and heuristic value, as well as empirical foundation for the evaluation of qualitative research.43 The critical discussion of this study is not included in this article. It was principally carried out in accordance with Larsson’s criteria on the grounds that these criteria are the latest ones to have emerged in research methodology.

The purpose of the present study was to create clarity in CLS as a science of its own. This has been achieved by means of capturing and describing facts and qualities, and thereafter presenting fundamental hypotheses in CLS. The results of this study give a thought structure for continued development and deepening within the theory and practice of CLS.

ACKNOWLEDGEMENT
The study upon which this article is based was originally published as a Master’s Thesis by the author.

REFERENCES

References continued on page 115.
A Procedure for the Detection of Stealth™ Adulterant in Urine Samples

SANDRA VALTIER, JOHN T CODY

Stealth™ is an adulterant that is advertised as not only preventing a positive drug test in urine, but also to be undetectable by currently available adulteration testing. It has previously been described as a peroxidase and peroxide that is added to urine for the sole purpose of preventing a positive drug test. The product was found to have a significant impact on the ability to detect several drugs of abuse, however, detecting the presence of the adulterant in urine had not yet been reported. A simple procedure to detect the presence of this adulterant in urine was developed. This simple color test procedure using commercially available reagents commonly used in clinical laboratories is based on the use of a chromogen to detect the peroxidase reaction in urine samples. If Stealth is present in the urine, the test sample will show an immediate color change from clear to dark brown. This qualitative test can also be adapted for use with a spectrophotometer or autoanalyzer.

ABBREVIATIONS: GC/MS = gas chromatography/mass spectrometry; LSD = lysergic acid diethylamide; PCP = phencyclidine; THC-COOH = 11-nor-delta-9-tetrahydrocannabionol-9-carboxylic acid; TMB = 3,3',5,5'-tetramethylbenzidine.

INDEX TERMS: adulteration; peroxidase detection; Stealth.


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Adulterants have always posed a problem in drug testing laboratories. In the past, many of these adulterants were easily detected in urine either by appearance, smell, pH or specific gravity measurements. In more recent years, the substances ingested or added to urine to prevent a positive drug test have become more difficult to identify and detect. Some of the more commonly used products include the fixative glutaraldehyde (UrinAid and Clear Choice), strong inorganic acid (Amber-13 and THC-Free), and strong oxidants such as nitrite (Klear, Whizzies, and Randy's Klear) and chrome (Urine Luck, LL 418, Sweet Pea's Spoiler, and Randy's Klear II). These adulterants were designed specifically to avoid detection of illicit drugs in urine.

One of the newer adulteration products, Stealth, was reported to consist of two vials, one containing a powder (peroxidase) and the other vial containing a liquid (peroxide). Combining the contents of both vials results in a strong oxidation potential, capable of oxidizing many compounds including several drugs and drug metabolites. The peroxidase catalyzes transfer of electrons between peroxide and another compound. This coupled reaction mechanism is used as the basis of a number of different clinical laboratory tests, e.g., cholesterol, glucose, etc. There are a number of commercially available assays designed to detect peroxidase activity, however, they are not routinely used to assess samples for adulteration. Often times, laboratories that perform drug screening assays are unaware of the various adulterants, detection methods, or their effects on the assay. Adulterants often have varying effects on different drugs-of-abuse testing assays. Even when there is reason to believe a sample has been adulterated, chances are that most clinical laboratories are not equipped with the appropriate materials to test for a specific adulterant.

In many cases, laboratory tests have been developed to detect the presence of some of the more commonly used adulterants and in some cases, manufacturers have designed test kits for use on autoanalyzers to detect the active component of these adulterants. However, most of the test kits provided for these purposes are designed for high volume drug testing laboratories. An automated test for detection of peroxidase will more than likely be available in the near future; however, for the small volume or clinical laboratories doing relatively few drug tests, purchasing a test kit for a few samples may prove to be unattractive due to the cost. A manual procedure using commercially available reagents for the detection of Stealth in urine was developed as part of this study. The color test is a simple and inexpensive procedure that can quickly and easily be performed in nearly any laboratory.
MATERIALS AND METHODS

Materials

TMB (Tetramethylbenzidine) Substrate Reagent Set for detection of peroxidase activity was obtained from Pharmingen and horseradish peroxidase (1,100 units/mg) was obtained from Sigma. Clinical dipsticks (Multistix SG) used for testing the samples were from Bayer Corp. Stealth was obtained from the supplier and provided to these investigators by the Research Triangle Institute and the Air Force Office of Special Investigation. Drugs were obtained from the following sources: Sigma [amphetamine, phencyclidine (PCP), morphine, morphine glucuronide, lysergic acid diethylamide (LSD), secobarbital, 11-nor-delta-9-tetrahydrocannabinol-9-carboxylic acid (THC-COOH)]; Alteich (benzoylcegonine, LSD, PCP); Radian (secobarbital, LSD); and Research Triangle Institute (THC-COOH). Immunoassay reagents for THC metabolite, cocaine metabolite, opiates, barbiturates, PCP, and amphetamines were OnLine reagents from Roche Diagnostics and CEDIA from Microgenics. LSD immunoassay reagents used were EMIT II from Behring and CEDIA from Microgenics.

Methods

Sample Preparation.

Drug free urine (no preservatives) was split into two portions. One was used as the negative control and the other was spiked with the drugs listed above in the Materials section. The spiked urine was further split into two portions, where one was used as the positive control and the other portion had Stealth added. The Stealth package contains two microcentrifuge plastic vials, one containing a powder (peroxidase) and the other containing a liquid activator (peroxide). As per Stealth package directions, the powdered catalyst is added to the empty sample cup, approximately 60 mL of sample liquid (urine) is added followed by the addition of the liquid activator and the sample is stirred briefly. (Note: for experimental purposes, smaller volumes of urine were prepared using proportionate portions of each vial).

Reagent Preparation

Horseradish peroxidase at concentrations ranging from 0.0002 to 0.1 mg/mL prepared in 0.1 M phosphate buffer, pH 7.0 were used as control samples. As per product insert, the TMB working solution was prepared by mixing equal volumes of Substrate Reagent A (hydrogen peroxide in a buffered solution) and Substrate Reagent B (3,3’,5,5’-tetramethylbenzidine in organic solvent).

Procedures

Test tube The test was performed by adding 10 µL of urine to a test tube containing 50 µL of TMB working solution in 500 µL of 0.1 M phosphate buffer (pH 7.0). The sample was mixed and observed for an immediate color change.

Microplate 100 µL of sample was pipetted into a microplate test well, followed by the addition of 100 µL TMB working solution and sample observed for a color change. Note: The normal procedure for these assays is to add acid to stop the reaction after a specified incubation period followed by measurement of the sample absorbance at a specific wavelength (450 nm). Addition of the acid not only stops the enzyme reaction, it changes the color of the complex to yellow. This procedure was modified by not adding the acid; thus the only samples that turned yellow were those that had strong redox potential.

Spectrophotometer: Peroxidase activity was monitored on the Beckman DU Spectrophotometer. Using the wavelength scan program, the instrument was first blanked against phosphate buffer. 10 µL sample was added to a spectrophotometer cuvette containing 50 µL TMB working reagent (TMB peroxide solution 1:1 v/v) in 500 µL 0.1 M phosphate buffer (pH 7.0). The sample and working reagent were mixed and immediately monitored. Spectrophotometer parameters used were: 10 scans per sample, interval time of 60 seconds, scan from 260 to 800 nm. Peroxidase activity was detected by monitoring peaks at 650 and/or 450 nm.

RESULTS AND DISCUSSION

Detection of peroxidase in samples was accomplished using 500 µL of 0.1 M phosphate buffer, pH 7.0 and 50 µL of the reagent mixture. Following the addition of sample to the reagent mix, the mixture was observed for an immediate color change. Horseradish peroxidase concentrations of 0.001 and 0.0002 mg/mL (1.1 and 0.22 units respectively) were monitored and compared to the activity seen in the negative, drug positive, and adulterated urine. No color change was seen for the negative or drug positive urine controls. The presence of Stealth was easily detected in the adulterated urines. In all cases, the color change observed for the adulterated urine was rapid and dramatic from clear to dark brown (Photo 1).

Results for the microplate assay were comparable to the test tube assay where all Stealth adulterated samples and peroxidase controls showed a dramatic color change to dark brown. Peroxidase activity in samples was also monitored using a spectrophotometer. Positive drug control, negative control, and Stealth adulterated urine results were based on the relationship between the sample
absorbance and the absorbance of the peroxidase control. The absorbance and wavelength of peroxidase activity in samples for the spectrophotometer were established by using the parameters described earlier. Evaluation of the spectral data showed the absorbance maxima associated with TMB following reaction with hydrogen peroxide in the presence of peroxidase were 450 and/or 650 nm. Initially, following a single electron transfer, TMB forms a complex that absorbs at 650 nm. Transfer of another electron results in an increase in absorbance at 450 nm with corresponding diminution of the peak at 650 nm. The absorbance of the Stealth adulterated sample was compared and found to show rapid increase in absorbance at 450 nm. When diluted, the Stealth adulterated samples showed the characteristic initial absorbance at 650 nm followed by formation of a peak at 450 nm with corresponding decrease in the 650 nm peak. It was demonstrated that low concentration of peroxidase produced a peak at 650 nm but, unless the amount of enzyme was high, there was little or no formation of the peak at 450 nm. The peak absorbance of adulterated samples was high enough to leave no question of the presence of Stealth in the urine sample. This dramatic difference in activity was used as the basis for the qualitative assay.

Because peroxidase activity can result from blood or bacterial contamination, 167 urine samples from the clinical laboratory that tested positive for blood and/or bacteria by clinical dipstick were tested for peroxidase activity using the color test procedure. Most samples showed no color change at all; the few that did, developed a faint blue-green tint. However, the blue-green color from these samples was easily distinguished from the dark brown color seen in samples adulterated with Stealth. Whole blood and hemolyzed blood were also used to directly assess the pseudoperoxidase activity of hemoglobin. These samples, along with the two clinical samples that had shown slight color development were monitored by spectrophotometer. No absorbance was seen for any of these samples at 450 nm under the experimental conditions described above. These results demonstrate that the possibility of getting false positives from samples containing blood and/or bacteria when using the parameters described is unlikely.

Horseradish peroxidase in buffer stored in a refrigerator has an extended shelf life, however, the stability of Stealth in urine samples is, to this date, unknown. In reality, there may be no predictable stability for peroxidase in urine samples. Peroxidase activity changes over time in individual samples. For example, one sample adulterated with Stealth was monitored on the same day. 15 days, and one month after Stealth was added. At 15 days, peroxidase activity showed a slight decrease; however after approximately one month, the sample showed no peroxidase activity. Refrigeration or freezing will help to prevent degradation, but may well depend on the individual sample matrix. Enzyme activity can be affected by many different variables that cannot be changed or controlled in random urine samples.

Evaluation of peroxidase controls in urine required considering the potential effect of sodium azide, a commonly used preservative in urine control samples, on the enzyme activity. To test the effects of the azide on peroxidase activity, 100 µL of 0.01% sodium azide in urine was added to phosphate buffer containing 0.001 mg/mL peroxidase. After the addition of TMB reagent, the sample was scanned from 400 to 800 nm. Sodium azide had a significant negative effect on peroxidase activity with absorbance seen at 450 nm; therefore, urine control samples containing this preservative cannot be used to control this assay. Controls must either be prepared fresh or be in a stable and predictable matrix such as a buffer.

Parameters normally used to assess sample adulteration did not reveal any significant changes of the urine samples following addition of Stealth. The color of the urine did change to a darker amber-brownish shade after addition of Stealth; however, the color change was not significant enough to warrant suspicion and there was no change in odor of the adulterated sample. Several other parameters were measured before and after adulteration of these samples. Specific gravity, pH, creatinine, urea, and chloride in each of the samples were measured over time (0, 24, 48, 72 hr and 7, 14, 21 days). Urea is a denaturant capable of inactivating peroxidase over time by changing the structural integrity of the enzyme. Chloride can have an effect on pH by reacting to produce hydrochlorous acid. There was little or no change in either urea or chloride measurements in the adulterated samples. The pH of the adulterated samples were consistently lower than the unadulterated, but still within pH range commonly seen in the clinical laboratory. Little or no differences were seen in specific gravity and creatinine results. Clinical dipstick results showed strong positive readings for glucose, blood, and nitrite in all samples adulterated with Stealth (Table 1). It should be noted the instructions with the Stealth adulterant indicate it should not be used for physicals, which would involve clinical testing. A strong positive for glucose, blood, and nitrite in a single clinical sample is unusual and might raise the veil of concern that the sample is contaminated with this adulterant.

| Table 1. Physical effects of Stealth on urine |
|-----------------|-----------------|
| **Urine**       | **Urine + Stealth** |
| pH              | 5.264           | 5.135          |
| Sp. Gr.         | 1.011           | 1.012           |
| Creatinine      | 43.3 mg/dL      | 41.2 mg/dL     |
| Dipstick*       |                 |                |
| Blood           | Neg             | +++             |
| Glucose         | Neg             | +++ (>2,000 mg/dL) |
| Nitrite         | Neg             | Positive        |

* Dipstick – Bayer Multistix SG
The impact of the adulterant on a sample can differ considerably depending on its methodology or on the assay used. The effect of Stealth was evaluated in several studies, including one reported by Davis that indicated this adulterant caused the screening assay for the THC acid metabolite (THC-COOH) to yield a negative result when the drug metabolite was actually present. The effect of Stealth on immunoassays for several drugs-of-abuse was studied in this laboratory (Table 2). Stealth had no effect on the assays for amphetamines, PCP, benzoylecgonine (cocaine metabolite), or barbiturates. It did cause samples positive for THC-COOH and opiate (morphine) to screen negative by both the OnLine and CEDIA immunoassays. Samples positive for LSD were also negative by EMIT II and CEDIA immunoassays following adulteration with Stealth. The THC-COOH and LSD positive controls adulterated with Stealth gave values that were comparable to the negative urine control. Although the result for the sample containing 2500 ng/mL morphine yielded a negative immunoassay result, some measurable activity was seen (approximately 30% of positive control value). Samples spiked with higher concentrations of opiates (6,000 ng/mL) did test positive, indicating the effect of Stealth on the immunoassays for opiates is dependent on drug concentration. Upon confirmation testing of these samples by gas chromatography/mass spectrometry (GC/MS), THC-COOH, morphine, codeine, and LSD were undetectable. Subsequent evaluation of opiates showed the initial interference with morphine/codeine confirmation could be reversed by addition of disulfite.

CONCLUSION
With new adulterants being developed at an alarming rate, it has become increasingly difficult to keep up with the development of methods to detect these products. Once a method is developed to detect presence of a specific adulterant, it will more than likely be provided commercially as a kit that may be more suitable for a high volume drug testing or toxicology laboratory. A color test using commercially available reagents for the detection of peroxidase was developed in our laboratory and found to be a reliable method in detecting Stealth in urine. The simplicity of the assay makes it ideal for laboratories that would test only a small number of samples. Using the reagents used for the manual procedure, however, the test could be adapted to most automated chemistry analyzers. The procedure is presented here to provide laboratories with a quick and inexpensive method for the detection of Stealth in urine.

Most assays designed for the analysis of peroxidase activity are designed to detect relatively small amounts of activity since normal urine samples have no activity. This sensitivity makes them valuable in the laboratory for routine assays but such sensitivity is not necessary when determining the presence of Stealth. The reduction-oxidation reaction of TMB involves first a single electron transfer that yields a maximum absorbance at 650 nm. This complex has a very faint blue color at neutral pH. If there is sufficient redox potential in the sample, the TMB complex undergoes another electron transfer to yield a complex with an absorbance maximum at 450 nm. Monitoring of the reaction using a scanning UV spectrophotometer showed the development first of a peak at 650 nm. This peak continued to grow until it eventually began to diminish with the appearance of a new peak at 450 nm. Under ordinary conditions, assays are conducted by allowing the reaction to occur for a specified amount of time at which point a strong acid is added. The purpose of the acid is to stop the reaction to accommodate reading all samples at a later time. Another consequence of the acid is to drop the pH of the reaction mixture which changes the absorbance to 450 nm. In the procedure described in this study, the pH was maintained at 7.0. This allowed the reaction of samples containing components that react with the reagent to do so but the resulting reaction gave absorbances in the 650 nm range. The presence of Stealth, owing to its high redox potential, quickly changed the solution to have a significant absorbance at 450 nm. Since the pH was maintained at 7.0, the only samples that demonstrated the absorbance peak at 450 were those adulterated with Stealth.

ACKNOWLEDGMENTS
Many thanks to Stephanie Martin, Rene Ramon, Ed Hubster, and Dan Castro for assistance in preparation and analysis of samples. Thanks also to Willford Hall Medical Center clinical laboratory personnel for creatinine, urea, chloride, glucose, blood, and nitrite measurements and also to Research Triangle Institute and the Air Force Office of Special Investigation for providing the Stealth used in this study.

The views expressed in this article are those of the authors and do not reflect the official policy of the Department of Defense or other Departments of the U.S. Government.

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Table 2. Effect of Stealth on drugs of abuse

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<th>OnLine</th>
<th>CEDIA</th>
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<tr>
<td>THC</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Cocaine</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Opiates</td>
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<td>–</td>
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<tr>
<td>Barbiturates</td>
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<td>PCP</td>
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<td>+</td>
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<tr>
<td>Amphetamine</td>
<td>+</td>
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<tr>
<td>LSD*</td>
<td>–</td>
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</table>

* LSD tested by EMIT II in place of Online and CEDIA immunoassay reagents
REFERENCES


Fetal Fibronectin (continued from page 98)


Knowledge Fields and Inner Patterns in Clinical Laboratory Science (continued from page 110)

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Developments in Component Therapy: Novel Components and New Uses for Familiar Preparations

MICHELLE S WRIGHT-KANUTH, LINDA A SMITH,

Over the years, the significant role of blood components in treating certain diseases or conditions has been recognized. The use of these components has expanded as patients undergo chemotherapy for bone marrow ablation and require short-term component support. On the other hand, these transfusions can cause reactions ranging from mild to severe. Despite advances in serological testing for infectious disease agents, the risk of infectious complications from transfusion still remains. In addition, newly identified agents that may be transmitted via transfusion are constantly identified.

The cellular components most people are familiar with include packed red blood cells (PRBC), washed PRBC, leukoreduced PRBC, and pooled or apheresis platelets. Plasma products such as fresh frozen plasma (FFP) or cryoprecipitated anti-hemophilic factor (CRYO), on the other hand, may not be as familiar. As our understanding of how the immune system functions and as technology has progressed, specialized components or manufactured products such as blood substitutes have been advanced as remedies to some of the complications with component transfusion or to meet the ever-increasing need for these products.

In this article we will focus on some of the new uses of common components and uncommonly used or newly developing components. We will discuss their origins, composition, and the conditions or diseases they are used to treat. These components include:
- donor leukocyte infusions
- dendritic cell vaccines
- blood substitutes
- novel platelet products and substitutes
- intravenous immunoglobulin (IVIG)
- fresh frozen plasma and cryosupernatant in therapeutic plasma exchange.

The variety of products and conditions reflect the ever-expanding role of immunohematology in the treatment of disease.

ABBREVIATIONS:
AML = acute myeloid leukemia; APT = antigen presenting cell; CML = chronic myeloid leukemia; CRP = cryoprecipitate reduced plasma; CRYO = cryoprecipitated anti-hemophilic factor; DC = dendritic cell; DCLHb = diaspirin cross-linked hemoglobin; DCGLHb = diaspirin cross-linked hemoglobin; DLI = donor lymphocyte infusion; DMSO = dimethylsulfoxide; FFP = fresh frozen plasma; GVHD = graft-versus-host disease; GVL = graft-versus-leukemia; HbOC = hemoglobin-based oxygen carrier; HLA = human leukocyte antigens; IPMs = infusible platelet membranes; IVIG = intravenous immunoglobulin; LEHb = liposomes containing hemoglobin; PAP = prostatic acid phosphatase; PBMC = peripheral blood mononuclear cells; PEG = polyethylene glycol; POE = polyoxyethylene; PRBC = packed red blood cells; TPE = therapeutic plasma exchange.

INDEX TERMS: blood and platelet substitutes; blood component therapy; blood components; novel blood components.


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Michelle S Wright-Kanuth PhD is the Focus Component Therapy guest editor.

Focus Continuing Education Credit: see pages 125 to 127 for learning objectives, test questions and application form.

LEARNING OBJECTIVES
At the end of the article the learner will be able to:
1. Identify the major diseases treated with each of the components discussed.
2. Discuss the preparation of DLI and why CD4 cells are retained, while CD8 cells are depleted.
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3. Describe the general process of making a dendritic cell vaccine.
4. Describe the different types of red cell substitutes and differentiate between them.
5. Explain at least two of the possible ways in which intravenous immunoglobulins may interact with the immune system.
6. Explain why cryoprecipitate reduced plasma is effective in treating thrombotic thrombocytopenia.
7. List and describe the platelet products under development.

The role of the routine blood bank in providing therapeutic products has changed dramatically within the past five years. More emphasis is being placed on new and improved blood components and alternate uses for products. In addition, new sources for blood products have been researched, particularly in the field of blood substitutes. A review of the state of the art in some of these areas is timely. Donor lymphocyte infusion (DLI) is a new use for the lymphocyte fraction obtained from apheresis. Blood substitutes are coming of age and several sources of hemoglobin based oxygen carriers are currently in Phase III clinical trials. A promising immunotherapeutic approach to cancer therapy is dendritic cell vaccines. A number of dendritic cell vaccines are in Phase I and II clinical trials. FFP and cryosupernatent (the supernatent left after cryoprecipitate is made) are being used in therapeutic plasma exchange (TPE). Intravenous immunoglobulin (IVig) has been used for over ten years; however, new applications for the use of this product are being studied. Cryopreservation and lyophilization of platelets and platelet substitutes are all being studied as remedies for the short shelf life of platelet components. These, then, are the areas that will be explored here.

DONOR LYMPHOCYTE INFUSION

Patients with chronic myeloid leukemia (CML) are offered the opportunity of a cure with allogeneic hematopoietic stem cell transplantation. Disease-free survival rates at five years reach 70% in transplanted patients. The cure is most likely partially due to the graft-versus-leukemia (GVL) effect mediated by donor-derived T lymphocytes. The GVL effect is primarily due to the derivation of the T cells from a healthy donor individual. The T cells in CML patients have been compromised by the tumor escape mechanisms that facilitate the growth of the CML in the patient.1 When transplanted patients relapse after achieving remission, the administration of donor T lymphocytes is considered the initial response. DLI is achieved by collecting the transplant donor’s white blood cells through apheresis. The donor cells are treated to deplete CD8+ T cells or other potentially harmful donor cells to prevent graft-versus-host disease (GVHD). The CD4+ T cells are necessary for the GVL reaction to occur.2

Various studies have shown that optimal numbers of CD4+ cells are required to induce remissions. Mackinnon and colleagues studied limiting the T cell dose given to induce remission. They found that most patients achieved remission at a dose of $1 \times 10^7$ T cells/kg body weight or above. However, the incidence of GVHD was greatly reduced at the lowest remission T cell dose of $1 \times 10^7$/kg.3 Mandigers also studied a target T cell dose along with CD8+ cell depletion and saw similar results.4

Because the treatment of early CML relapse with DLI after stem cell transplant induces remission in the majority of patients studied, it is becoming an important treatment option. There is also promising data indicating that the use of DLI will affect remissions in relapsed acute myeloid leukemia (AML) patients.5 These remissions may not be as common as those for CML patients, but some patients have stayed in remission for up to two years. In addition, DLI has been shown to have a graft-versus-myeloma effect in multiple myeloma patients.6 As DLI becomes an increasingly documented and effective treatment, it will likely become the standard of care for such patients. Undoubtedly, blood centers and blood banks will be involved in the future procurement and cell manipulation of the DLI and in DLI storage and thawing, as they are becoming similarly involved in stem cell transplantation.

DENDRITIC CELL VACCINES

Dendritic cells (DCs) are the most potent of the antigen presenting cells (APCs). DCs can be found in most organs, the T cell areas of secondary lymphoid tissues, and circulating in the peripheral blood. During a normal immune response, the APCs phagocytize and process antigen and then present it along with MHC Class II molecules. The individual’s T cells specific to that antigen will bind to the APC through the presented antigen and MHC molecule. The T cell will then be stimulated to respond and initiate the primary immune response. It is known that many tumor-associated antigens are weak immunogens and do not stimulate the immune response well. This lack of immunogenicity may be due to tolerance to self-antigens that is normally induced in the immune system during the education of T cells in the thymus.7 Because it appears to be difficult to encourage natural antigen presentation of tumor-associated antigens, several groups of investigators have tried exposing the patient’s DCs to exogenous sources of these antigens in vitro.

A phase I clinical trial was conducted in patients having prostate cancer. The investigators used mouse prostatic acid phosphatase (PAP) instead of the patient’s own PAP to stimulate DCs obtained from the patient by peripheral blood leukapheresis. The DCs and mouse PAP were incubated together overnight at 37 °C. The resulting antigen-treated DC vaccines were then reinfused into the patient. A T cell response to the self-PAP was then seen in 11 of 21 patients treated. Six of the patients showed stabilization of a previously progressing prostate cancer. No toxicity to the vaccine was seen.7

In another phase I clinical trial, solid tumors from children were reduced to single cell suspensions and cultured. The tumor cells were then lysed and the cell suspension, presumably containing tumor-associated antigens, was incubated with DCs collected from the patient by peripheral blood leukapheresis. The resulting DC
Hemoglobin-based oxygen carriers (HbOCs) are being studied as oxygen-carrying substitutes for blood cells. They are purified cell-free hemoglobins, where the globin portion of the molecule has been modified chemically by conjugation, cross-linking or polymerizing. Modification increases the oxygen releasing ability of the hemoglobin. HbOCs fall into three categories: surface modified hemoglobins, cross-linked hemoglobins, and polymerized hemoglobins. Surface modified Hbs have molecules attached to the lysine residues on the surface of the hemoglobin molecule. Such attachments can be made using polyethylene glycol (PEG) and polyoxyethylene (POE). Small molecules stabilize the hemoglobin and increase its molecular weight. Two of these products, PEG-Hb and pyridoxyl Hb-POE, are currently in clinical trials. Cross-linked Hbs consist of Hb subunits attached to each other using internal covalent bonds. Diaspirin cross-linked hemoglobin (DCLHb) is produced by using a reagent that cross-links the lysine residues in the Hba chains. These cross-links delay clearance of the free Hb from the circulation by stabilizing the Hb tetramer. Most of the clinical studies have been done using human DCLHb. DCLHb trials were halted in 1999 due to increased mortality in some trial enrollees. Polymerized Hbs are cross-linked at lysine residues with glutaraldehyde, which then has active aldehyde groups at both ends of the molecule. This allows polymers of Hb tetramers to form. Human polymerized Hb is currently in clinical trials, as is a polymerized bovine Hb product. The bovine HbOC has completed phase III clinical trials and has been approved in South Africa for treatment of perioperative anemia in adult surgical patients.

Perfluorocarbon-based red cell substitutes consist of carbon backbones highly substituted with fluorine. While they can dissolve large amounts of oxygen, the perfluorocarbons themselves are not water-soluble. To deliver them intravenously, they must be emulsified. This is accomplished using a surfactant such as a phospholipid. Perfluorocarbons were the original red cell substitutes and have potential due to the ability to synthesize them from non-biological sources. This not only allows large-scale production, but also eliminates the transmission of diseases to recipients. The perfluorocarbons are biologically inert; however, the phospholipids required to emulsify them are not, leading to complications when they interact with the immune system.

Three perfluorocarbons have entered clinical trials. The first to do so was marketed as Fluosol-DA and was licensed by the FDA in 1989. However, it was withdrawn from the market due to lack of sales. Oxygent, an emulsion of perfluorodichloroactane and egg yolk phospholipid with safflower oil, began clinical trials. However, its development has been discontinued. The only perfluorocarbon that remains in clinical trials is Oxygent, an emulsion of perfluoroctyl bromide and egg yolk phospholipid. Oxygent is being studied for use in perioperative hemodilution to allow more extensive hemodilution.

Hemoglobin-containing liposomes (LEHb) are formed using spheres of phosphatidylcholine to form a lipid bilayer that replicates the red cell membrane. Hb solution is then introduced inside the bilayer. Since this is not a cell-free Hb, some of the potential for toxicity is diminished. Replicating the cellular format also results in a longer half-life in the circulation than the perfluorocarbons and most of the HbOC preparations. LEHb does, however, have a higher affinity for oxygen than some of the other red cell substitutes. Standardizing the size of liposomes is also problematic.

Platelet products and substitutes
Platelets participate in primary hemostasis by initially adhering to the vascular subendothelium and then using interactions between glycoproteins on the platelet surface and fibrinogen to initiate aggregation with the eventual formation of a platelet plug. Patients with low platelet counts may have petechiae or ecchymoses and those with extremely low platelet counts are at risk for spontaneous hemorrhage.

Major indications for transfusing platelets include prophylaxis in inheritable conditions that result in thrombocytopenia or dysfunctional platelets and to end active bleeding in thrombocytopenic patients. A little over 50 years ago, the only sources of platelets were from fresh whole blood or platelet rich plasma. Since that
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In recent years platelet transfusion therapy has focused on the use of two products—random donor pooled platelets or apheresis platelets. Obtaining a ‘pooled platelet’ preparation is a two-step procedure. First, one unit of platelets is harvested from a unit of red cells. Then four to six of these individual units (from different donors) are ‘pooled’ together in a single pack to be given to a thrombocytopenic patient. Apheresis platelets, on the other hand, are those collected from a single donor using cell separator instrumentation. As blood cycles through the machine, platelets are removed and all other blood constituents returned to the donor. The amount of platelets collected with this procedure represents the equivalent of four to six units of random donor platelets. Leukoreduction filters can be used with either of these to remove the majority of white blood cells before infusion and therefore decrease the risk of sensitization to human leukocyte antigens (HLA), symptoms caused by production of cytokines in the stored PRBCs, or the risk of transmission of cytomegalovirus.

The risks associated with sensitization include development of alloantibodies to HLA antigens or to platelet-specific antigens. These antibodies may cause the patient to experience a febrile non-hemolytic transfusion reaction or become refractory to a platelet transfusion. A patient who is ‘refractory’ does not have the expected increment in the post-transfusion platelet count due to antibody-mediated destruction of transfused platelets. In some cases in which the patient has developed antibodies to HLA antigens and become refractory, apheresis platelets that are HLA matched to the patient’s antigens may be used. A summary of problems and biological risks associated with platelet transfusions are listed in Table 1.

Platelets have short shelf life and also develop changes in functional ability during storage. Even with the short shelf life, storage at room temperature increases the risks of bacterial growth. Over the past 40 years, unsuccessful attempts were made to cryopreserve or lyophilize platelets to overcome these problems and today the search for alternative ways of preserving platelets or creating platelet substitutes continues. Numerous criteria that novel platelet products or platelet substitutes should meet have been described in the literature and some of these are listed in Table 2. Platelets include: cryopreservation with or without synthetic additives, lyophilized platelets, photochemically treated platelets, infusible platelet membranes, and fibrinogen coated albumin microspheres.

Cryopreservation
Platelets suspended in dimethylsulfoxide (DMSO) at -80 °C have been preserved up to ten years and represent the ‘gold standard’ of preserved platelet products. During the thawing and post-thaw processing however, these platelets develop functional and morphologic defects. Although there is some loss of functional activity when compared to fresh platelets, cryopreserved platelets do demonstrate a reduced level of primary hemostatic activity. The numbers of platelets that are recovered is about 75% of the original number and they have a short circulation time in vivo.

Because of the complexities of storing, processing, and thawing frozen platelets, the current use is limited. Several studies have been done using a decreased concentration of DMSO with a platelet-stabilizing solution (ThromboSol™) to decrease problems such as clotting of the infusion set and platelet membrane destruction.

<table>
<thead>
<tr>
<th>Table 1. Biological risks associated with platelet transfusion</th>
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<tr>
<td>Alloimmunization (development of antibodies to HLA or platelet specific antigens)</td>
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<tr>
<td>- refractory state</td>
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<tr>
<td>- febrile non-hemolytic transfusion reactions</td>
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<tr>
<td>Bacterial, viral or parasitic contamination</td>
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<tr>
<td>- disease transmission</td>
</tr>
<tr>
<td>- septic shock</td>
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<tr>
<td>Immune system effects [uncommon]</td>
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<tr>
<td>- immunosuppression</td>
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<td>- graft-versus-host disease</td>
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<table>
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<tr>
<th>Table 2. Selected criteria for platelet substitutes or novel platelet products</th>
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<tr>
<td>Function hemostatically as ‘live platelets’</td>
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<tr>
<td>- attach to vascular surfaces</td>
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<tr>
<td>- provide a procoagulant surface</td>
</tr>
<tr>
<td>Avoid initiating consumptive coagulopathy or thrombosis</td>
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<tr>
<td>Not transmit infectious diseases</td>
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<tr>
<td>Be non-immunogenic</td>
</tr>
<tr>
<td>Have a long shelf life and simple storage requirements</td>
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<tr>
<td>Be easy to prepare</td>
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as decreased recovery and short circulation time that occur with current methods of cryopreserving platelets. This solution inhibits platelet activation pathways and protects against cold storage lesions. Results of these studies have shown higher recovery rates and longer survival times than with the 6% DMSO method as well as fewer processing steps. There are investigations under way to develop methods that do not require processing after freezing and can be directly infused after thawing.

**Lyophilized platelets**

Lyophilized platelets are created after treatment with a paraformaldeyde solution and then freeze-dried. Specific advantages of this product include storage measured in years instead of days, reduced storage space and true sterility. Once rehydrated, they appear to retain structural integrity and attach only to damaged subendothelial surfaces. They will also change shape and extend pseudopods in preparation for plug formation. Thus it appears that the rehydrated lyophilized platelets have hemostatic efficiency—measured by bleeding time—similar to that of fresh platelets; however this effect continues for only several hours.

**Infusible platelet membranes**

Infusible platelet membranes (IPMs) are manufactured from outdated platelet units in an attempt to provide a stable product that mimics the actions of the platelet-derived microparticles. Platelet derived microparticles (microvesicles) are the particles that form spontaneously from a platelet during collection and processing of components. They have been found in platelet concentrates, fresh frozen plasma, and cryoprecipitate. They appear to have the ability to function as a platelet—they are procoagulant active, adhere to vascular subendothelium, and enhance platelet adhesion to form a primary hemostatic plug. Studies have shown that the IPMs do retain some function of GP Ib receptor and bind to VWF and can initiate local fibrin formation, but much of the GP IIb/IIIa is lost. One application for IPMs may be in patients who are refractory to platelet transfusions and for whom finding HLA matched plateletpheresis donors is difficult. One problem appears to be a relatively short life (less than 24 hours) in vivo.

**Miscellaneous microspheres**

There are a number of products that use formaldehyde fixed platelets, liposomes, or 10% albumin spheres as a basis on which to coat fibrinogen or platelet membrane glycoproteins. Results from some of the pre-clinical trials show that these products appear to be able to enhance the adhesion of platelets and formation of aggregates but in vivo stability remains a problem.

**FOCUS: COMPONENT THERAPY**

**Contamination of platelets**

A peripheral but important issue with transfusion of human pooled platelets is the risk of transfusion transmitted diseases—especially bacterial and the associated potential for septic shock and death. While serologic tests for transfusion transmitted viruses such as hepatitis B have reduced the incidence of viral transmission significantly, there have not been concurrent advances for detecting bacterial contamination. Platelets stored at room temperature create an ideal incubation environment for growth of bacteria. Studies indicate that 1 in 2,000 to 1 in 3,000 platelet units are bacterially contaminated, with sepsis occurring with about 1/6 of the contaminated units transfused. Units at the end of the four to five day storage period are the most likely to be contaminated. Contamination can originate from occult bacteremia in the donor, induction of skin bacteria such as *Staphylococcus epidermidis* during phlebotomy, or contaminated collecting devices. Detection of contaminated units is difficult and a number of methods have been proposed to determine contamination prior to transfusion. These include examination of Gram’s stains of units at day four or five, or surrogate methods such as measuring low pH or glucose levels of units with a urine dipstick. The major disadvantage of these methods is that they are not sensitive and require large numbers of organisms for detection. One study showed that detection methods must be sensitive enough to detect 100 CFU/ml by day three of storage. Several researchers have evaluated an automated culture system which could detect organisms with concentrations as low as 10 to 100 colony forming units /mL in 9 to 26 hours. The results indicated that short-time culture in automated systems may be useful in screening platelet units for contamination. Methods used to prevent contamination have also been investigated. One method is use of a photochemical agent and ultraviolet light (UV) to inactivate bacteria and viruses in conventional platelet units. The chemical, in the presence of UV light, will bind to DNA to prevent transcription and replication. Studies have shown this treatment will inactivate high concentrations of bacteria and viruses without significantly affecting the hemostatic activity of the platelets.

**Intravenous immunoglobulin**

Once the fractionation of immunoglobulins was successfully performed in the 1940s, the use of immunoglobulins (especially gamma globulin) became an established method of providing protective, passive immunity for some diseases. However, intravenous administration was not possible because the method of preparation often resulted in a variety of patient side effects including anaphylaxis. During the 1980s and 1990s changes in manufacturing allowed fractionation of the product into IgG portions that could be solubilized and used intravenously.

Intravenous immunoglobulin (IVIG) is made from large pools of donor plasma (hundreds to thousands of donors). This polyclonal preparation contains 90% to 98% IgG and small amounts of IgA and IgM. Bacteria are removed by filtration and viral agents are inactivated by a variety of mechanisms. This pooling of donor
plasma provides a diversity of antibodies that have led to the use of IVIG for treatment in a wide spectrum of diseases. In contrast, monoclonal antibodies have a use that is limited to a specific disease. For example anti-tumor necrosis factor can be used as adjunct treatment for rheumatoid arthritis.

The mechanism of how IVIG works is not completely known. Studies with specific diseases and animal models have shown that the therapeutic action includes one or more of the mechanisms listed in Table 3. The most commonly recognized mechanisms appear to be those of competition for binding sites on the Fc receptors of phagocytic cells and the binding of anti-idiotypic antibodies (antibodies to human antibodies) to autoantibodies by attaching to the Fab portion of the immunoglobulin molecule.

IVIG was first licensed in the early 1980s to be used as treatment for primary immunodeficiency diseases characterized by hypogammaglobulinemia and/or recurrent infection. For individuals with these diseases, it provides a source of antibodies and decreases the incidence and severity of infections in this population. After its initial use as a replacement therapy, it was also found to have an immunomodulatory effect and its use expanded to include selective treatment for hematologic, inflammatory, and infectious diseases that have an immunologic component. The FDA has approved the use of IVIG for treatment of more than 30 disease conditions including primary immune deficiency, B-cell chronic lymphocytic leukemia, idiopathic thrombocytopenia purpura (ITP), pediatric human immunodeficiency virus infection, Kawasaki syndrome, and neuroimmunologic diseases such as Guillain-Barre syndrome and selected obstetric conditions. In addition, it has been approved for use in allogeneic bone marrow transplant patients to prevent GVHD as well as infections. The relative success of IVIG in many conditions, however, has also led to use in treating many other conditions for which it has not been approved.

One of the first conditions in which IVIG was recognized as effective treatment was ITP. In ITP the two major mechanisms for action of IVIG include blocking Fc receptors on splenic macrophages and reaction of anti-idiotypic antibodies with autoantibodies. It appears that more immediate effects are due to inhibition of the RES and the anti-idiotypic antibodies may function in a long term protective role. A study of antibody coated platelets showed that the Fc fragments of immunoglobulins in IVIG gave protection by inducing expression of an inhibitory receptor on effector cells. This decreased or prevented the clearance of the antibody-coated platelet. In another study, high-dose IVIG therapy accelerated clearance of autoantibodies but could only explain 20% to 40% of the decrease in autoantibody concentration after therapy. When ITP occurred in pregnant women the IVIG was also effective in decreasing platelet damage in the fetus.

Another obstetrically-related condition in which IVIG has been used is neonatal alloimmune thrombocytopenia (NAIT). In this disease, the mother develops antibodies against fetal platelet antigens, most commonly the Human Platelet Antigen 1a, formerly known as PL1. Infants with this condition are born with clinical indications of moderate or severe thrombocytopenia and may be at risk for intracranial hemorrhage. As with other fetal-maternal alloimmune conditions, the risk to the fetus and the severity of the condition can become more severe with each subsequent pregnancy. Once the condition has been identified, IVIG can be given to the mother during the pregnancy. IVIG crosses the placenta and provides protection to the fetus. It may also inhibit maternal immunoglobulin synthesis through a feedback mechanism or inhibit transport of the maternal antibodies across the placenta. This is effective in decreasing platelet destruction in 50% to 80% of cases. A study by Gaddipati linked the initial fetal platelet count to the subsequent efficacy of IVIG therapy. If the fetal platelet count was >20,000/microliter then approximately 89% of future counts were above that level. If the platelet count was <20,000 then only 51% had an increased count after the IVIG.

Although the use of Rh immunoglobulin (RhIg) has successfully reduced the number of cases of Rh (D) hemolytic disease of the newborn due to anti-D, there are some RhIg failures. In addition hemolytic disease of the newborn may be due to antibodies to other blood group system antigens. In cases where the maternal antibody is extremely high and intravascular transfusion is unable to be performed, IVIG has been used to decrease maternal antibody titer.

Because neonates have an immature immune system and may be at increased risk for infection, the use of IVIG in treating sepsis has also been studied. Studies as well as a meta-analysis of studies of IVIG use in treating neonatal sepsis showed that IVIG may be of significant benefit in addition to standard treatment for neonates early in the onset of sepsis but had minimal benefit when used prophylactically.

Autoimmune diseases are another area in which IVIG has been used. These diseases present challenges for treatment. One is bal-

### Table 3. Potential mechanisms of IVIG

- Binding to complement proteins
- Inhibition and regulation of cytokine action
- Interference with antigen recognition by T cells
- Activation of neutrophils
- Competition for binding to Fc receptors
- Interaction with superantigens
- Binding to autoantibodies
FOCUS: COMPONENT THERAPY

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Clinical Laboratory Science

Inhibiting the suppression of the immune system against the risks of infection. Another challenge is dealing with exacerbation or crises in the disease when the antibody titer reaches very high levels. IVIG has been useful in treating autoimmune diseases such as myasthenia gravis. The culprit in this condition is an autoantibody to acetylcholine receptors that interferes with nerve impulse transmission. It is characterized by weakness of voluntary muscles and affects both women and men of any age. Although drugs are the usual long-term therapy, IVIG is a temporary treatment to decrease antibody production. One study determined that there may be some efficacy in using IVIG as a replacement treatment for patients with Guillain-Barre syndrome who could not undergo plasma exchange.53

Kawasaki syndrome is a leading cause of acquired heart disease in North America and Japan. Its cause is unknown although an infectious agent has been suggested. It is a self-limiting disease that leads to coronary artery lesions.64 Therapy with IVIG along with aspirin during the first ten days of the illness decreases risk of coronary artery damage. There is some evidence to suggest that the IVIG may also decrease circulating cytokines that mediate much of the damage.

There are multiple studies of other possible applications of IVIG therapy in diseases with infectious or immunologic origins.54-56 In pediatric HIV patients who have hypergammaglobulinemia but the impaired ability to produce specific antibodies, IVIG was used to decrease episodes of acute pneumonia but unfortunately did not increase survival.64 Another study looked at whether IVIG could be used in treatment of acute rheumatic fever.55 Despite the underlying immunologic basis for acute rheumatic fever, IVIG showed no effect on clinical progress or other disease parameters. In another study IVIG was studied as a supplemental treatment in patients with sepsis and septic shock.65 Again there was no overwhelming improvement in those who received the IVIG, but it appeared to decrease morbidity and mortality in some patients when used as part of the treatment protocol.

COMPONENTS USED IN THERAPEUTIC PLASMA EXCHANGE

Fresh frozen plasma

Fresh frozen plasma (FFP) is the component created when plasma is removed from a unit of blood and frozen at −18 °C within eight hours after collection. It contains stable and labile coagulation factors, immunoglobulins, and proteins and has been used in treating a number of conditions (Table 4). One of the most common ways it is used is in therapeutic plasma exchange (TPE). TPE involves removal of a patient’s plasma and a return of the cellular elements in a liquid medium replacement. FFP is the preferred medium over crystalloids such as physiologic saline or albumin because it is not only a volume expander, but is also a source of proteins and immunoglobulins. Over the years, TPE has become accepted therapy for a number of diseases such as cryoglobulinemia, myasthenia gravis, Guillain-Barre syndrome, and thrombotic thrombocytopenic purpura (TTP).67-69 It has been used with varying degrees of success in diseases such as cold agglutinin disease, systemic vasculitis, chronic inflammatory demyelinating polyneuropathy, hemolytic uremic syndrome (HUS), and to remove high levels of antibody in pregnant women when uterine transfusion cannot be accomplished. Although TPE generally will not cure the underlying condition, the procedure will often temporarily alleviate symptoms by decreasing the concentration of the underlying problematic plasma component. Table 5 lists some of the specific components that can be removed by TPE.

The disease in which TPE has been used most successfully is TTP and this disease will be used as an example of how TPE may alleviate underlying conditions.

TTP is characterized by a pentad of symptoms including thrombocytopenia, microangiopathic hemolytic anemia, fever, neurological symptoms, and renal dysfunction. It may manifest as a single acute episode or a chronic relapsing condition. The cause of the disease is unknown but it may be triggered by a variety of conditions including pregnancy and infections. In TTP a combination of endothelial cell damage and platelet aggregation results in microthrombi and a consumptive thrombocytopenia. Research has shown that in contrast to the usual platelet plugs that are composed of platelets and fibrinogen, those in TTP are composed of platelets and ultra large multimers of vonWillebrand Factor (uLvWF).61,62 The presence of these uLvWF multimers led researchers to investigate why these multimers were present. Findings indicate it may be an absence of a vWF cleaving protein in the plasma of patients with TTP. Plasma exchange using FFP removes some of the multimers and provides a source of enzyme, however, the FFP itself remains a source of vWF.63-65 Although TPE treatments are successful in many cases, there were a number of patients who did not respond. The research of causes and the identification of vWF as a possible cause led to the use of another blood component in TPE—cryoprecipitate reduced plasma (cryosupernatant or cryo-poor plasma).63-66

Table 4. Indications for use of fresh frozen plasma

| Indications for use of fresh frozen plasma |
|-------------------------------|---------------------|
| Consumptive coagulopathies such as disseminated intravascular coagulation (DIC) |
| Multiple coagulation factor deficiencies |
| Liver disease |
| Dilutional coagulopathies such as those seen in massive transfusion |
| Thrombotic thrombocytopenia purpura (TTP) |
| Deficiencies of Protein C, Protein S |

Table 5. Specific components that can be removed by TPE

<table>
<thead>
<tr>
<th>Component</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelets</td>
</tr>
<tr>
<td>Proteins</td>
</tr>
<tr>
<td>Immunoglobulins</td>
</tr>
</tbody>
</table>

Deficiencies of Protein C, Protein S
FOCUS: COMPONENT THERAPY

Cryoprecipitate reduced plasma (CRP)

Cryoprecipitate reduced plasma (CRP) is the plasma remaining once cryoprecipitate has been prepared from the FFP. Preparation of the cryoprecipitate removes much of the fibrinogen, Factor VIII, and vWF from the plasma. However, the vWF enzyme remains. This eliminates a source of vWF for multimer formation and provides the patient with the deficient enzyme to degrade the existing multimers. TPE is the only disease in which the component is used as therapeutic treatment.

The major type of transfusion reaction associated with the use of either component in TPE is allergic (reaction to plasma proteins). In a few cases these may be anaphylactic when the recipient lacks serum IgA and has developed antibodies to plasma IgA (anti-IgA antibodies). The risks are relatively small in comparison to the high mortality of untreated TTP.

In summary, this article has addressed the use of some novel component preparations in treatment of specific disease conditions and the status of substitutes for conventional components. The constantly changing technology, the increased knowledge about how the immune system functions, the increased numbers of patients needing component support, and the spectrum of transfusion-transmitted diseases will assure that the research and clinical trials of new components will increase in the coming years.

### Table 5. Removal of specific substances with therapeutic plasma exchange

<table>
<thead>
<tr>
<th>Factor</th>
<th>Disease or condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelet aggregating factors</td>
<td>TTP</td>
</tr>
<tr>
<td>Immune complexes</td>
<td>SLE</td>
</tr>
<tr>
<td>Antibodies causing hyperviscosity</td>
<td>Waldenstrom’s macroglobulinemia</td>
</tr>
<tr>
<td>Autoantibodies</td>
<td>SLE</td>
</tr>
<tr>
<td>Alloantibodies</td>
<td>Hemolytic disease of the newborn</td>
</tr>
<tr>
<td>Antibodies blocking receptors</td>
<td>Myasthenia gravis</td>
</tr>
</tbody>
</table>

### REFERENCES

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Continuing Education Questions

SPRING 2002

To receive 2.0 contact hours of intermediate level P.A.C.E.® credit for Focus: Component Therapy, insert your answers in the appropriate spots on the immediately following page; then complete and mail the form as directed. Refer to the first page of each article for the learning objectives for that article.

NOTE: There may be more answer spaces on the answer sheet than needed. If so, leave them blank. Make sure the number of the answer space you fill in matches the number of the question you are answering.

LEARNING OBJECTIVES

1. Identify the major diseases treated with each of the components discussed.
2. Discuss the preparation of DLI and why CD4 cells are retained, while CD8 cells are depleted.
3. Describe the general process of making a dendritic cell vaccine.
4. Describe the different types of red cell substitutes and differentiate between them.
5. Explain at least two of the possible ways in which intravenous immunoglobulins may interact with the immune system.
6. Explain why cryoprecipitate reduced plasma is effective in treating thrombotic thrombocytopenia.
7. List and describe the platelet products under development.

CONTINUING EDUCATION QUESTIONS

1. The CD4+ T cells are necessary for:
   a. graft-versus-host disease to develop.
   b. graft-versus-leukemia effect to occur.
   c. engraftment of CD8+ cells.
   d. CD8+ cell depletion to occur.

2. Dendritic cells:
   a. engulf and process antigen from foreign material.
   b. present antigen along with MCH class I.
   c. phagocitize MHC class II molecules.
   d. cannot be found in the peripheral blood.

3. A hemoglobin-based oxygen carrier is a:
   a. perfluorocarbon backbone structure.
   b. hemoglobin encased in liposomes.
   c. cell-free hemoglobin.
   d. product derived only from human sources.

4. Fibrinogen-coated albumin microspheres are being studied as:
   a. red cell substitutes.
   b. platelet substitutes.
   c. dendritic cell vaccine carriers.
   d. a method for CD8+ cell depletion.

5. Cryoprecipitate reduced plasma (CRP) retains normal amounts of:
   a. von Willibrand’s factor.
   b. factor VIII.
   c. fibrinogen.
   d. von Willibrand’s enzyme.

6. In ITP, the clearance of immunoglobulin coated platelets from the circulation is inhibited by treatment with:
   a. cryosupernatant.
   b. perfluorocarbons.
   c. DC vaccines.
   d. IVIG.

7. Chronic myeloid leukemia relapses are being treated with:
   a. IVIG.
   b. DC vaccines.
   c. DLI.
   d. cryoprecipitate reduced plasma.

8. Therapeutic plasma exchange is performed using:
   a. cryosupernatant.
   b. fresh frozen plasma.
   c. cryopreserved platelets.
   d. donor lymphocyte infusion.

9. Acetylcholine antibodies are the source of damage in:
   a. diopathic thrombocytopenic purpura.
   b. thrombotic thrombocytopenic purpura.
   c. myasthenia gravis.
   d. graft-versus-leukemia effect.
10. Carbon backbones substituted with fluorine are characteristic of:
   a. hemoglobin-based oxygen carriers.
   b. cell-free hemoglobins.
   c. perfluorocarbons.
   d. liposome encased hemoglobins.

11. Phosphatidyl choline is characteristic of:
   a. myasthenia gravis.
   b. liposome encased hemoglobins.
   c. donor lymphocyte infusion preparation.
   d. perfluorocarbons.

12. Cryopreservation of platelets is accomplished using:
   a. DMSO.
   b. hydroxyethyl starch.
   c. glycogen.
   d. glycerol.

13. Paraformaldehyde solution is used in preparation of:
   a. infusible platelet membranes.
   b. DMSO.
   c. liposome encased hemoglobins.
   d. lyophilized platelets.

14. IVIG interacts with the immune system by:
   a. competing for binding sites on the Fc portion of phagocytes.
   b. binding to the Fab portion of phagocytic cells and anti-idiotypic antibodies.
   c. clearing autoantibodies from the peripheral circulation.
   d. inducing hypogammaglobulinemia.

15. The source of dendritic cells used in making a DC vaccine is:
   a. donor leukocytes.
   b. patient peripheral blood.
   c. mouse spleen.
   d. none of the above.

16. CD8+ T cells are involved in the development of:
   a. GVL effect.
   b. DLI product.
   c. GVHD.
   d. DC vaccines.
Continuing Education Registration Form

To earn continuing education (P.A.C.E.®) credit, (1) complete the form below, (2) record your answers, and (3) tear out and mail this form with a check or money order ($18 for ASCLS members, $28 for non-members for all articles) to:

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A certificate and credit will be awarded to participants who achieve a passing grade of 70% or better. Participants should allow 8 weeks for notification of scores and receipt of certificates.

Focus Component Therapy carries 2.0 contact hours of intermediate level credit. This form can be submitted for credit for up to one year from the date of issue.

Print or type carefully.

(01) NAME ______________________________________________________ ASCLS membership number ____________________

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(08) CREDIT CARD # ____________________________ TYPE (CIRCLE)    AE     MC     VIS       EXP . DATE __________

Check all that apply
❑ I am an ASCLS member
❑ I am not an ASCLS member
❑ I would like to receive ASCLS membership information
❑ I have previously participated in Focus
❑ I would like information on other continuing education sources

Answers

Circle correct answer (questions are on previous two pages).

1. a  b  c  d  e  8. a  b  c  d  e  15. a  b  c  d  e  22. a  b  c  d  e
2. a  b  c  d  e  9. a  b  c  d  e  16. a  b  c  d  e  23.a  b  c  d  e
3. a  b  c  d  e  10. a  b  c  d  e  17. a  b  c  d  e  24. a  b  c  d  e
4. a  b  c  d  e  11. a  b  c  d  e  18. a  b  c  d  e  25. a  b  c  d  e
5. a  b  c  d  e  12. a  b  c  d  e  19. a  b  c  d  e  26.a  b  c  d  e
6. a  b  c  d  e  13. a  b  c  d  e  20. a  b  c  d  e  27. a  b  c  d  e
7. a  b  c  d  e  14. a  b  c  d  e  21. a  b  c  d  e  28. a  b  c  d  e

Participant Information

Please circle the most appropriate answers.

1. Is this program used to meet your CE requirements for:
   (a) state license (b) NCA (c) employment (d) other

2. Specialty: (a) biochemistry/urinalysis (b) microbiology
   (c) lab administration (d) hematology/hemostasis (e) education
   (f)immunology (g) immunohematology

3. Workplace: (a) hospital over 500 beds (b) hospital 200–499
   beds (c) hospital 100–199 beds (d) hospital under 100 beds
   (e)private lab (f ) community blood bank (g) group practice
   (h) private physician (i) clinic (j) other

4. Salary range: (a) under $10,000 (b) $10,000 to $20,000
   (c) $20,000 to $30,000 (d) $30,000 to $40,000
   (e) over $40,000

5. Did these articles achieve their stated objectives?
   (a) yes      (b) no

6. How much of these articles can you apply in practice?
   (a) all (b) some (c) very little (d) none

7. Employment status: (a) full time (b) part time (c) student
   (d) not employed (e) retired

8. How long did it take you to complete both the reading
   and the quiz? ___________ minutes

9. What subjects would you like to see addressed in future
   Focus articles?
Trends and Technology: Spring 2002

MARY JANE GORE

Trends and Technology welcomes releases and information about new products, services, Web sites, trends, and upcoming events. If your company has a Web site that you would like for us to review, please send us news for our Online section, or tell us about sites that would interest clinical laboratory scientists. These sites, as well as the new product information, are offered for reader information only. We cannot vouch for them and their presence here does not constitute an endorsement by CLS or ASCLS.

ONLINE

I felt I was unearthing a real treasure when a routine search took me to Clinical Laboratory Science Internet Resources®, compiled by Louis B. Caruana, Ph.D. (http://members.tripod.com/~LouCaru/index-5.html). Caruana is professor emeritus of the Clinical Laboratory Science Program, college of Health Professions, Southwest Texas State University in San Marcos. I hope that those of you unfamiliar with it will visit and share in the wonder.

He has compiled what looks to be the most comprehensive list of laboratory related sites anywhere. The main pages are divided into the traditional categories of laboratory medicine, including mycology and parasitology, but he also includes education resources, laboratory management resources, phlebotomy, professional associations and organizations, and student resources. Just to be esoteric, here are some of the links I found:

The Academy of Medical Laboratory Science—The AMLS is an academic body representing the majority of medical laboratory scientists in Ireland. Five separate sites providing information on myeloproliferative disorders. Clip-Art Alley, which claims to be the largest clip-art gallery online, plus many other sites for using technology effectively, creating web sites, learning HTML, and so on.

This review space cannot do it justice—so many of the major diseases and their diagnostic tests, all of the laboratory professional associations I could think of, government and industry resources, handy documents, recommended reading lists—it was all there. My only beef is that he includes absolutely everything—I started to count the sheer number of links but gave up: you must visit this site yourself. Perhaps the sitemaster could sponsor a contest by popular vote of the most valuable clinical laboratory sites. P.S. Dr. Caruana encourages you to contact him if you find any of the lists are not functional: loucaruana@rocketmail.com.

NEW PRODUCTS

The new VIDAS assay from bioMérieux is a reliable test for monitoring prostate cancer. The VIDAS TPSA assay provides an accurate means for determining total PSA and delivers high-quality results for precise and reliable monitoring. Single-dose reagents and calibration concepts ensure the cost of analysis remains the same when running single tests or batches. Contact Bob Bokerman (800) 638-4835, ext. 8090.

The Heraeus HERAsafe® HS 12 biological safety cabinet (Class II, type A/B3, according to NSF Standard 49) offers unmatched operator and sample protection. There is an aerosol-tight, motor-driven front window that seals the inner chamber to protect users and samples. The SampleGUARD™ system also eliminates the need for time-consuming taping before decontamination. North American Kendro customers contact (800) 522-7746.

Zeiss has a new release of the KS Elispot image analysis software for microscopic examination and measurement of large serum quantities, for both routine and research applications. For example, the software can be used to monitor tumor or AIDS therapies. The KS Elispot 4.3 release system provides high sample throughput and optimum measuring accuracy, which is extremely important to immunologists and oncologists. Zeiss also has introduced a new 3D Deconvolution software module to improve image quality in fluores-
The BD Vacutainer™ Anaerobic Specimen Collector maintains an oxygen-free environment for fragile anaerobic swab, tissue, or liquid specimens that maintain an oxygen-free environment up to 72 hours. When the plunger on top of the system is pressed, an oxygen-eliminating system is activated, which converts oxygen and hydrogen into water. This media-free device is provided in a sterile, easy-peel pouch designed for use in the operating room or other sterile environments. Contact Joy Sussman at (410) 316-4467.

The Olympus OLA4000 Workcell automation system is designed for laboratories in medium- and high-volume hospitals and commercial reference laboratories. The OLA4000 fully automates the labor-intensive tasks associated with sample processing by automating sample identification, centrifugation, decapping, and output sorting of specimen tubes. It also integrates Olympus AU analyzers for automated rack loading and unloading along with centralized data processing. Sample tracking capabilities allow for quick identification of specimens while reducing biohazard and blood-borne pathogen contact by laboratory personnel. OLA 4000 can process a wide variety of sample tubes and specimen closure containers that use the most common bar code formats. Contact Timothy Votapka at (631) 756-7160.

Polaroid PhotoMAX PDC 2300Z digital camera, with 1792 x 1200 image resolution and is available with a seven-inch or 11-inch hood. The Polaroid GelCam includes sophisticated image analysis software, Gel-Pro® Express 4.0. Contact Kim Reingold at (781) 386-3573; reingok@polaroid.com.

Quater Research & Development announces the release of its new XYZ-1000 Series of high-precision micropositioners. These small devices provide for ultra-precise manual positioning of probes, test heads, lasers, optics and numerous other subassemblies in a broad range of test, instrumentation, and analytical applications. The XYZ-1000 Series provides X-, Y- and Z-axis positioning with 1 inch (25mm) of travel on each axis. Designed for both space and cost efficiency, these positioners measure just 3.75 x 4.0 x 4.75 inches. For further information, visit the Quater website: www.quater-research.com.

**NEW PURCHASING ARRANGEMENTS**

Dade Behring and Consorta Catholic Resource Partners today announced they have signed a sole source contract for Dade Behring’s MicroScan® line of microbiology instruments, reagents, and supplies. With this contract, Dade Behring now provides the group purchasing and resource management company with its complete line of diagnostics equipment and supplies. Consorta is the third largest group purchasing organization (GPO) in the country in purchases per facility. Dade Behring has also struck a deal with MedAssets HSCA to renew and expand current contracts for laboratory products. “With its broad range of equipment for small, medium and large-sized laboratories, as well as an extensive service network, Dade Behring provides solutions that meet the needs of our diverse membership base,” said Mary Ellen Kimmeth, MedAssets HSCA to renew and expand current contracts for laboratory products.

**KEYLOGIC SYSTEMS**

TeamLeader 2002, the latest release of its business process reengineering. The 2002 release strongly resembles the way small-business teams work together, making an out-of-the-box implementation much easier than traditional workflow systems. TeamLeader 2002 allows users to assign, track and manage work, documents, forms and other types of information without replacing existing systems. Contact Cary Landis at (304) 296-9100.

KeyLogic Systems, Inc. unveiled TeamLeader 2002, the latest release of its team automation system designed to help people work together more effectively. TeamLeader 2002 offers fast relief to organizations like laboratories that want to automate teamwork functions without investing heavily in workflow customization or business process reengineering. The 2002 release strongly resembles the way small-business teams work together, making an out-of-the-box implementation much easier than traditional workflow systems. TeamLeader 2002 allows users to assign, track and manage work, documents, forms and other types of information without replacing existing systems. Contact Cary Landis at (304) 296-9100.