Changes in Clinical Laboratory Technology During the Last Half of the Twentieth Century, Part 1

Part 1 Contributors: Chris Ferrell, BS, Wayne Chandler, MD, Sandra Krueger-Nielsen, BS, Mark Wener, MD, Mary Lampe, PhD, Sharon Miller, MS, Lee Anne McGonagle Malott, MPH, Kathleen Clayson, MS

The Medical Technology Program at the University of Washington (UW-MTP) was established in 1948 and the first student graduated in 1952. As we consider the more than 50 year history of the UW-MTP, it seems appropriate to reflect on the tremendous changes in clinical laboratory instrumentation and techniques during the last half of the 20th century and to acknowledge the continuing and critical role that medical technologists have in the clinical laboratory and in medicine.

In the 1950s, instruments used for laboratory testing were monocular light microscopes with reflected light sources, simple photocell colorimeters with various colored filters for colorimetric procedures, the Van Slyke apparatus to measure CO₂ combining power and O₂, and the analytical balance to prepare standards and reagents and perform gravimetric procedures. The pH meter was in its infancy, blood cell counts were performed with hemocytometers, assays were done manually, the coagulation technique was the tilt-tube method, and the simplest of incubators and autoclaves was available. Calculations were done manually using graph paper and slide rules. Strict safety standards had not yet been developed so pipetting was done by mouth, and gloves were not worn; results were handwritten on request forms and manually filed in patient charts; glassware was hand washed and reused; there were no dishwashers or disposables; needles for blood draw were reused - filed to remove barbs, washed and sterilized before the next use. Quality control was just beginning; acceptability of results relied on duplicate analyses and recoveries. Instrumentation and techniques not available in 1950 included computers, calculators, fibrometers, flame photometers, fluorometers, ion selective

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The University of Washington’s Department of Laboratory Medicine is the major contributor to Laboratory Errors and Patient Safety (LEPS; www.laboratoryerrors.org), a newsletter dedicated to improving the quality of laboratory testing. Our contributions consist of feature articles, cases, and interviews with experts in patient safety. Employees who are interested in viewing LEPS can do so at www.labmed.washington.edu on the “Staff Only” website under the heading “Health and Safety”.

In this edited excerpt from the 5th issue of 2005 LEPS, we talk with Dr. Kaveh Shojania about tips for improving incident reporting. Dr. Shojania is from the University of Ottawa, and he is an international expert in patient safety, with a particular interest in incident reporting. His ideas can help our Department as we seek to better implement the Patient Safety Net (PSN) online incident reporting system.

LEPS: Incident reporting systems have been the subject of much research. Can you translate some of the key research findings into practical tips for laboratory leaders?

Dr. Shojania: Here are key principles for improving incident reporting systems.
1. Use a streamlined incident reporting system that captures a few key points about the event.
2. Relay the incident reports quickly to front-end managers who can triage them.
3. Actually use the incident reports to fix something.

LEPS: Can you give us some detail about the third principle regarding actually acting on the incident reports?

Dr. Shojania: You actually have to use incident reporting to fix things. The purpose of incident reporting is not simply to collect and store a large amount of data. Management will kill the morale of staff if they put all the quality improvement effort into implementing a complex incident reporting system and little or no effort into interventions that improve patient safety.

LEPS: How can a lab avoid the trap of putting too much effort into incident reporting and insufficient effort into interventions?

Dr. Shojania: Cycling is the useful concept here (Figure 1). Labs can focus on incident reporting for a particular period in a particular division of the lab, for example specimen processing, phlebotomy, the core lab, or chemistry. Then you stop and change your focus to analyzing the incident reporting data, developing interventions based on the analysis, and implementing the interventions. After a successful intervention is implemented you can repeat the cycle by going back to focus on incident reporting perhaps in another division of the laboratory. This will help labs avoid two common mistakes. The first mistake is trying to solve all its incident reporting problems before implementing any interventions. The second mistake is trying to do all the steps at the same time, thereby providing insufficient resources to any one step.

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In addition to these new columns, this issue contains two feature articles. The first, by emeritus faculty Kathy Clayson and Lee Anne McGonagle Malott, is part one of a two-part series on the history of laboratory technology in the last half of the 20th century. It is a thought-provoking read and reminds us that it is easier to understand where you are going if you know where you have been. The other feature article is an inspirational piece penned by Dr. Gottfried Schmer, who discusses his colorful career with an emphasis on his recent work in fighting disease in developing countries.

I hope you enjoy this new format, and please share the newsletter with a friend or colleague. If you have any questions, comments, or ideas for future versions of the newsletter, please email me at mastion@u.washington.edu.

Sincerely,
Michaël Aston, M.D., Ph.D
Associate Professor, and Director of Reference Laboratory Services
Profiles: What are some examples of tumor markers?

Aston and Wener: CA-125 is a tumor marker for ovarian cancer. AFP is a tumor marker for certain kinds of testicular cancer, and certain kinds of liver cancer. CA27.29 is a tumor marker for breast cancer. Prostate specific antigen (PSA) is a tumor marker for prostate cancer. There are many others.

Profiles: What is the most commonly ordered tumor marker?

Aston and Wener: PSA

Profiles: What is the most common misconception that the public has regarding tumor markers?

Aston and Wener: With the possible exception of PSA, tumor markers are usually not used to screen asymptomatic patients for the presence of cancer.

Profiles: Why not?

Aston and Wener: The tests are not sufficiently sensitive and specific to be used in patients who have a low probability of having cancer, as is the case with asymptomatic patients with no significant family history. A positive test result may be a false positive, and this can cause worry, and unnecessary further diagnostic testing that can be expensive, invasive, and potentially lead to morbidity.

Profiles: Why is PSA an exception?

Aston and Wener: PSA may or may not be an exception. There are a number of published guidelines for its use and these guidelines do not always agree. Some distinguished organizations, like the American Cancer Society, recommend that men greater than age 50, with more than 10 years of remaining life expectancy, be screened for prostate cancer using a PSA. Other distinguished organizations, like the United States Preventive Services Task Force, feel that there is not sufficient evidence to make a recommendation for or against PSA screening.

Profiles: What are the usual uses of tumor markers?

Aston and Wener: The usual uses are determining the stage of the cancer, and monitoring therapy. By staging, we mean determining the severity of the disease. This can be illustrated with CA-125, an ovarian tumor cancer marker. The test for this tumor marker is not used to screen patients for ovarian cancer. However, once the cancer is diagnosed by other methods - for example physical exam, imaging and biopsy - a CA-125 is usually ordered. The test can be used for helping determine the severity of the disease and monitoring the response to therapy. More severe cases, which unfortunately have a worse prognosis, are associated with higher levels of CA-125. A post-treatment drop in the CA-125 level indicates successful therapy. Figure 1 illustrates in a generic fashion the use of CA-125 and other tumor markers.

Profiles: These results must be very important to patients with cancer.

Aston and Wener: They are, and that is why the laboratory staff put so much effort into maintaining and improving the quality of these tests.

![Figure 1. Most tumor markers are used for monitoring treatment and disease progression.](image)

Research Roundup: HIV Transmission

In this feature, PROFILES presents a short question and answer with a faculty member regarding the importance of their research. The interview for this issue is with Dr. Robert Coombs, Professor and Vice-Chairman for Research in the Department of Laboratory Medicine.

Profiles: What is the main focus of your research laboratory?

Dr. Coombs: Our goal is to more fully understand the source of human immunodeficiency virus (HIV) shedding from mucosal surfaces and how this shedding effects the sexual transmission of HIV from men to women, from women to men, and from men to men.

Profiles: How many people work in your research laboratory and where is it located?

Dr. Coombs: There are two research scientists and 12 technologists that work in the laboratory along with four administrative support staff. We are located on the 7th floor of the Harborview R&T building and have a magnificent view of Mount Rainier.

Profiles: Your research laboratory is internationally recognized for its excellent work. Can you name some particular accomplishments that would be of interest to our readers?

Dr. Coombs: In collaboration with investigators from the University of Washington and elsewhere, we have gained a detailed understanding related...
After working five years as a general practitioner in a rural area in Austria, I decided on a change of lifestyle and studied Biochemistry at the University of Vienna. Dr. Neurath, the then Chairman of the Department of Biochemistry at the University of Washington and Dr. Earl Davie invited me to come to Seattle in 1967 on a postdoctoral fellowship in coagulation chemistry. A NIH Career Fellowship Award made it possible to extend my stay until 1970, when I isolated the Von Willebrands factor/ factor VIII complex. Dr. Paul Strandjord, the chairman of the newly founded Department of Laboratory Medicine, offered me the position of Chief of Clinical Coagulation in 1970, a position I held until 1998. During this time I was mainly involved in the synthesis of biocompatible artificial organs in a wonderful collaboration with Dr. Belding Scribner and the Nephrology Division of the UWMC. Coagulation was widely expanded and a consultation network was set up with the practitioners of our state. Through the generosity of the UW, I was able to train in tropical medicine and public health at Tulane University in 1992-1993, planning to work in this area after my retirement.

The real adventures in my life started with my retirement on June 30, 1998, when I decided to dedicate the years I have left to the impoverished population in the tropics as a volunteer physician. After a training at the Instituto de Medicina Tropical in Lima/Peru I was “let loose” to attend to the Quetchua Indios in the Altopiano. An attempt on my life left me gravely injured and forced my return to the United States. After my recovery I had the great fortune, to be received with open arms by the great leprologist Sinesio Talhari in Manaus, Amazonas, Brazil where I trained and worked for more than two and a half years attending to a low income population. The area around Manaus is hyperendemic for malaria, leishmaniasis and leprosy. The highlights of my volunteer activities were our medical expeditions up the Rio Negro and Rio Amazonas to attend to the settlers and the Indios, the “riverinhos” (Amazonas has practically no roads). The brutal climate with its humidity of 100% and the temperature between 95 and 100 degrees F make life miserable. The overcrowded quarters on the small boat don’t help but the indescribable beauty of the jungle, the camaraderie on board and the gratitude of the patients are rewards I would not exchange for anything else. A very positive result of this work is the possibility of bringing back the experience of working in International Medicine to our residents. Furthermore I obtained through my work clinical privileges in Tropical and non-Tropical Dermatology as well as in Parasitology. I also work in the Leprosy Clinic at Harborview Medical Center. The story would not be complete without mentioning my lover, companion, and wife of forty-seven years Elisabeth, who shared my trials and tribulations through most of the time.

Editor’s note: In response to requests by faculty and staff, we asked Dr. Schmer to give us an autobiographical sketch with special emphasis on his most recent humanitarian activities. Dr. Schmer is a role model for us all, and this brief autobiography will show you why.
electrodes, osmometers, electrodes for blood pH, spectrophotometers, automated instrumentation for blood cell counting, antimicrobial susceptibility testing and organism identification, electrophoresis (not even paper), chromatography, immunochemical, radioisotope and polymerase chain reaction (PCR) tests, and the list goes on. There was a dress code: women medical technologists wore white uniforms, nylon hose and white shoes; the few men MTs wore white -shirts, pants and shoes.

To highlight the changes, specific examples in chemistry, coagulation, blood bank, hematology and microbiology follow.

**Hyperparathyroidism detection**

Diagnosis of hyperparathyroidism demonstrates the marked change in the usefulness of the clinical chemistry laboratory. In 1950 the only laboratory assay of any value for this diagnosis was the measurement of serum calcium, which is affected by many pathophysiological states and thus elevated levels were not a specific indicator of hyperparathyroidism. One method for assay of calcium was direct precipitation as calcium oxalate; ammonium oxalate was added to 2 mL serum, incubated, centrifuged, the precipitate was washed to remove excess oxalate, centrifuged, the precipitate was dissolved in dilute sulfuric acid at 100°C and oxalic acid was titrated with potassium permanganate at 70°C. This three-hour procedure was not offered on a stat basis! Opportunities for error were great so all assays were done in duplicate (4 mL serum required); repeat assays were often required thus prolonging the turn around time.

In contrast, assays for parathyroid hormone (PTH) now available facilitate the diagnosis of hyperparathyroidism and are performed so rapidly that PTH levels can actually be monitored during the surgical removal of the tumor or hyperplastic tissue responsible for primary hyperparathyroidism. PTH, synthesized by the parathyroid gland, specifically measures hormone produced by that gland. Baseline levels are measured on the day of surgery, minutes before removal of tissue and the blood specimen is rapidly sent to the laboratory via pneumatic tube or runner. Testing is performed (sample size, 0.5mL) on an automated immunoassay platform capable of producing a result within minutes. Ten minutes post removal of tissue, a second specimen is drawn and sent to the laboratory for analysis. Clinicians look for at least a 50% decrease in PTH from the baseline. Since the half-life of PTH in blood is <5 minutes, successful removal of a parathyroid adenoma is demonstrated by a rapid decline in the PTH level within minutes of removal of the tumor. If the necessary decrease is not obtained, the surgeon removes more tissue and submits a third sample ten minutes later. The surgeon continues in this fashion until the desired fall of PTH concentration is obtained. This intraoperative testing saves the patient from future invasive procedures as well as time and money associated with second or third surgeries.

**Coagulation**

In the 1950s there were only three known coagulation factors; little was known about the etiology of bleeding disorders so little was known about thrombosis problems. There were no coagulation instruments — only tilt-tube prothrombin times and a stopwatch. Evaluating platelet function entailed slicing a patient’s arm or ear with a razorblade, and platelet adhesion was tested by running whole blood over glass beads then counting the platelets before and after.

The 1960s brought an understanding of the coagulation cascade with its waterfall activation of nine clotting factors (later discovered to be somewhat different in vitro rather than in vivo). The activated PTT expanded the battery of tests for coagulation and the semi-automated fibrometer made testing easier.

Over the next three decades discoveries of antithrombin, protein C, Protein S, factor V-Leiden and prothrombin 20210A mutations, and the lupus anticoagulant improved our understanding of the thrombotic patient. We can now prevent thrombosis with numerous drugs developed from leaches, worms and blood-sucking insects. More than 60 assays are now run on fully automated instruments to evaluate more than 40 coagulation factors. Instrument evaluation of platelet function is now performed without any razorblades! ♦

To be continued in the next issue of this newsletter.
The Medical Technology Program Scholarship Committee has begun an initiative to increase the principal amount in available funds so that the annual interest/dividends generated will provide help to undergraduate Medical Technology Program students in the form of scholarships. Currently, funds include the Undergraduate MT Scholarship Fund, the Western Pathology Quality Assurance Association Endowed Fund and the Fritz D. Schoenknecht Clinical Microbiology Award Fund. Gifts can be made in a variety of ways including annual gifts through payroll deduction, online via credit card, checks sent by mail, gifts of securities, and matching and planned gifts. For more information, go to the “Make a Gift” link at www.labmed.washington.edu.

Contributions made through payroll deduction can be specified as a total gift amount and a fraction will be automatically deducted from each paycheck. A gift of $120 per year is made by contributing $5 per pay period. Authorization forms and additional fund information are available online at www.uwfoundation.org/staff. If your spouse or partner works for a company that matches charitable donations, you may be eligible for matching gift funds so that amount would double to $240. For more information about matching gifts, go to www.uwfoundation.org/match.

A new way to support scholarships for medical technology students was created with the “Campaign for Students”. Faculty, staff, and retirees can establish a named endowed undergraduate scholarship through a matching gift initiative, with a minimum pledge commitment of $5,000, or $1,000 per year for five years. The university will match the gift dollar for dollar up to $10,000. Dr. James Fine, Chair of Laboratory Medicine, and his wife, Dr. Meredith Fine, were some of the first Laboratory Medicine faculty to establish a fund using this initiative to create the James and Meredith Fine Fund for Undergraduate Medical Technology student education. For more information on ways you can support Lab Medicine, including the “Campaign for Students”, please contact Caroline Anderson, UW Medicine Development at (206) 221-2899 or cmanders@u.washington.edu or UW Foundation at 1-877-UW-Gifts or www.uwfoundation.org.

Our thanks go to all who have made contributions to these funds. We encourage faculty, staff, and retirees to consider making a gift to support scholarships for medical technology students.