Errors in Pathology and Laboratory Medicine: Consequences and Prevention

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Reducing errors and improving quality are an integral part of Pathology and Laboratory Medicine. The rate of errors is reviewed for the pre-analytical, analytical, and post-analytical phases for a specimen. The quality systems in place in pathology today are identified and compared with benchmarks for quality. The types and frequency of errors and quality systems are reviewed for surgical pathology, cytopathology, clinical chemistry, hematology, microbiology, molecular biology, and transfusion medicine. Seven recommendations are made to reduce errors in future for Pathology and Laboratory Medicine.


KEY WORDS: pathology; laboratory medicine; errors; quality improvement

Intelligence is not to make no mistakes,
But quickly to see how to make them good.
Bertolt Brecht, The Measures Taken

INTRODUCTION

According to the National Academies Institute of Medicine (IOM), medical errors lead to an estimated 44,000–98,000 deaths and perhaps as many as 1 million injuries per year in the United States [1]. The Joint Commission on Accreditation of Hospitals Organization (JCAHO) has begun to address this by issuing patient safety goals for 2004 [2]. An important goal is improved accuracy of patient identification, while another is improved effectiveness of communication among caregivers. Both of these goals have implications in the practice of pathology and laboratory medicine, and indeed, have been recognized before these formal declarations.

The following comments are heard far too often in pathology and laboratory medicine: “This result can’t be right. The laboratory messed up again!” Clinicians for decades have attributed many patient results that do not fit expected findings to laboratory error. Only recently have pathologists and laboratorians begun to scientifically investigate the root cause of analytical and operational errors in pathology and the clinical laboratory. It has been estimated that up to 75% of laboratory errors generate “normal” results, approximately 12% produce absurd results, and approximately 12% are significant errors that may impact patient care [3]. The validity of such data has been influenced in the past by the lack of adequate reporting of laboratory errors, by the culture of litigation in healthcare in general, and by the slow migration of quality assurance tools used in other industries to pathology and the clinical laboratory arena.

A transitional point in the movement of pathology and the clinical laboratory towards improved industry standards was the implementation of the federal government Clinical Laboratory Improvement Amendments of 1988 (CLIA’88) [4]. Although the impetus for this regulation was due to media investigative reports of patient deaths related to erroneous cytopathology reports, the legislation incorporated standards for general laboratory quality performance. A second regulatory document having major impact on laboratory quality assurance was the publication by the US Food and Drug Administration (FDA) in 1995 giving guidance to blood bank establishments [5]. Shortly thereafter, the major accrediting agency for blood establishments, the American Association of Blood Banks (AABB), issued Quality System Essentials (QSEs) for their membership [6]. Other business and industry groups were also formulating “quality” manufacturing initiatives which culminated in the publication in 1998 by the International Organization...
for Standardization (IOS) of their guidelines—ISO 9000 [7]. Quality systems were beginning to arise in all sectors to improve consumer confidence and safety.

Although the definitions of “error” are varied, a reasonable definition for clinical laboratories is “any defect from ordering tests to reporting results and appropriately interpreting and reacting on these” [8]. This definition of a total testing process begins and ends with patient care and incorporates the classic three phases of performing laboratory testing: (1) pre-analytical, (2) analytical, and (3) post-analytical (Fig. 1) [9]. Each of these phases when carried out properly plays an important role in preventing laboratory errors.

**Pre-analytical Phase**

The traditional laboratory approach to correct pre-analytical tasks has involved providing appropriate clinical history, proper patient preparation, proper collection of laboratory specimens (patient and specimen identification, appropriate sample collection containers), proper preparation of these samples (transportation, handling, accession), and assurance that the testing equipment was “in control” for testing. Newer models for the pre-analytical phase also include patient satisfaction with the collection process (demeanor and knowledge of staff), professional staff satisfaction with this phase (request forms easy to understand, availability of satellite drawing stations, adequate specimen transport), and general customer service satisfaction with the menu of testing offered.

In a recent study by an ISO 9002:1994 certified clinical laboratory, 84.5% of errors detected in their laboratory occurred in the pre-analytical phase [10]. Patient care units using non-laboratory personnel accounted for 95.2% of these mistakes. The causes attributed to these errors in both the inpatient and outpatient areas are listed in Table I. As all the errors in this study resulted from human error, more effective processes, technology (barcode readers), and educational tools are needed to decrease the pre-analytical causes of error.

Pathologists and clinical laboratory scientists are aware of other less controllable sources for potential pre-analytical error that include cyclic (circadian) variation and patient-related physical variables (exercise, diet, stress, positional effects). When combined with other known pre-analytical sources of error (incorrect blood collection technique, anticoagulants, and sample tubes), the errors in just obtaining the optimum sample for analysis can add additional cost to healthcare.

**Analytical Phase**

The traditional laboratory approach to the analytical process has involved the actual test performance and result calculation. Enhancements to the analytical phase now include adequate turn-around time (TAT), easy understanding of test result reports (manual or electronic format), availability of add-on and repeat testing, and general customer service in timely and accurate response to questions. Newer audit criteria in anatomic pathology are focusing on correctness of diagnosis, number of deferred diagnoses, and physician performance assessment.

Anatomic and clinical laboratories have the responsibility for research and development of newer test methods, implementing and communicating to their customers revised laboratory test protocols, current laboratory terminology and normal/abnormal test result criteria. Rejection of a specimen because it does not meet laboratory requirements is not well received by the clinical staff, but is a necessary component of the analytical phase of testing. Analytical timeliness (TAT) has been a common audit tool for the analytical phase of laboratory testing. However, a rapid TAT for an erroneous result will not improve laboratory operations or patient care. Adherence by the clinical laboratory to standard

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**TABLE I. Types of Pre-analytical Error in Laboratory Testing** (Modified From Wiwanitkit [10])

<table>
<thead>
<tr>
<th>Type of error</th>
<th>Percent of pre-analytical errors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inaccurate quality of specimen</td>
<td>47.0</td>
</tr>
<tr>
<td>Wrong identification of the patient</td>
<td>26.8</td>
</tr>
<tr>
<td>Missing physician order</td>
<td>14.0</td>
</tr>
<tr>
<td>Inappropriate quantity of specimen</td>
<td>11.6</td>
</tr>
<tr>
<td>Use of inappropriate container</td>
<td>0.6</td>
</tr>
</tbody>
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operating procedures (SOPs) and manufacturers/regulators instrument calibration and preventative maintenance schedules, providing an adequate number of staff to perform the analytical phase of testing who are properly trained in their job tasks, and participation in external reviews of analyte testing (proficiency testing) will help ensure that the laboratory provides quality service during the analytical phase of patient testing.

Post-analytical Phase

The traditional laboratory approach to the post-analytical phase has involved routine generation and transmission of the test results. Newer models include billing issues (correct codes, user-friendly bill format), patient safety issues (reporting STAT results and critical values in a timely manner), and general customer satisfaction surveys (wait times, informational materials, use of the lab in the future).

The inability of the clinical laboratory to report results has been attributed by Stahl et al. to: (1) patient-related (patient not available for sample procurement); (2) specimen-related (pre-analytical errors); (3) specimen-transport related (broken tubes, incorrect transport conditions); (4) laboratory-related (pre-analytical/analytical); and (5) calculation/evaluation of results [11]. Approximately 16% of the laboratory mistakes in the study were due to a post-analytical mistake. In another study, post-analytical mistakes accounted for 18.5% of errors in STAT testing [12]. The majority of these errors resulted from failing to correct an erroneous result and not notifying the physician of a laboratory-testing problem.

Advancement in computer technology has assisted clinical laboratories in reducing problems in the post-analytical phase of testing. However, keyboard entry errors occur and hospital and/or laboratory computer down-time can have major consequences in resulting patient tests. The cost for many of the information technologies now available may be prohibitive to many laboratories in an era of budget reduction.

What is the impact of errors in the three phases of clinical laboratory testing on patient outcomes? In anatomic pathology, the outcome of an erroneous frozen section diagnosis resulting in surgery modification, termination or a new procedure has been shown to be 39% [13]. In the laboratory medicine, 70–74% of the laboratory errors had no significant impact on patient outcome [12,14]. However, in 7–20% of the errors, inappropriate patient care resulted. These were, for the most part, avoidable negative patient outcomes.

The clinical laboratory must continue to pursue higher quality initiatives in order to minimize “blunders” in any aspect of patient testing. Reduction of human error through root-cause analysis, process control, enhanced metric utilization, use of newer information technologies, and constant education and communication can be achieved.

What concerns everyone can only be resolved by everyone.

Freidrich Durrenmatt

QUALITY SYSTEMS ESSENTIALS IN PATHOLOGY

Definitions of quality abound depending on the industry in question, as stated by Moore and Foss [15]. “Quality, like pornography, is somewhat difficult to define, but is usually recognizable when it is seen.” Healthcare organizations have lagged behind their manufacturing counterparts in recognizing the importance of implementing quality systems as an integral component of their operations. The impetus for improvements in the quality mission in healthcare facilities has been spearheaded by greater regulatory and/or accreditation oversight. More knowledgeable patient consumers have also required this industry to intensify their focus on error management and outcomes assessment.

The official definition of a “quality system” comes from the ISO 9000 Quality Standards used in business and industry [16]: A quality system is the organizational structure, responsibilities, procedures, processes, and resources for implementing quality management [12,16]. The quality system represents only one level of a multilevel quality model as shown in Figure 2 [17].

Laboratory Medicine specialists have traditionally emphasized the quality control (QC) level in this model in the daily operations of the clinical laboratory. Instrument calibration and validation, reagent performance, linearity measurements, and result output undergo robust analysis and monitoring. Surgical pathology utilizes control tissue slides with special stains and peer review of tissue diagnoses. Progression to the higher levels of...
Total Quality Management (TQM) is rapidly being undertaken in this setting as greater emphasis on total facility quality becomes the norm. QSEs represents the keystone of achieving “world class quality” status.

What are QSEs? They represent what the organization says it will do to have a quality system in place to prevent errors and then do what they say they are going to do. Components of a QSE plan usually incorporate the following items [16,18,19]:

- policies (statement of what the facility will do),
- processes (written documents describing the who, what, when, where of the operation),
- organization
- personnel (staffing, job descriptions, training, competency)
- equipment (proper use, validation, maintenance, adjacencies with other departments)
- supplier issues (qualifications, contracts)
- process control, final inspection, handling (performance of task, evaluation of task, minimize handoffs)
- documents and records (design, user friendliness, storage/retention, legibility)
- incidents, errors, and accidents (reporting, investigating, corrective actions, effectiveness checks)
- assessments (internal and external)
- process improvement
- facilities and safety (space, design, review of safety policies)
- standard operating procedures (SOPs), forms, records.

Hospitals and other healthcare organizations voluntarily accredited by the JCAHO have been required to report serious adverse patient occurrences (sentinel events) since 1998 [20]. The requirement was later revised to have accredited facilities develop a system to detect, evaluate, and track such cases in a more proactive manner [21]. A recent report on the status of errors in medicine has generated renewed interest by both regulatory and volunteer accrediting organizations in developing quality mechanisms for preventing patient errors before they occur [1].

The Transfusion Medicine section of the clinical laboratory has been the earliest unit to develop quality procedures to evaluate the frequency, cause, and prevention of errors. This was in response to the realization that catastrophic consequences occur in patients who may receive a wrong unit of blood. Due to the strict regulation of the blood industry by the FDA blood centers, blood banks, and transfusion services implemented QSEs prior to other patient care departments. The AABB members were introduced to these concepts in 1997 [22] and implemented with the publication of the 18th edition of Standards for Blood Banks and Transfusion Services [23]. It has taken the blood banking community several years to master the essentials, but now noncompliance (observations) as shown by FDA and AABB external assessments is now decreasing (Fig. 3) [24,25].

Manufacturing companies are now advancing into the next generation of quality improvement essentials. This new quality tool, Six Sigma, incorporates management commitment and support, a basic problem-solving methodology relying heavily on metric analysis, and a management system that supports continual improvement [26]. Sigma is an approximation of the average distance from the peak of a bell shaped curve. This is typically represented in laboratory statistics as the standard deviation (SD), which measures the variability of testing data around the mean of that data set. Laboratory deviation for QC is normally acceptable at /C6 2 SD. This equates to Two Sigma (approximately 1 out of 20) or results within 95.44% dispersion from the mean. The average American company operates at the Four Sigma level or a 99.4% yield [27]. Examples of Four Sigma operations in healthcare include: 5000 incorrect surgical procedures per week, or 200,000 incorrect drug prescriptions per year [28]. A decrease of errors to Six Sigma equates to 3.4 errors per million actions, compared to 6,210 per million actions for a Four Sigma process. In order to raise the bar of QSEs to this nearly perfect performance in process control, the healthcare organizations will need to improve the “will, ideas, and execution” of their quality approach for success in error reduction [29].

In conjunction with Six Sigma, many manufacturing organizations include Lean Thinking as a methodology for identifying opportunities to eliminate errors [30]. A “lean” laboratory organization delivers the service at the right time, reduces waste, and improves overall efficiency in the pre-analytical, analytical, and post-analytical phases of specimen testing. Such improvements in performance should assist the organization in meeting or exceeding the “customer” expectations.
Although there is a 12% vacancy rate in the nation’s clinical laboratories, an example of Lean Thinking would be to prioritize technologist assignments on value-added tasks that yield greater productivity and improve morale [31].

Several models have been proposed to identify and reduce hospital errors. One such model is a modification of the aviation safety model which now has reduced the airlines industry error rate to 1 in 2,000,000 tasks [32]. As depicted in Figure 4, the model depicts three paths a hospital error may take: (1) an unidentified problem without a negative patient outcome, (2) an identified problem through safety policies and processes designed to improve quality (QSEs), or (3) an error that results in a patient adverse event.

Pathology as a hospital-based profession is in a unique position to facilitate the incorporation of QSEs into the operation models of their hospital colleagues. Representation by pathologists on hospital quality councils for utilization of their quality expertise, participation by clinical laboratory professionals/technologists in assisting other medical/surgical unit staff on how to implement QSEs in their division, open communication by all hospital groups to detect and report process failures and patient errors, and strong support by hospital administrators and boards to promote the use of QSEs both financially and philosophically can only help lead the organization to the top hierarchy of TQM.

The greatest mistake you can make in life is to be continually fearing you will make one.

Elbert Hubbard (1856–1915)

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**Fig. 4.** A PROCESS model for the reduction and prevention of hospital errors [32].

**ERRORS IN ANATOMIC PATHOLOGY**

Emphasis on error reduction as a response to public concern is not new to anatomic pathology. In 1987, a series of articles regarding accuracy of Papanicolaou (Pap) smears appeared in the press [33,34]. The concern raised about false-negative Pap smears led to federal regulation for all laboratories practicing gynecologic cytology under CLIA’88, and subsequently to the Bethesda system for reporting cervical cytology diagnoses in a standardized way with clinically accepted terminology [35]. Experience with the response to these mandates by cytopathology services is also helpful in addressing the current concerns about patient safety and medical error reduction in anatomic pathology.

**Surgical Pathology**

Many of the points discussed for cytopathology error reduction have similar applications for anatomic pathology and tissue examination. However, the task may be more difficult, as surgical pathology is more complex, involving neoplastic and non-neoplastic lesions, classification, staging, and grading of malignancies. Studies involving review of consecutive cases for surgical pathology errors have identified false-negative errors (missing a lesion completely) to be the most frequent. This is in contrast to studies regarding error as determined by consultative pathology services, where false positive diagnosis, threshold errors (a difference of opinion involving a spectrum of a process, but not an error in identifying the process), and typing and grading of tumors were the most frequent errors [36].

Guidelines for performance of quality work in the areas of gross and histologic examinations, performance of frozen sections, and autopsy examinations have come from the College of American Pathologists (CAP) and JCAHO. Communication between clinicians and pathologists is again essential for arriving at the correct pathologic diagnosis. Although most request forms for surgical pathology exam have a place for a brief history, the availability of medical records through hospital information systems has greatly aided the pathologist in obtaining pertinent clinical history for a surgical pathology examination. In many instances, an organ can only react in a few ways to different stimuli, and addition of clinical history, physical examination, and results of laboratory tests can help greatly in narrowing a differential for the surgical pathologist. Clinical correlation of pathologic findings is then instrumental in arriving at the correct diagnosis for the patient.

The timely reporting of interpretive results for small biopsies, and complex large anatomic specimens is also important for patient care, and many laboratories will monitor their TAT for anatomic pathology with the goal...
of having the majority of cases signed out within a day or two of receipt of the specimen within the anatomic pathology section. TAT of a frozen section diagnosis is also monitored, along with correlation of frozen section interpretation with that of permanent sections. Discrepancies should be communicated to the clinician, and tracked for trends that could offer opportunities for the improvement of frozen section diagnoses.

Correct patient identification of tissues and subsequent tissue slides and blocks is crucial for error reduction, as is record keeping through the surgical report of gross and microscopic observations. Digital imaging has been used in some institutions to provide the inclusion of gross photographs and microscopic fields into the patient’s report. Since glass slides and paraffin blocks deteriorate over time, the storing of such digital images with the patient’s report may be the best option for maintaining a patient record of pathologic tissue exam. Automated faxing of tissue examination results, immediately performed by computer after the case is finalized, has aided the laboratory in the quick dissemination of results.

A standardized approach to the gross and microscopic examination of tissue, using concise terminology for reporting is useful for quality assurance by reducing errors of omission, and for providing referring physicians with the information necessary to plan treatment, estimate prognosis, and follow outcome. Checklists and protocols are available to the pathologist, especially for reporting of findings in malignancies. Cancer protocols have been developed by the Cancer Committee of the CAP, and published in the *Archives of Pathology and Laboratory Medicine* [37]. Similar recommendations have been developed by the Association of Directors of Anatomic and Surgical Pathology and published in the *Human Pathology* and the *American Journal of Clinical Pathology*. The protocols provide a basis for development of consistent written reports, an outline for the narrative portion of the report, and a basis for research designs. They are written in a standard format that suggests handling of macroscopic and microscopic examinations, as well as histologic grading and pathologic staging, by organ. The protocols provide a framework of information that should be included in surgical pathology reports, but the format of the reporting is left to the individual pathologist or institution for flexibility. The protocols are revised as needed to include new information regarding specimen examination. Interestingly, the effort to make a report complete does not ensure that a clinician will understand its content. A study involving questionnaires completed by surgeons regarding pathology reports indicated that surgeons misunderstood pathologists’ reports 30% of the time [38]. Surgical experience reduced but did not eliminate the problem, and stylistic improvements to report formats had the potential to interfere with comprehension and increase misunderstandings. As laboratories are consolidated and reports disseminated widely by the Internet, the communication gap is likely to increase, unless ways to correct it are delineated [38].

In addition to optimal communication with clinicians and proper specimen identification, peer review of difficult cases is imperative for error reduction in the anatomic service. Seeking consultation with one’s peers or at an expert level is usually based on a pathologist being familiar with his or her limitations, and being aware of pathologic processes for which one has minimal experience. When an experienced pathologist finds that immediate recognition of a pathologic process does not occur, and that applying familiar rules and criteria do not lead to a diagnosis, the pathologist enters unfamiliar territory and is prone to the same types of error as the novice in the field. The difference between the novice and the expert is that the expert has a larger repertoire of skill-based and rule-based diagnoses. It is important for the pathologist to identify cases where a better diagnosis could be made if the case were referred to another pathologist [39]. Selection of cases for peer review and/or consultation may also be based on the severity of consequences of error [40]. A study involving 180 laboratories established a multi-institutional extra-department aggregate consultation rate of 0.5% [41], and this finding can be used as a target rate in quality assurance plans for anatomic pathology.

Once a decision has been made to seek consultation, the next consideration is the expertise required of the consultant. Using institutional peers for consultation should be done regularly, but may not resolve the diagnostic issue. In these cases, consultation with an expert at another institution is wise. Consultants who have published studies, books, and book chapters about the process in question usually have the most experience with diagnostic problems that can arise in the organ system of their expertise [42]. No system is perfect, however, and rarely an error in diagnosis is made even after peer review and expert consultation has been obtained, because of agreement on the erroneous diagnostic impression.

Occasionally, more than one diagnosis is “right” for a given pathologic process, depending on interpretation of criteria. Every pathologist is aware of variation in interpretation among pathologists for the same slide, as well as his or her own variation in diagnosis of the same case on different days, and is a complex issue for surgical pathology [42]. Cramer and colleagues have classified sources of variability among pathology observers that include mistakes, ambiguous qualitative terms, lesion heterogeneity, difficult diagnoses, imprecise quantitative terms, and relative importance of criteria (Fig. 5) [43]. A study by Schnitt et al. involved the review of 24 breast tissue slides by 6 pathologists, in which the diagnoses
Sources of Variability in Histopathologic Classification

**MISTAKES**

*After careful study, I think this is Type A, because...*

*I'm tired, but I think this is Type B, because...*

**UNCATEGORIZABLE SLIDES**

*There is no problem. This is Type C.*

*This material cannot be classified without a special stain.*

**AMBIGUOUS QUALITATIVE TERMS**

*Term A means □.*

*Term A means ○.*

**IMPRECISE QUANTITATIVE TERMS**

*Rare means 1% or less.*

*Rare means 10% or less.*

**TUMOR HETEROGENEITY**

*I see □, so this is Type A.*

*I see □, so this is Type B.*

**RELATIVE IMPORTANCE OF CRITERIA**

*I see □ and □, so this is more important, so this is Type D.*

*I see □ and □, so this is Type E.*

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Fig. 5. Six types of diagnostic variability in histopathologic classification [43].

represented a spectrum of duct hyperplasia for usual, to atypical to noncomedo ductal carcinoma in situ [44]. Before looking at the slides, all 6 pathologists were given instruction regarding Page's criteria for intraductal lesions and 15 slides to illustrate the criteria were included in the training session [45]. The "pretraining" allowed agreement among all 6 pathologists in 14 of the cases, agreement of 5 pathologists in 17 cases, and agreement of 4 pathologists in 22 of the unknown cases. The study indicates that a high degree of reproducibility in tissue diagnosis can be obtained when standardized criteria are applied.

The exact process of how the brain recognizes visual images and converts them to a diagnosis is mostly unknown; however, a general understanding of the process has been described [42,46–48]. Bartels described the process of human visual perception as having first a high speed stage in which an overview of the image is obtained, and then a slower, sequential stage which focuses on smaller areas and details of the image. For the surgical pathologist this is a quick scan of a slide under a microscope using low power, to see the number of fragments, the slide quality, and the intricacy of the process. This is usually followed by a study under high power of individual fields and cells, to apply rules and criteria that must be met to establish a definitive diagnosis, or a differential diagnosis. Bartels describes visual patterns in the surgical pathology diagnostic work.
as “good” patterns, or “poor” patterns. Good patterns are easily recognized, and are correctly classified even when the differential diagnosis is broad. Poor patterns represent a spectrum of changes so subtle that much experience is required to make a diagnosis, even when as few as two choices exist. Examples of such poor patterns are the spectrum of intraductal lesions of the breast, as mentioned in the Page study above, and the subtle differences of dysplastic nevi and melanomas. Examples of good patterns are the easily recognizable features of the classic seborrheic keratosis, basal cell carcinomas, and keratinizing squamous cell carcinomas. As experience is gained and a broader understanding of the interrelationships of patterns is obtained, the pathologist that has mastered the good patterns will also become proficient in the poor patterns, although total interobserver agreement may not exist in all cases.

Although proficiency testing is not required in surgical pathology for CAP accreditation, as it is in gynecological cytopathology, many surgical pathologists opt to study unknown cases periodically throughout the year to test their knowledge and gain continuing medical education [4]. The programs are very helpful for self assessment, for staying current in the field of surgical pathology, and as supplementation for pathology meetings and training courses. However, the nature of such self-testing means that the unknown slides must be excellent examples of the processes they are representing, with high agreement among observers for the diagnosis. For this reason, performance on a set of unknown slides may not always accurately reflect the competency of a pathologist in actual practice, since many variables that effect performance are present in the day-to-day work load, and cannot be reproduced in a testing situation [42]. Computerized interactive video programs may enhance future proficiency tests, as inclusion of cases with small amounts of tissue would be possible, and not limited by the number of slides that could be prepared from the material, with dispersion to a large number of participants [40].

Computer technology is becoming a convenient tool by which pathologists can share information, obtain education, and obtain consultation. Digital photography and the internet allow the possibility of immediate consultations, without the time delays of preparing and mailing slides for outside consultation. Telepathology [49,50] and telecytology are promising tools for the future that would allow pathologists with subspecialty training to view difficult cases both nationally and internationally. A recent study indicates that digital images are suitable substitutes for glass slides, and telecytology can be used for the cytologic diagnosis of cervical smears, as well as in quality assurance programs [51]. Informatics training is being added to pathology residency programs, to help pathologists contribute to the need for clinical information management [52,53]. Informatics can be used to organize work, correlate findings from different areas of the laboratory, and to store findings. Future growth in the areas of genomics and proteomics will make information management even more critical for correlating all findings for the proper diagnostic impression.

Perhaps one of the best ways to reduce errors in anatomic pathology is for the pathologist to avoid fatigue and physician burnout. Physician burnout increases in those who consistently experience work overload with a perceived lack of control over the extent to which the work exceeds the individual’s capacity. Symptoms of burnout include impaired job performance, headaches, sleep disturbances, irritability, fatigue, hypertension, anxiety, and depression. These symptoms can lead to physician error, and the errors perpetuate the burnout, leading to a devastating emotional impact for the practicing physician [54]. Certainly it is difficult to be useful to others when one’s own emotional and physical reserves are depleted.

**Cytopathology**

Quality improvement measures for the practice of cytopathology mandated limits of workload for cytologists, rescreening of some Pap smears initially screened as negative, and computation and maintenance of laboratory statistics. Also required by CLIA’88 was periodic proficiency testing for all laboratories screening or interpreting Pap smears [8]. To properly select the cases for rescreening, patients at high risk for developing cervical cancer had to be recognizable by the laboratory. This necessitated communication between the clinician and the laboratorian, and is often indicated on the test request for the Pap smear through history or designation as “high risk” by a checkbox on the requisition form. Laboratory computer systems are also helpful for obtaining a past record of the patient’s cytotology and surgical pathology findings [55].

Efforts to limit the work load of a cytotechnologist, and thus decrease errors related to fatigue have been tempered by the issues of reimbursement by third party payers, which seek to increase productivity and decrease cost in the evaluation of Pap smears. This has become a major challenge for the health care system in general, as high demand for services stress available providers and available funding. Thus, efficiency in maintaining the statistics regarding laboratory performance becomes critical, and computer software designed specifically for meeting the cytology requirements of CLIA’88 is available. These statistical requirements include number of specimens processed by specimen type, percentage rate of cases interpreted as abnormal by diagnosis, and correlation with histology.
Of these statistical requirements, the following two areas have been particularly helpful in identifying areas for quality improvement: the statistics regarding the number of specific diagnoses and the comparison of discrepant cytologic and histologic findings. These are statistics that can be benchmarked with large databases [55]. Discrepancy between cytologic and histologic diagnoses may result from errors including patient sampling, as well as screening and interpretation of the slides prepared at time of patient exam. Investigations of the discrepancies have revealed a majority to be due to sampling error, either in procuring the Pap smear or a tissue biopsy [56–58]. In a study by Cioc et al., 3,486 cervical biopsies were correlated with their corresponding Pap smears and noncorrelation was found in 13.1%. Noncorrelation was due to cytology smear screening and/or interpretive errors in 1.2%, as compared to noncorrelation accounted for by cytology sampling error in 5.1% and biopsy sampling error in 6.8% [59]. The study emphasized the need to share the findings of such correlations with clinicians and to direct the management of the patient for maximum diagnostic and patient benefit. Cytologic findings in non-gynecologic specimens and from fine needle aspiration biopsies are also correlated with histology when available to improve cytologic diagnosis and decrease errors in cytology interpretation.

A survey of 186 office-based clinicians using the same major commercial laboratory for cytology services was performed by Morrell et al. to gain knowledge about the clinician’s understanding of the technical aspects of obtaining an adequate Pap smear [60]. The survey results indicated differences among clinicians by gender and medical specialty in reported knowledge, understanding, and technique in cervical cancer screening. For example, respondents reported variation in the rotation of the cytobrush while obtaining a Pap smear from 90° to over 360°. Of all clinicians that used a cytobrush for obtaining the Pap smear, 33.9% indicated rotation of the brush more than 360°. This is regarded as overrotation; with increased risk for damage to cells on the smear and increased bleeding and discomfort (180° rotation is recommended by the manufacturer). The study suggested that targeted education of this population of clinicians may be useful in improvement of the quality of cervical cancer screening. Similar findings were noted in a survey of clinicians regarding performance of superficial fine needle aspiration biopsies. It was concluded that the quality of diagnosis could be improved by placing greater emphasis on training and education regarding technique and specimen adequacy in the procedure [61].

The CAP has been instrumental in helping laboratories address the requirements regarding cytopathology mandates by CLIA’88. The CAP has programs directed toward improvement of laboratory practices through peer review, interlaboratory comparison, education, and development of practice standards and guidelines. Two major programs exist for cytopathology, including the Laboratory Accreditation Program (LAP), section on cytology, and the Interlaboratory Comparison Program in Cervicovaginal Cytology (PAP). The LAP program involves on site inspections for cytopathology laboratories every 2 years to maintain the laboratory’s accreditation to perform cytology services. Under the PAP program, laboratories receive quarterly mailings of five slides for evaluation and diagnosis. Participation in this type of proficiency testing provides opportunities for participants to discover weaknesses in proficiency, and to compare their performance with other laboratories. Review of the data collected by the PAP program indicates higher error rates with interpretation of the cytology proficiency test slides in small-volume laboratories, and in laboratories new to the program as compared to experienced participants. The data indicated that Pap smear evaluation is enhanced by a team approach (pathologist and cytotechnologist), ample case volume, and participation in an external comparison program, such as PAP [62]. A collaborative study between several centers compared the results of screener’s work performance, as determined by results of rescreening, with computer-based proficiency tests. The study found that proficiency-testing scores gave some indication of the true performance of screeners, and that computer-based proficiency tests offered a valuable vehicle for assessment of work performance and for continuing education [63].

The PAP program has also allowed analysis of data collected through the program from thousands of laboratories in the United States, so that benchmarking data may be provided, by which laboratories may compare their own performance. The data include percentages by diagnostic category of abnormal smears [55], and has noted an overall annual laboratory error rate (false negatives and false positives) of about 4% [62].

Emphasis has also been placed on the follow-up of patients with abnormal cytology results. In 1998, a study conducted by the CAP investigated the patient care follow-up for 16,132 abnormal cytology results. The study found that young patients (<30 years), pregnant patients, and those with low grade intraepithelial lesions were shown to have lower follow-up percentages [64]. Investigations such as this could prompt practices to standardize the way patients are informed of test results, to bring patients with abnormal results back in a timely manner for follow-up care, and to lead the health system in establishing monitoring processes and providing data analysis [65].

Despite these successes, areas of error reduction in cervicovaginal cytology remain. A basic problem persists in how to define an error regarding Pap smear
interpretation. Because of differences in definition of errors and calculation of error rates, published reports on errors may show wide variation among laboratories [66]. Before such laboratory comparison can become meaningful, “error” needs to be defined for every area of laboratory work, and statistical analysis should be similar to allow comparison between institutions. The mandates of CLIA’88 were especially concerned with the reduction of false negative Pap smears. A statistical formula for calculating the false-negative fraction for Pap smears has been proposed, and is an example of efforts to standardize data generation for interlaboratory comparison [67].

Another area of concern is how to address an error that is discovered in order to provide optimal patient care. CLIA’88 requires that an amended report be issued when a significant cytology/histology discrepancy that would affect patient care is discovered. However, a survey by Stastny et al. revealed that a standard of practice for issuing of such amended reports does not exist, and that the phrases “significant discrepancy” and “affects patient’s care” are vague and subject to a variety of interpretations [68]. Risk management issues influence the decision as to how to reveal communication of errors to physicians and their patients, and are at times handled on a case-to-case basis. One of the problems in dealing with error in Pap smear interpretation is society’s goal of eradication of cervical cancer mortality through perfect performance of Pap smear interpretation. Unfortunately, the Pap test cannot control the behavioral risk factors associated with cervical cancer, and a 0% error rate is not attainable. Rather errors are inevitable, and analysis of system characteristics is necessary to know why errors happen. Attributing each error to an individual prevents the identification of system errors. Reducing error is dependent on admitting it, forgiving it, and learning from it. To implement this, accepted standards of performance would be determined by pathology professional societies, and the overall performance of a laboratory would be evaluated in response to an error, rather than the performance of the individual [69].

Technology for automation of cytology screening has been introduced, and has been used to select Pap smears for manual rescreening, rather than a random 10% of Pap smears screened as negative, with finding of an increased false negative rate for initial screening [70]. Concerns about cost, however, prevent additional efforts to prevent error, including manual secondary rescreening of all negative Pap smears or adding machine screening to routine processing, as health care payers and patients are unlikely to be prepared for increases in payments for the service.

Diagnostic errors may also occur with the interpretation of fine needle aspiration biopsy material. An article by Skoumal et al. makes several pertinent points [71]. Although examination of such material is expected to result in a diagnostic impression, the impression as to benign or malignant may be less evident than with surgical material. For this reason, cytology is sometimes regarded as a screening laboratory test that exhibits uncertainties and errors. In some cases, the best cytopathological impression is one that relates diagnostic uncertainty with such terms as “suspicious” or “atypical cells, favor…” so that a more diagnostic specimen may be procured. Problematic fine needle aspiration biopsies usually fall into two categories: (1) a decision as to whether cells are benign or malignant cannot be made or (2) a diagnosis is made, but uncertainty and errors are associated with the procedure (i.e., pancreatic and thyroid aspirates). False negative results may occur due to sampling errors, in which the malignancy is not apparent on aspiration smears, but is later diagnosed on tissue examination. Understanding and communicating these limitations are important for patient care, as clinicians and patients may not be aware of diagnostic errors associated with cytological procedures. Once again, communication between caregivers (and ultimately patients) and the pathologist is necessary.

Failure is the seed of success. Kaoru Ishikawa

ERRORS IN LABORATORY MEDICINE

The clinical laboratory will play a great role in the future in helping to provide patient safety. The medical laboratories of the nation generate billions of pieces of data that are used for patient diagnosis and treatment, and often serve as a source of general information regarding laboratory testing and interpretation for physicians. The laboratory is the hub from which information is generated that helps to turn the great wheel of health care. Fortunately, the clinical medical laboratory has a long history of putting patient safety first, by complying with national, state, and accrediting agency rules and regulations. Because of this emphasis, error relating to performance of a laboratory test is greatly reduced. Whether laboratory services can benefit patient care, however, is dependent on more than mere generation of a correct analytical result. The total testing process begins with a clinical question and ends by applying the information from the laboratory study to patient care, and error is possible in any step of the process.

TAT of results becomes an important factor in patient care, when the effect of delayed test results is studied. According to JCAHO in a Sentinel Event Alert delayed test results is the second most common reason for treatment delay [72]. The desire to speed up TAT once the laboratory receives a sample has spurred interest in
automation of sample processing. These processes include sample log in, centrifugation, and sample sorting, by using bar coded labels attached to the specimens. Automation incorporated in these stages can reduce clerical and labeling errors that occur when laboratorians transport and aliquot patient samples, and eliminate some of the rote work that causes errors due to fatigue or distraction [72]. Automation may also be used to check the quality of a sample, with instruments designed to detect substances that interfere with testing such as presence of hemoglobin, bilirubin, and lipemia. Interfacing of laboratory information systems allows computers to transfer results directly to the patient’s report to avoid transcription errors. The reports, once manually or auto-verified, can then be immediately faxed to a physician or printed to a clinical service area providing care for the patient.

Errors made in the actual performance of a laboratory test are rare because of efforts to provide accurate analytical methods. Bonini et al. has summarized the literature on laboratory errors from January 1994 to June 2001 [8]. The findings indicated a very limited number of studies of the topic of laboratory errors, and the results were heterogeneous. A common finding, however, was the distribution of errors across different phases of the entire testing process. A large percentage of laboratory errors occurred in the pre- and post-analytical phases, with fewer mistakes being the result of an analytical process. Another study, a survey of laboratory incident reports by Astion et al. was done to help identify problems that jeopardize patient safety [73]. In this study the most common specific impact on patient care of an adverse laboratory event was delay in receiving test results (85%). The pre-analytic testing phase was involved in 71% of incidents, the analytic in 18%, and the post-analytic in 11%. The most common pre-analytic problem was specimen transportation (16%), and the most frequently implicated error in laboratory function was specimen processing (31%). This information from formal studies can help to identify the most common type of errors and to improve system processes to prevent them.

Clinical Chemistry

The discipline of clinical chemistry has actively introduced systems to reduce analytical error beginning more than 50 years ago. In the late 1940s, proficiency testing among laboratories began in Philadelphia under the direction of Dr. William Sunderman and the CAP [74]. This concept has been greatly expanded over the years and now involves all aspects of laboratory medicine and pathology. The Clinical Laboratory Improvement Act of 1967 (CLIA’67) required all laboratories to participate in proficiency testing programs. However, CLIA’88 established a passing grade of 80% for proficiency testing and used results to accredit laboratories. In 1950, Levey and Jennings published their classic study on the use of control charts in clinical chemistry and clinical laboratories [75]. Westgard et al. developed a number of QC rules based on statistics for effectively using a Levey–Jennings chart to reduce error [76]. These are some of the milestones that have helped to identify and reduce analytical errors and improve quality for clinical chemistry. Today, an extensive QC program is in place in most clinical chemistry laboratories that continues to reduce the error rate.

Only a few studies have been done to specifically evaluate the analytical error rate of a clinical chemistry laboratory. For essentially any laboratory, the majority of results come from the clinical chemistry section. Clinical chemistry more than the other sections of the laboratory usually produces a quantitative result that facilitates statistical QC and error detection. In an early report, McSwiney and Woodrow reported an error rate of 2.3% (number of documented errors within the laboratory/ number of tests performed) [77]. Several years later, Chambers et al. reported the rate of erroneous results from a clinical chemistry laboratory was 0.3% [78]. For this study, an error was defined as an erroneous result which was issued or would have been issued by the department if the final cumulative reports were not checked. Failure to perform or report requested analyses were also considered an error. Errors detected before analysis were not included; these were analyses when blood samples were received more than 12 hr after phlebotomy, inappropriate samples and samples with an inadequate or wrong identification. Technical errors or omissions detected at the bench level were also excluded. The denominator was the number of test results reported during the time interval. Lapworth and Teal reported a rate of error of 0.05% [79]. For this study, an error was defined as an incident leading to an incorrect result/set of results either being reported or detected at the final checking-out stage in the laboratory. Errors detected before or during analysis, or before the final validation stage were not included. The denominator was the number of accessions that may have included several different test results and not the number of individual test results. This study also found that the number of errors was approximately the same in the pre-analytical, analytical, and post-analytical phases. Further, this study found a higher error rate for proficiency testing than patient analyses that the authors attributed to the need for reconstituted in some cases, transcription errors and calculation steps that are required with these specimens. Thus, the error rate within the laboratory for patient specimens should be less than that documented for proficiency
testing based on the results of this study. Another study used methods comparison data with over 200,000 results obtained over several years and found an error rate of 0.045% [80]. In this study, each result was prospectively compared with its replicate, comparative, or repeat value to identify differences from expected values. The results were expressed as unacceptable results/errors per million results. The error rate was higher for patients' samples compared with control samples. These four studies show a progressive decrease in the rate of errors over time. However, it is difficult to determine if we have made progress over time based on these four studies since the denominator may have been different for each study. In the study by Chambers et al. the denominator was the number of test results reported, but the study by Lapworth and Teal used accessions (a set of results) for the denominator. Since, to date, there has not been a standardization of what constitutes an “error,” it is difficult to make a comparison among studies, but we seem to be heading in the right direction.

The error rate in STAT laboratories has also been studied. Plebani and Carraro reported an error rate of 0.47% based on the number of test results reported in four different STAT laboratories in a hospital [12]. This is approximately 10-fold higher than Witte et al. reported for chemistry laboratories in the same year [80]. The distribution of errors in the study was the following: pre-analytical 60.2%, analytical 13.3%, and post-analytical 18.5%. A review study evaluating several reports of errors in laboratory medicine also found that most errors occur in the pre-analytical phase [8], which differs from the similar distribution of errors among the three phases reported by Lapworth and Teal [79].

Interference with clinical laboratory analyses that primarily occurs in clinical chemistry is an important source of error. Interference by endogenous or exogenous substances with assays for clinical analytes is a common problem. Interference has been defined as the effect of a substance present in the sample that alters the correct value of the result, usually expressed as concentration or activity, for an analyte [81]. The following four major endogenous compounds when present in excess consistently interfere with laboratory test results: hemoglobin, bilirubin, lipids, and paraproteins. The major exogenous sources of interference are drugs prescribed for the patient. Evaluating interference may be tricky since it may increase or decrease the concentration of the analyte and the interferent may interact with the analyte (analyte dependent interference) or alter the assay result independent of the analyte concentration (analyte independent interference). The frequency of interference with clinical laboratory analyses is difficult to determine. A study of 100 outpatients found that the percentage of tests effected by interference was 7% when the patient took one drug, 16.7% when the patient took two drugs, 66.7% when the patient took three or four drugs, and 100% when the patient took five or more drugs [82]. It is important to think of interference when a patient has a highly abnormal laboratory result that is inconsistent with the clinical picture. There are several sources of information to assist the laboratorian with the resolution of an interference problem. A starting point is the manufacturer’s package insert in which the description of the method usually includes an analysis of probable interfering substances. In most clinical laboratories, the publication by Dr. Donald Young on the Effects of Drugs on Clinical Laboratory Tests is a great resource for resolving interference problems [83]. The information in this publication is organized by laboratory tests and drugs, and an index lists all laboratory tests and drugs. Thus, for unusual laboratory results, it is important to review the patient’s laboratory values and chart for medications that may interfere with the abnormal result for the analyte in question.

Hematology

Proper collection and labeling of specimens is extremely important for the hematology and coagulation services, where special attention to the quality of a sample is necessary for an optimal laboratory result. Clots in whole blood samples, even small ones, cause errors in results in both complete blood counts (CBC) and coagulation parameters. Incorrect coagulation test results can be caused by contamination of blood samples incorrectly drawn from heparinized intravenous lines or catheters. For the prothrombin time (PT) and activated partial thromboplastin time (aPTT), the ratio of blood to anticoagulant (sodium citrate) must be correct for the patient’s hemoglobin and hematocrit. Less anticoagulant is used for patients with elevated hemoglobin and hematocrits, to avoid incomplete utilization of the anticoagulant by plasma, leaving excess anticoagulant present to falsely prolong clotting assays [84]. Such issues are familiar to clinical laboratory scientists working in the hematology/coagulation area; however, many blood samples are now drawn by non-laboratorians, who must be informed of such nuances as part of the laboratory quality assurance programs.

Timeliness of specimen transport to the hematology/coagulation laboratory is also an important factor in obtaining reliable results. Cells exposed to EDTA degenerate and appear dysplastic over time, so that peripheral blood and bone marrow aspirate specimens obtained for morphologic review and placed in EDTA are best delivered promptly to the laboratory [84]. When available, bedside assistance in making bone marrow aspirate smears directly from the aspiration needle by a
trained assistant ensures optimal preparations. Samples from patients being evaluated for heparin therapy by the aPTT should be assayed as soon as possible, as heparin is eventually neutralized by platelets in the test tube, and delay of testing may lead to a falsely low aPTT value. These criteria are often addressed in an instructional manual and made available to services sending specimens for analysis to the clinical laboratory. Timeliness of specimen transport also helps to improve the TAT for generating test results.

The analytical phase of laboratory testing is becoming more challenging, however, as work forces dwindle due to attrition and lack of incoming trained medical technologists and technicians. This makes automation even more necessary, to handle routine work and free technical personnel to concentrate on problematic results. For example, in the hematology laboratory, normal differential counts are performed by the instrument and reported, leaving only those flagged by the blood counting instrument to be counted manually.

In addition to maintaining an adequate laboratory labor force by raising the esteem of the profession and maintaining an adequate number of training programs, this group of health care providers needs access to continuing medical education to stay current with new laboratory tests and theory. Providing the latest and most accurate tests is a critical service for the clinical laboratory, necessitating constant review of test menus and implementation of new equipment and procedures. JCAHO cites offering of “outmoded” tests as a critical risk factor for clinical laboratories. As an example, the most sensitive testing method now for paroxysmal nocturnal hemoglobinuria is flow cytometry using anti-CD 55 and anti-CD 59, replacing the veritable Ham’s and sucrose hemolysis tests previously used for diagnosis and screening. Examination of bone marrow aspirate specimens from patients with leukemia now routinely incorporates findings from flow cytometry and cytogenetic studies. These ancillary tests improve diagnostic accuracy by providing additional information to morphologic examination (immature cells of different lineage can look alike), and providing information regarding classification and prognosis.

The natural adjunct to performing updated laboratory tests is providing laboratory consultative services to physicians, to help them best utilize the laboratory’s armament of tests and interpret them correctly (post-analytical services). In an editorial written by Lundberg in JAMA [85], proper interpretation and action must be accomplished before the laboratory test loops are actually completed. This type of closed loop testing approach is particularly suited to hematology, where many morphologic impressions are converted to numerics, and to coagulation where theory is complex. A survey conducted by Sandhaus and Meyer [86] examined the perceived usefulness of CBC and reticulocyte reports to clinicians at the University Hospitals of Cleveland—Case Western Reserve. The study surveyed 1,353 attending and 689 house staff physicians to determine which of the CBC parameters were regarded as useful to clinical practice. Only 4 of the 11 reported parameters were selected as frequently or always useful by more than 90% of physicians: hemoglobin, hematocrit, platelet count, and WBC count. Among primary care physicians, the mean cell volume (MCV) was also selected as frequently useful in the evaluation of anemia. Physicians practicing less than 10 years infrequently used this parameter. The study indicated that modifications of report formats were needed to facilitate physician perception of hematology laboratory results. Currently this is being accomplished through clinical pathology consultative reports, such as a pathologist’s interpretation after review of a peripheral smear and CBC. This method enhances only a few of the reports generated daily from the hematology laboratory, however, correlation with clinical history and laboratory results could be beneficial for all patients being studied in the laboratory. Computers could assist with this in the future, by linking interpretive comments for certain laboratory results with key words in the provided clinical history. Of course, it is the clinician who ultimately interprets laboratory data and applies it to patient care, but improved relationships with clinicians and laboratorians could help eliminate errors, as the ultimate quality assurance of a laboratory test is whether it is a rational result given the patient’s condition.

Interpretation of coagulation tests can often be perplexing, and coagulation test results are highly dependent on methods performed. Coagulation test results are also greatly influenced by pre-analytical factors, including therapy and techniques of phlebotomy. A survey of hospital coagulation laboratory practices in the United States was conducted by the Centers for Disease Control and Prevention in 2001 [87]. A part of the survey dealing with clinical service and laboratory capacities found that only 57% of hospital coagulation laboratories had a clinician available for consultation with expertise in coagulation disorders. A minority of the hospitals were associated with outpatient coagulation services, specifically, only 20% of the responding hospitals had a clinic specializing in adjustment of oral anticoagulants, and only 9% offered outpatient clinics specializing in diagnosis and treatment of coagulation disorders. Results of a portion of the survey dealing with coagulation laboratory practices found departure from certain accepted coagulation laboratory practices which may result in adverse outcomes, and called for laboratorians and clinicians to work together to understand the reasons behind the variabilities. Coagulation laboratories clearly have an
opportunity to positively impact patient care by making interpretive consult reports regarding specialized coagulation laboratory work-ups available to clinicians, and by establishing dedicated phone lines or e-mail addresses within the laboratory to facilitate communication between laboratorians and care givers. Becoming involved with outpatient clinics and point of care coagulation testing is another way to ensure that high quality laboratory methods are being made available to outpatients as well as hospitalized patients. Point-of-care laboratory testing accuracy is improved when the service has a quality assurance plan, including proficiency testing for those performing the assays.

Microbiology and Molecular Biology

Microbiology may be the area of laboratory medicine that is most difficult to detect and to quantify errors. The pre-analytical part of microbiology is the most important factor for successful analytical and post-analytical phases of a culture. If a specimen is contaminated when obtained from the patient, the laboratory has no way to resolve this error. The rate of blood and urine culture contamination has been evaluated by the CAP Q-Probe Studies. In a Q-probe study evaluating just under one-half million cultures and 640 institutions showed the median adult inpatient blood culture contamination rate was 2.5% by laboratory assessment [88]. Factors associated with a significantly lower contamination rate were a dedicated phlebotomy service, use of a tincture of iodine for skin disinfecting, and application of an antiseptic to the top of the collection device before inoculation. There was no significant difference in the contamination rate between inpatient and outpatient cultures. Further, teaching institutions and high numbers of occupied beds with demographic factors associated with higher contamination rates for inpatients by not for outpatients. Contamination rates were not significantly affected by the type of blood culture method used, or use of a double-needle collection procedure.

The contamination rate for urine cultures in this country is more problematic. A CAP Q-probe study with 906 institutions each reporting results on 250 urine cultures from outpatients showed the median urine culture contamination rate was 18.1% [89]. The 10% of institutions with the lowest urine contamination rate reported 5.6% or fewer of their cultures were contaminated. In contrast, the 10% of institutions with the highest contamination rates reported that 36.8% or more of their urine specimens were contaminated. Institutions with lower contamination rates tended to process a lower proportion of specimens from female patients. Thus, contamination of outpatient urine cultures is a common occurrence and facilities differ significantly in their overall frequency of urine culture contamination.

Very little data are available about errors that occur during molecular testing. The results of survey data from 42 laboratories in this country reported significant errors in 0.33% of tests performed [90]. Of the errors identified, 60% occurred in the pre-analytical phase, 32% in the analytical phase, and 8% in the post-analytical phase. Moderate or high levels of harm to the patient occurred in only 0.008% of the total cases. The study involved 227,000 molecular tests with no lawsuits, judgments, or disciplinary action reported. Further, the overall frequency of errors in a given laboratory did not correlate with laboratory age, test volume, accreditation status, proficiency testing performance, or institution type. Thus, errors with molecular testing occur infrequently, and harm to a patient is a rare event.

Transfusion Medicine

The first blood transfusion to a human occurred in 1666 in Paris performed by Jean Baptiste Denis [91]. Lamb’s blood was used as the source, and 3 of the 4 patients transfused survived. However, due to the one patient death and subsequent lawsuits, human blood transfusion was banned in Europe until the early 1800s. James Blundell revived human transfusion in England in 1818 [92] and the practice evolved through the next 150 years, which included many discoveries: blood group antigens, blood anticoagulants, blood group inheritance, and transfusion-transmitted agents. These discoveries were all crucial to the development of safe blood transfusions.

In 1990, approximately 41% of transfusion related deaths reported to the FDA were acute hemolytic transfusion reactions [93]. According to the FDA Center for Biologics Evaluation and Research (CBER), 189 transfusion-related deaths were reported during the period 1999–2001 [94]. The major etiologies of these deaths were bacterial contamination (15.4%), acute hemolytic transfusion reaction (14.3%), and transfusion-related acute lung injury (TRALI; 12.7%). Transfusion-transmitted diseases have come full circle since the 1940s when open vented glass bottles were used for plasma and blood infusion and the risk of bacterial contamination was high. The only infectious disease test was for syphilis, and the donor questionnaire elicited only information related to a history of hepatitis, IV drug use, and international travel to malarial areas. Today the blood manufacturers utilize nine tests for potential donor infectious disease (Human Immunodeficiency Virus/HIV antibody(ies), Human T-cell Lymphotrophic Virus/HTLV antibody(ies), HIV p24, Hepatitis B surface antigen/HBsAg, antibody to Hepatitis B core antigen/anti-HBc, Hepatitis C Virus antibody(ies), HIV RNA and HCV RNA [Nucleic Acid Test/NAT], and syphilis). The donor history questionnaire now has over 40 questions related to social,
medical, and infectious disease risks. Figure 6 demonstrates the significant steps from blood donor recruitment to patient transfusion [95].

As can be appreciated from the steps involved to prepare a blood component for transfusion, the possibility of errors exists at any point in this complex process. Most of the errors reported are associated with clerical (human) error. A review of the literature on transfusion errors in hospitals revealed that contributing factors included patient wristbands (multiple, incomplete, erroneous, illegible), wrong blood tube collected or mislabeled, and patient misidentification (transfusion to wrong patient, phlebotomy errors, multiple errors) [8].

In the hospital transfusion services alone, 24 quality assurance steps have been identified for the transfusion process [96]. The step descriptions for 88,038 transfusion defects found in a CAP Blood Bank Quality Improvement questionnaire are listed in Table II.

This study identified that the majority of errors related to transfusion of a blood component occurred outside the transfusion services. Miscollected blood samples (the wrong blood in the tube) were found to occur in a 10-nation study in 1 in 2,000 collections; mislabeled samples (samples with labels not meeting locally accepted standards) occurred in a 1 in 165 frequency [97]. The FDA has proposed point-of-care bar code requirements for medication and blood transfusions in order to reduce these errors of patient identification [98]. Experience with several barcode technologies to reduce mistransfusions has proven successful [99,100].

With the discovery of acquired immune deficiency disorder (AIDS) and the causal agent HIV in the early 1980s, the public became more attuned to blood transfusion risks, the regulatory agencies and blood industry responded, and transfusion medicine transformed itself into a “zero risk” operation. The FDA published their guidelines on quality assurance in blood establishments [101], and have subsequently revised multiple regulations to reduce the errors in blood manufacturing. Areas included in reporting errors (Biological Product Deviation Reporting [BPD]) to the FDA now required of both blood/plasma collection centers and transfusion services include the following [102]:

- donor suitability
- blood collection (donor and patient)
- component manufacturing/preparation
- product testing
- compatibility
- labeling
- storage and distribution

From October 1, 2000 through September 30, 2001, there were 23,839 reportable BPDs submitted from the blood industry. Table III shows the breakdown of the various reporting categories.

The majority of errors (76.6%) in licensed blood establishment and plasma centers result from information supplied by the donor after the donation that would have...

**TABLE II. Twenty-four Quality Assurance Steps for Transfusion [99]**

<table>
<thead>
<tr>
<th>Testing phase</th>
<th>Step description</th>
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<tr>
<td>Pre-analytic—35,922 defects (40.8%)</td>
<td>1. Physician’s order missed</td>
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<td></td>
<td>2. Orders misinterpreted</td>
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<td></td>
<td>3. Donor/recipient misidentified</td>
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<td></td>
<td>4. Wrong container used for collection</td>
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<td>5. Specimen container/requisition misidentified</td>
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<td></td>
<td>6. Specimen mishandled</td>
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<td></td>
<td>7. ABO/Rh performed incorrectly</td>
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<td></td>
<td>8. Antibody detection performed incorrectly</td>
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<td></td>
<td>9. Cross-match procedure performed incorrectly</td>
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<td></td>
<td>10. Blood testing incomplete on component release</td>
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<td>Analytic—3,727 defects (4.2%)</td>
<td>11. Results misinterpreted</td>
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<td>12. Results misidentified</td>
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<td></td>
<td>13. Transcription error</td>
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<td>14. Results on wrong patient</td>
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<td>15. Results sent to wrong physician</td>
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<td>16. Results not charted correctly</td>
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<td>17. Turn-around time exceeded</td>
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<td>18. Physician not notified of problem</td>
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<td></td>
<td>19. Blood component administered improperly</td>
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<td>20. Component date expired</td>
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<td></td>
<td>21. Patient or component misidentified</td>
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<tr>
<td></td>
<td>22. Baseline vital signs not recorded</td>
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<tr>
<td></td>
<td>23. Patient not observed during transfusion</td>
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<tr>
<td></td>
<td>24. Patient not observed after transfusion</td>
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<tr>
<td>Post-analytic—48,389 defects (55.0%)</td>
<td>25. Results misinterpreted</td>
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<tr>
<td></td>
<td>26. Results misidentified</td>
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<td></td>
<td>27. Transcription error</td>
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<td>28. Results on wrong patient</td>
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<td>29. Results sent to wrong physician</td>
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<td>30. Results not charted correctly</td>
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<td>31. Turn-around time exceeded</td>
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<td>32. Physician not notified of problem</td>
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<td></td>
<td>33. Blood component administered improperly</td>
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<td>34. Component date expired</td>
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<td>35. Patient or component misidentified</td>
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<td>36. Baseline vital signs not recorded</td>
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<td>37. Patient not observed during transfusion</td>
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<td>38. Patient not observed after transfusion</td>
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disqualified them at the time of donation (post-donation information). Errors in viral testing account for only 0.3% of total errors reported by all facilities. In transfusion services which only began reporting errors to the FDA during FY01, errors in QC and distribution accounted for 42.0% of total errors reported. These errors were made up of human errors in not following procedures (component not leukoreduced, 13.0%; component not irradiated, 11.5%; improper ABO/Rh selected, 11.0%). Labeling errors in transfusion medicine (31.3%) were the result of human error in not following procedures that led to missing/incorrect labels on blood components. Routine testing errors by the transfusion services (24.6%) were due to human error in not correctly performing the compatibility testing or antibody screening, or because of sample misidentification.

Although blood centers and transfusion services are among the most heavily regulated and externally inspected department in the clinical laboratory (FDA, CLIA, CAP, AABB, Nuclear Regulatory Commission/NRC, state laboratory license), errors still occur. In order to further reduce errors (deviations in manufacturing), newer technologies and automation are being developed and implemented. Figure 7 highlights these new technologies [95].

For the blood donation process, new requirements by the AABB and CAP to reduce bacterial contamination in platelets took effect on March 1, 2004 [103,104]. Leukoreduction of red blood cells and platelets, although not required universally by FDA, is being performed routinely by many blood collection agencies. Nucleic Acid Testing (NAT) is now required of all blood donations to improve the detection of HIV and HCV. Pathogen reduction technology (PRT) is in various clinical trials and soon will be available to reduce pathogen transmission by blood transfusion. New automated blood collection devices are either currently being used or are under investigation to allow fully automated component preparation during the donation process (minimize human error). Transfusion services have integrated more automation including bar-coding into their operation to reduce labeling errors (patient blood specimens and blood components) and electronic crossmatching to decrease costs and staff benchwork. New patient typing, antibody screening, and compatibility testing technology (gel and solid phase) have been introduced and have the capability for automation (standardization) which will also assist in reducing human errors (analytic phase).

Can an error free (zero risk) transfusion medicine service be achieved? Probably not as long as there is a human element (from the raw material—the donor—to the hanging of the blood component for patient transfusion) involved even in the best of a quality system culture. As stated by AuBuchon, “It is to be hoped that we will continue to devise new strategies, uncover new facts, and develop new solutions to continue to move forward toward the universal goals of improved transfusion safety and supply while balancing economic pressure and patient and society needs” [105]. Transfusion medicine safety has progressed radically since Blundell’s first human transfusion in 1666. World-class quality in transfusion medicine that is essentially error free can be achieved!

It takes a long time to bring excellence to maturity. 
Publilius Syrus (~100 BC), Maxims

ERROR REDUCTION FOR THE FUTURE

The approach to reducing errors in pathology and laboratory medicine is similar to that for most systems.
At present, the error rate for pathology and laboratory medicine does not approach Six Sigma (3.4 errors per million events), which has become a goal for many companies that manufacture products. Automation and computers have greatly improved quality and reduced the error rate in pathology and laboratory medicine, but a large component of this field is still manual. Further, each physician office laboratory and hospital laboratory, for the most part, are independent entities and have varying approaches to quality and error reduction. However, the approach to error reduction for the future has certain commonalities for all pathology and laboratory medicine departments. We will comment on the generic approach to error reduction (improve quality) and then make specific suggestions for the three phases of the process.

Error reduction and improved quality are essentially two names for the same goal; you can’t have one without the other. Probably the most important factor for error reduction is a commitment by the team (pathologists, technologists, phlebotomists, etc.) to reduce errors/improve quality. The tools for the team are spelled out in the Juran trilogy; quality planning, QC, and quality improvement [106]. These concepts are not foreign to pathology and laboratory medicine. We continually monitor the quality/error rate of our service through delta checks, blood culture contamination rate, patients receiving a mismatched unit of blood, comparing cytologic diagnosis with tissue diagnosis for lesions of the cervix, etc. These and many other error rates have been monitored for many years by pathology and laboratory medicine with a modicum of improvement. Most of these are outcome measurements. W. Edwards Deming emphasized that outcome measures after the service or product is completed are an indication of performance but not the key to the solution. Dr. Deming emphasized the importance of improving the process to achieve better quality/fewer errors. The fifth point of Deming’s 14 points is “improve constantly and forever every process for planning, production, and service” [107]. Dr. Deming postulated the 85–15 rule based on his research which indicates that 85% of what goes wrong is with the system or process, and only 15% with the individual person or thing [108]. Thus, the key to error reduction is continuous quality improvement of the many systems and processes in the thousands of individual clinical laboratories and pathology departments throughout the country. However, since each one of these laboratories/departments is an independent entity, the resources, commitment and knowledge for improvement/error reduction differs in each entity, and this is a significant factor for reducing the error rate.

Recommendation #1. Establish a continuous quality improvement program that focuses on improving the processes in the laboratory/pathology.

The majority of errors for the laboratory occur during the pre-analytical phase [80,108]. A study by Nutting et al. found that 56% of the errors for laboratory testing involved test ordering and specimen handling—pre-analytical components [109]. In a study by Witte et al.,
62.2% of the errors were pre-analytical [80]. A CAP Q-probe study involving 660 institutions found that 4.8% of outpatient requisitions had at least one order entry error and the median participant reported one or more order errors on 6% of requisitions [110].

**Recommendation #2.** Have a user-friendly computer system that facilitates direct physician ordering for laboratory and pathology services.

Another Q-probe study in 712 hospitals showed a wristband identification error rate of 2.7% [111]. The most significant factor in the error rate was the policy governing the initial placement of the wristband by the nursing staff.

**Recommendation #3.** Develop a quality wristband policy and use bar codes on the wristband and specimen labels to insure positive patient identification.

There are two important components of the analytical phase of the laboratory: personnel and instrumentation. Assessing laboratory employee competence is a challenge and has only been done recently. The CLIA’88 requires a laboratory to have policies and procedures for evaluating personnel competency and the regulations include appropriate evaluation factors. In a Q-probe study, 89.8% of institutions had a written competence plan and 98.1% reported reviewing employee competence at least yearly [112]. Personnel failure rate ranged from 0.9 to 6.4%, depending on the competence evaluated. The authors concluded that opportunities for improvement in employee competence assessment are numerous.

**Recommendation #4.** Establish quality programs for continuing education and personnel competency assessment.

The choices for laboratory instrumentation have increased greatly in the past several years. It is a challenge to laboratory personnel to select equipment that improves quality and reduces error. A recent study documented that an automated robotic workstation does decrease the number of laboratory errors that occur with sorting, labeling, and aliquotting [113].

**Recommendation #5.** Use automated systems where feasible in the laboratory and use error reduction/improved quality as a factor when selecting instrumentation.

The pathology/clinical laboratory report and transmitting abnormal results to the patient care physician are the key components of the post-analytical process. The rate of errors in pathology/laboratory reports is difficult to measure since it depends on the error detection systems used by a given pathology department. A study of errors in reports found greater than 61,000 errors over a 3-month period in reports from 641 laboratories [114]. This study also noted that the error rate is lowest in transfusion medicine and highest in hematology.

**Recommendation #6.** An effective system for error detection in patient reports should be present in all pathology departments.

It is important for a pathology department to define how it transmits abnormal results such as a tissue specimen positive for cancer or a markedly abnormal laboratory result, to the patient care physician. A study has documented that physicians frequently do not respond appropriately to an abnormal laboratory result due to a variety of reasons [115].

**Recommendation #7.** Pathologists and laboratory personnel must have policies and procedures in place that insure abnormal results are promptly received by the patient care physician and provide consultation for the abnormal results.

Current climates are supportive of changing reaction to medical error from a system that is determined to find individual fault to a system that examines all aspects of the process that contributed to the error [116]. Often the individual associated with a medical error has inherited a number of problems inherent with the task that include organizational or system factors, including work environment and management decisions [117]. Enhancing total laboratory testing practices is the goal of the federally funded cooperative agreement between the American Society for Clinical Pathology and the Centers for Disease Control and Prevention. The title of the agreement is *Enhancing Testing Practices in the Clinical Laboratory by Developing Specific Training Activities for Medical Technologists, Medical Laboratory Technicians, and Pathologists.* The project will encompass a number of laboratory functions, and help to prepare laboratories for challenges of the future including chemical terrorism testing and clinical tasks involved with spin offs from the human genome project. Such collaboration will give the individual working daily in clinical laboratories the support and information needed to perform the highest quality of laboratory practices [118].

We began this chapter with statistics from the IOM indicating the large number of deaths and injuries in the United States attributed to medical errors. Pathology and laboratory medicine are a diagnostic arm of the health care team and contribute to these statistics. However, pathology and laboratory medicine in this country have focused on quality, improving the process for service and error reduction since their inception. In every pathology and laboratory medicine department in this country, there are many systems in place to insure high quality and minimize errors. The standards set by CLIA’88, the
JCAHO, AABB, and the CAP are maintained by the inspection and accreditation process and proficiency testing. The goal of pathology and laboratory medicine is to provide an error free service to physicians and their patients. The pursuit of this goal is in the commitment they have made when they have chosen a career in pathology and laboratory medicine.

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